VNIVERSITAT DE VALÈNCIA

VNIVERSITAT DE VALÈNCIA Facultat de Ciències de l'Activitat Física i l'Esport

EFFECTS OF ELASTIC-BASED EXERCISE INTERVENTIONS ON OXIDATIVE STRESS, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH AND PHYSICAL FUNCTION IN OLDER WOMEN

Training intensity and modality as key exercise programming parameters

INTERNATIONAL DOCTORAL DISSERTATION presented by:

Pedro Gargallo Bayo

Supervised by:

Dr. D. Juan Carlos Colado Sánchez

Dr. D. Guillermo Sáez Tormo

-Valencia, Enero 2021-

UNIVERSIDAD DE VALENCIA

Facultad de Ciencias de la Actividad Física y el Deporte

Programa de Doctorado: 3161 Actividad Física y Deporte

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Juan Carlos Colado Sánchez, Profesor Titular de Universidad del Departamento de Educación Física y Deportiva de la Universidad de Valencia y Director del Grupo de Investigación en Prevención y Salud en el Ejercicio y el Deporte (PHES) de la Universidad de Valencia,

I N F O R M A que la memoria presentada por Pedro Gargallo Bayo con el título, "**EFFECTS OF ELASTIC-BASED EXERCISE INTERVENTIONS ON OXIDATIVE STRESS, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH AND PHYSICAL FUNCTION IN OLDER WOMEN**" ha sido realizada bajo mi co-dirección en el Dpto. de Educación Física y Deportiva, Dto. De Bioquímica y Biología Molecular y Hospital Universitario Dr. Peset de la Universidad de Valencia, cumpliendo los objetivos experimentales planteados en su proyecto inicial y satisfaciendo los requerimientos de formación en investigación biomédica del doctorando. Por lo que informo favorablemente sobre su presentación y defensa ante el tribunal competente.

Lo que suscribo a efectos del interesado en Valencia a veintiocho de enero del dos mil veintiuno.

JUAN CARLOS| COLADO| SANCHEZ

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Dr. Juan Carlos Colado Sánchez

VNIVERSITAT DE VALÈNCIA Facultat de Medicina i Odontologia

HOSPITAL UNIVERSITARI DOCTOR PESET

Sercicio de Análisis Clínicos

Departament de Bioquimica i Biologia Molecular
Secció Departamental de Medicina i Odontologia

Guillermo Sáez Tormo, Catedrático de Bioquímica y Biología Molecular de La Facultad de Medicina y Odontología de La Universitat de Valencia y Jefe de Sección de Análisis Clínicos Del Hospital Universitario Dr. Peset de Valencia,

I N F O R M A que la memoria presentada por Pedro Gargallo Bayo con el título, "**EFFECTS OF ELASTIC-BASED EXERCISE INTERVENTIONS ON OXIDATIVE STRESS, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH AND PHYSICAL FUNCTION IN OLDER WOMEN"** ha sido realizada bajo mi co-dirección en el Dto. De Bioquímica y Biología Molecular, Hospital Universitario Dr. Peset y Dpto. de Educación Física y Deportiva de la Universidad de Valencia, cumpliendo los objetivos experimentales planteados en su proyecto inicial y satisfaciendo los requerimientos de formación en investigación biomédica del doctorando. Por lo que informo favorablemente sobre su presentación y defensa ante el tribunal competente.

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Guillermo Sáez Tormo

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Guillermo Sáez Tormo

“Elige un trabajo que te guste

y no tendrás que trabajar ni un día de tu vida”

Confucio (551 – 478 a.C.)

A mis padres, Mª Dolores y Pedro,

por los valores que me han transmitido,

por apoyarme en cada meta, sueño y objetivo,

por ser mi fuerza y fuente de inspiración. GRACIAS.

A mi mujer, Paula,

por ser mi apoyo incondicional,

mi amiga, mi confidente, mi compañera de viajes,

por dar tanto sin esperar nada a cambio,

por estar "simplemente" ahí, en los buenos y malos momentos. GRACIAS

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- Ayudas a la Salud y Prevención Ignacio Hernando de Larramendi 2014 (Fundación Mapfre; Resolución: 18 de Diciembre de 2014). Duration: 6 months. (Grant reference number: OTR2015-140931NVES).

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SCIENTIFIC CONTRIBUTIONS AS A PhD CANDIDATE

Publications arising from my PhD candidature

This section contains the publications as a PhD student resulting directly or indirectly from this dissertation which have been published or are under review (extracts of publications collected in Appendix B):

Peer reviewed publications

1. **Gargallo, P**., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research For Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877

2. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & **Gargallo, P.** (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

3. Fritz, N. B., **Gargallo, P.,** Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High-and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press).*

4. Fritz, N. B., Juesas, Á., **Gargallo, P**., Calatayud, J., Fernández-Garrido, J., Rogers, M. E., & Colado, J. C. (2018). Positive effects of a short-term intense elastic resistance training program on body composition and physical functioning in overweight older

women. *Biological Research For Nursing, 20*(3), 321-334. https://doi.org/10.1177/1099800418757676

5. Colado, J.C., Smolkay, R., Calatayud, J., **Gargallo, P.,** Flández, J., & Page, P. (2020). Effects of strength training with variable elastic resistance across the lifespan: a systematic review. (Efectos del entrenamiento de la fuerza con resistencia variable elástica a lo largo de la vida: una revisión sistemática). *Cultura, Ciencia y Deporte, 15*(44), 147-164. http://dx.doi.org/10.12800/ccd.v15i44.1458

6. Colado, J. C., Pedrosa, F. M., Juesas, A., **Gargallo, P.,** Carrasco, J. J., Flandez, J., Chupel, M. U., Teixeira, A. M., & Naclerio, F. (2018). Concurrent validation of the OMNI-Resistance Exercise Scale of perceived exertion with elastic bands in the elderly. *Experimental Gerontology, 113*, 11-16. https://doi.org/10.1016/j.exger.2017.12.009

7. Flandez, J., Belando, N., **Gargallo, P**., Fernández-Garrido, J., Vargas-Foitzick, R. A., Devis-Devis, J., & Colado, J. C. (2016). Metabolic and functional profile of premenopausal women with metabolic syndrome after training with elastics as compared to free weights. *Biological Research For Nursing, 19(*2), 190-197. https://doi.org/10.1177/1099800416674307

Manuscripts under preparation

1. **Gargallo, P**., Colado, J. C., Juesas, Á., Estañ-Capell, N., & Sáez, G. The effect of moderate-versus high-intensity resistance training on lipid peroxidation, protein carbonilation, muscle strength and physical function in older women (Redox Biology).

2. **Gargallo, P**., Colado, J. C., Fernández-Garrido, J., & Sáez, G. The effect of multi-component and power strength training programs on oxidative stress in older women. (Free Radical Biology and Medicine).

3. **Gargallo, P**., Guzmán J. F., Fernández-Garrido, J., Sáez, G., & Colado, J. C. Are power strength or multi-component training more effective than high-intensity resistance training to improve bone status in older women? A 20-week randomized controlled trial (Bone).

4. **Gargallo, P**., Flández, J; Guzmán J. F., Sáez, G., & Colado, J. C. Differential effects of elastic-based multi-component and power strength training programs on bone health, body composition and physical function in older women (Age and Ageing).

Publications as a PhD student not directly related to the this PhD dissertation

1. **Gargallo, P**., Juesas, A., Bruño, A., Guzmán, J. F., Lisón, J. F., Baños, R. M., Flández, J., Rogers, M., & Colado, J. C. (2020). Physiological and psychological effects of a new racket sport in children with and without overweight at primary school (Efectos fisiológicos y psicológicos de un nuevo deporte de raqueta en niños con y sin sobrepeso en la escuela primaria). *Cultura, Ciencia y Deporte, 15*(45), 363-375. http://dx.doi.org/10.12800/ccd.v15i44.1458

2. Gene-Morales, J., Flández, J., Juesas, Á., **Gargallo, P**., Miñana, I., & Colado, J.C (2020). A systematic review on the muscular activation on the lower limbs with five different variations of the squat exercise. *Journal of Human Sport and Exercise, 15*(4), 1277-1299. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.28

3. Muñoz, V., **Gargallo, P**., Juesas, Á., Flández, J., Calatayud, J., & Colado, J. C (2019). Influencia de los distintos tipos y parámetros del ejercicio físico sobre la calidad seminal una revisión sistemática de la literatura. *Cultura, Ciencia y Deporte, 14*(40), 25-42.

4. Moya-Nájera, D., Moya-Herraiz, Á., **Gargallo, P.,** Calatayud, J., Escrig-Sos, J., & Colado, J. C. (2019). Clinical relevance of a balance training program on liver transplant patients. A randomized controlled trial. *Transplantation, 103*(5), 965-972. https://doi.org/10.1097/tp.0000000000002415.

5. Calatayud, J., Casaña, J., Martín, F., Jakobsen, M. D., Colado, J. C., **Gargallo, P**., Juesas, Á., Muñoz, V., & Andersen, L. L. (2017). Trunk muscle activity during different variations of the supine plank exercise. *Musculoskeletal Science and Practice, 28*, 54-58. https://doi.org/10.1016/j.msksp.2017.01.011.

6. Calatayud, J., Martin, F., **Gargallo, P.,** García-Redondo, J., Colado, J. C., & Marín, P. J. (2015). The validity and reliability of a new instrumented device for measuring ankle dorsiflexion range of motion. *International Journal of Sports Physical Therapy, 10*(2), 197.

Scientific oral communications arising from my PhD candidature

This section contains the oral communications as a PhD student resulting directly or indirectly from this dissertation which have been presented in international congress and conferences (certificates of oral communications compiled in Appendix C):

1. **Gargallo, P**.,Fernández-Garrido, J., Flández, J., Saez, G., Colado, J.C. Effects of Power and Multi-component training with elastic resistance on oxidative stress, physical function and strength. *25th Annual Congress of the European College of Sport Science.* 28-30th October 2020, Sevilla, Spain.

2. Flández, J., **Gargallo, P.,** Gene-Morales, J., Modena, N., Martín, F., Colado, J. C. Effects of a power strength training with elastic bands on body composition, physical function and muscle strength in older women. *Summer Event-Costa Blanca Sports Science.* 25-26th September 2020, Alicante, Spain.

3. Martín, F., **Gargallo, P**., Sáez, G. T., Bañuls, C., Flández, J., Juesas, Á., Colado, J. C. Effects of moderate versus high-intensity resistance training on oxidative stress markers and antioxidant capacity in older women. *NCSA National Conference.* 8-11th July 2020, Las Vegas, USA.

4. **Gargallo, P**., Sáez, G. T., Fernández-Garrido, J., Juesas, Á., Colado, J. C. Differential effects of Multi-component, Power and Traditional resistance training on balance and gait speed in older men. *V Congreso internacional optimización del entrenamiento y readaptación físico-deportiva.* 29-30th May 2020, Sevilla, Spain.

5. **Gargallo, P**., Sáez, G. T., Juesas, Á., Flández, J., Colado, J. C. Comparison effects of Multi-component, Power and Traditional resistance training with elastic bands on

strength in older men. *V Congreso internacional optimización del entrenamiento y readaptación físico-deportiva.* 29-30th May 2020, Sevilla, Spain.

6. **Gargallo, P.**, Juesas, Á., Sáez, G., Guzmán J. F., Flández, J., Colado, J. C. Effects of multi-component, power and traditional resistance training on cardiovascular risk in older men. *II congreso internacional sobre prescripción y programación de deporte y de ejercicio en la enfermedad crónica.* 5-6th March 2020, Murcia, Spain.

7. **Gargallo, P.**, Flández, J., Calatayud, J., Fernández-Garrido, J., Sáez, G., Colado, J. C. Multi-component vs Power training using variable resistance: effects on bone health in older women. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

8. **Gargallo, P.**, Tamayo, E., Guzmán, J. F., Calatayud, J., Fernández-Garrido, J., Sáez, G., Colado, J. C. Effects of Power and Multi-component training with elastic resistance on metabolic, lipidic and inflammatory profile in older women. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

9. Juesas, Á., **Gargallo, P.**, Flández, J., Casaña, J., Sáez, G., Colado, J. C. Which training modalities are most effective for improving gait speed and balance in older women. A 5-month randomized controlled trial. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

10. Juesas, Á., **Gargallo, P.**, Flández, J., Casaña, J., Sáez, G., Colado, J. C. Improvement of muscle quality in older women with different exercise interventions. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

11. Gené, J., **Gargallo, P.**, Calatayud, J.,Flández, J., Sáez, G., Colado, J. C. Comparison effects of Multi-component, Power and Traditional resistance training with elastic bands on body composition and cardiovascular risk in older women. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

12. Gené, J., **Gargallo, P.**, Navarro, J., Baños, R. M., Casaña, J., Sáez, G., Colado, J. C. Differential effects of Multi-component, Power and Traditional resistance training on health-related quality of life, anxiety and depressive symptoms in older women. *VI congreso internacional de Readaptación y prevención de lesiones en la actividad física y el deporte de JAM Sport y IV congreso internacional de salud y ejercicio físico de JAM Sport.* 24-26th January 2020, Valencia, Spain.

13. **Gargallo, P.** Efecto osteogénico del ejercicio físico en la edad adulta y la vejez. *4º Congreso Internacional de Fisioterapia* Momentum. 5-7th October 2017, Puebla, Mexico.

14. **Gargallo, P.** Tejido óseo, muscular y graso, interconexión e influencia sobre la funcionalidad del adulto y adulto mayor. *4º Congreso Internacional de Fisioterapia Momentum.* 5-7th October 2017, Puebla, Mexico.

Conference abstracts arising from my PhD candidature

This section contains the posters as a PhD student resulting directly or indirectly from this dissertation which have been presented in international and national congress and conferences (certificates of posters compiled in Appendix D):

International

1. Rogers, M., **Gargallo,P.,** Juesas, Á.,Tamayo, E., Torkamanech. S., Guzmán, J. F., Fernández-Garrido, J., Sáez, G., Rogers, N., Colado, J. C. Multicomponent, Power, and Resistance Training With Elastic Resistance: Effects On Physical Function In Older Women. *66th American College of Sport Medicine Annual Meeting*. 28th-1st May and June 2019, Orlando, Florida (USA).

2. Rogers, N., **Gargallo,P.,** Juesas, Á.,Tamayo, E., Torkamanech. S., Guzmán, J. F., Fernández-Garrido, J., Sáez, G., Rogers, M., Colado, J. C. Effects Of Resistance, Power, And Multicomponent Training With Elastic Resistance On Strength In Older Women. *66th American College of Sport Medicine Annual Meeting*. 28th-1st May and June 2019, Orlando, Florida (USA).

3. Colado, J. C., **Gargallo, P.,** Juesas, A., Torkamaneh, S., Tamayo, E., Guzmán, J. F., Fernández-Garrido, J., & Sáez, G.T. (2018). Effects of multicomponent and power training programs using elastic devices on motor function, body composition, and metabolic, bone and inflammatory profile in older adults. *Journal of Performance Health Research,2* (2), 4-5.

4. **Gargallo, P.,** Munoz, V., Juesas, A., Saez, G., Hernando-Espinilla, A., Iradi, A., Colado, J. C. Adaptations in muscle mass and motor function during resistance

training with elastic bands at different intensities in older adults. *21st Annual Congress of the European College of Sport Science*. 6-9th July 2016, Vienna, Austria.

5. Munoz, V., **Gargallo, P.,** Juesas, A., Saez, G., Estañ-Capell, N., Colado, J. C. Effects of resistance training with elastic bands at different levels of intensity on the immune system of older adults. *21st Annual Congress of the European College of Sport Science*. 6-9th July 2016, Vienna, Austria.

6. Fritz,N., Colado JC., Juesas, Á., **Gargallo, P.,** Muñoz, V. Short-term effects of strength training with elastic bands at different levels of intensity on body composition, motor function and wellness in older adults. *VI Congreso Internacional de Ciencias del Deporte*. 18-19th December 2015, Santiago de Chile, Chile.

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RESEARCH STAYS

The PhD candidate has completed two research stays in the following destinations:

- Center of Physical Activity and Aging, Department of Human Performance Studies, Wichita State University (Wichita, Kansas, USA). Supervisor: Michael Rogers, PhD. Chair, professor and Research Director Center for Physical Activity and Aging. Date: from 17th Septermber 2018 to 15th December 2018. Duration: 3 months. Corresponding to the Grant reference number EST17/00925. (Appendix E).

- Leon Levine Hall, Department of Health & Exercise Science, Appalachian State University. Supervisor: Travis Triplett, PhD. Chair, professor and Physiology of Exercise, Exercise Science Undergraduate Program Director. President of the National Strength and Conditioning Association (NCSA). Date: from 30th June 2019 to 30th December 2019. Duration: 6 months. Corresponding to the Grant reference number EST18/00793. (Appendix F).

ENGLISH ABSTRACT

Background

The aging of the global population is recognized by the World Health Organization (WHO) as a major issue due to the disabilities and comorbidities related to this process, with women being the gender most affected. Due to the physiological and psychological age-associated declines, physical activity and exercise are proven strategies for reducing the impact of aging. However, it is still unknown what kind of training program could be the most effective in reversing deleterious age-related changes in older women. Regarding this, the type of training intensity and exercise modality are two key training parameters in exercise programming, and, therefore, different adaptations could be induced in older adults through the modification of these parameters. Furthermore, the type of training device is a significant factor and can act as a barrier or facilitator in older adults' participation in physical activities and exercise programs. Therefore, this dissertation's primary goals are to compare the effects of a 32-week elastic resistance training program at high and moderate intensity and 20-week elastic-based multi-component, power strength and traditional high-intensity resistance training programs on oxidative stress, bone health, body composition muscle strength and physical function in older women.

Methods

This dissertation is composed of two projects/studies involving two cohorts of female volunteers (first project: 93 subjects aged 60–88 years [69.93± 6.27]; second project: 136 subjects aged 60–82 years [67.97± 4.77]). In the first project, the subjects were randomly assigned to a 32-week progressive elastic-based resistance training program at high (HI; n = 39) or moderate intensity (M; n = 31) or a self-management control group (C; n = 23). In the second project, the participants were randomly assigned to a 20-week multi-component (MT;

n = 34), power strength (P; *n* = 34) or traditional high-intensity resistance training (T; *n* = 34) elastic-based interventions or to a self-management control group (C; *n* = 34).

In the first project, the exercise groups engaged in progressive elastic-based resistance training twice a week with three to four sets of six (HI) or 15 (M) repetitions including six overall body exercises at a rate of perceived exertion (RPE) of 6–7 in the first four weeks and 8–9 in the remaining weeks on the OMNI-Resistance Exercise Scale (RES). Members of the control group were instructed to continue their everyday lives. In the second project, the P and T groups performed the same progressive elastic-based resistance training in terms of exercises (six whole-body exercises) and sets (three to four sets per exercise) twice a week, but the P group displaced the load in the concentric phase as fast as possible, while in the T group the speed of execution was 2s for the concentric phase and 2s for the eccentric phase. The P group performed 12 submaximal repetitions in each set in the first two weeks to consolidate the technique and 10 during the rest of the program with a perceived exertion of 3–4 (very low) on the OMNI-RES scale in the first repetition, which is equivalent to 40%–60% 1RM (low-load or low intensity), never exceeding the value 6 at the end of the 10 repetitions. The T group performed six submaximal repetitions, equivalent to 85% of the 1RM per exercise, at OMNI-RES scale values of 6–7 in the first four weeks and 8–9 in the remaining 16 weeks. The multi-component training was composed of balance, strength, aerobic, flexibility, and coordination exercises in the same session and was also performed twice a week.

Oxidative stress, bone health, body composition, neuromuscular strength, and physical function were assessed in both studies. Oxidative stress status was assessed in deoxyribonucleic acid (DNA) (urinary 8-oxo-2-deoxyguanosine [8-oxo-dG] in both projects), lipids (F_2-isoprostanes[8-iso-P] in both projects; malonaldehyde [MDA] in the first project), and proteins (protein carbonyls in the first project) products together with antioxidant

enzymes (superoxide dismutase [SOD] and glutathione peroxidase [GPx] in both projects; catalase [CAT] in the second project) and thiol redox state (reduced glutathione [GSH], oxidized glutathione [GSSG], and the GSSG/GSH ratio in both projects; total glutathione and the GSH/GSSG ratio in the second project). Bone health was integrated by measures of areal bone mineral density (aBMD) and the T-score of the lumbar spine (L1–L4 segments, L2–L4 segments, and L1, L2, L3, and L4 individual vertebrae, in both projects) and proximal femur (femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip in both projects) assessed by dual-energy X-ray absorptiometry (DXA). Additionally bone health was also composed by fracture risk (the 10-year probability of a major osteoporotic fracture and the 10-year probability of a hip fracture), bone turnover markers (BTMs) of bone formation (procollagen type I N propeptide [P1NP] in both projects, a bone-specific isoform of alkaline phosphatase [bALP] in the first project, and osteocalcin [OC] in the second project) and bone resorption (a β-isomerized form of C-terminal telopeptide of type I collagen [β-CTx] in both projects), and their relationship (bALP/ β-CTx ratio in the first project). Body composition (total body mass, total fat mass, total fat-free mass, and total body fat percentage) was measured in both projects by DXA, while in the second project the cardiovascular risk was assessed through anthropometric measures (waist circumference [WC], hip circumference [HC], the waist-to-hip ratio [WHR], and the waist-to-height ratio [WHtR]). Moreover, the neuromuscular strength of upper limbs (elbow flexor and extensor muscles) and lower limbs (hip abductor and hip adductor along with knee flexor and extensor muscles) was assessed through isokinetic dynamometry at low (60°/s) and high (180°/s) velocities in both projects. Finally, physical performance was measured using various functional tests and batteries widely used in the literature, such as the 30 seconds chair stand (30sec-CS) and 30 seconds arm curl (30sec-AC) for muscle strength/endurance of the lower and upper limbs (used in both projects); time up and go (TUG) for dynamic balance/agility (used in both projects); the

six-minute walking test (6MWT) for aerobic endurance (used in both projects); five sit-to-stand (5STS), stair-climbing, stair-climbing speed (SCS), and stair-climbing power (SCP) for muscle power of the lower limbs (used in the second project); and the functional reach test (FRT) for proactive balance (used in the second project).

Data were analyzed using the intention-to-treat (ITT) and per-protocol analysis (PPA) approaches in both projects. After applying Kolmogorov-Smirnov and Levene tests for checking data distribution and homogeneity, the non-normally distributed data were transformed using a natural logarithm (log10). A two-way analysis of variance (ANOVA) for repeated measures was used to examine time, group, and interactions effects, and Bonferroni corrections were then applied. A two-way analysis of covariance (ANCOVA) for repeated measures adjusting for baseline values and age was also applied. The Cohen's d effect size (ES) and delta percentage (Δ%) were also calculated. Data are reported as the means ± the standard deviations (*SD*) with 95% confidence intervals (CI). Statistical significance was set at $p \leq 0.05$. The SPSS Version 25.0 commercial software was used for the statistical analysis.

Results

Regarding oxidative stress, in the first project, after 16 weeks of training, the M group achieved significant decreases in 8-oxo-dG (-21.34%), 8-iso-P (-15.85%), and MDA (-19.12%), with moderate ES in all these, while the HI group showed significant increases in 8-oxo-dG (+60.49%; large ES) and 8-iso-P (+24.40%; moderate ES). No significant differences by time were found in protein carbonyls. Significant time × group interaction was found in MDA in the M and C groups. After the ANCOVA, differences in 8-oxo-dG were found in the HI vs M and HI vs C groups, and differences in MDA were found in the M vs C groups. In addition, the M group showed an increase in CAT levels (+5.40%; small ES) ($p \leq 0.05$), while the HI group showed a significant decrease in the GPx (-8.95%; moderate ES) and

GSH (-9.31%; moderate ES). In the second project, after 20 weeks both the MT and P groups improved their oxidative stress status by decreasing the 8-oxo-dG (MT: -48.56%, moderate ES; P: -65.79%, large ES) and 8-iso-P (MT: -30.49%, moderate ES; P: -26.98%, small ES). Additionally, the MT group significantly increased the values of the SOD enzyme (small ES). Significant differences in 8-oxo-dG were found between the P and C groups, and significant differences in SOD were found between both experimental groups and the C group. The P group also achieved positive changes in the thiol redox state ($p \leq 0.05$) (an increase in total glutathione, GSH, and the GSSG/GSH ratio and a decrease in GSSG). After ANCOVA, the MT group showed a significant decrease in GSSG and the GSSG/GSH ratio. The ES of the thiol state changes ranged from small to large.

Regarding bone health, in the first project, after 32 weeks both the HI and M groups achieved a significant increase in total lumbar spine aBMD (M: +0.89%; HI: +1.12%) with trivial ES, but only the HI group showed a significant difference from the C group. In the proximal femur scores, both the HI and M groups increased ($p \leq 0.05$) aBMD of femoral neck (M: +1.57%; HI: +1.39%), Ward's triangle (M: +2.59%; HI: +2.47%), and total hip (M: +1.13%; HI: + 1.21%), while the HI group also improved significantly the trochanter aBMD (+ 1.38%). The ES were all trivial, and no significant differences between groups were found. Moreover, the risk of major osteoporotic or hip fracture was also reduced ($p \leq 0.05$) in the HI and M groups. The changes in aBMD were accompanied by significant changes in bone formation and bone resorption biomarkers after 16 weeks, as was the case for P1NP (M: +11.24%; HI: +8.23%), bALP (HI: +4.68%), β-CTx (M: -6.65%; HI: -8.07%), and the bALP/β-CTx ratio (M: +13.71%; HI: +9.58%). These changes were also seen after 32 weeks for P1NP (M: +19.76%; HI: +23.89%), bALP (M: +8.07%; HI: +9.95%), β-CTx (M: -7.24%; HI: -9.80%), and the bALP/β-CTx ratio (M: +20.86%; HI: +19.56%). In all the parameters, the magnitude of the change was considered trivial or small. An ANCOVA revealed

significant differences between the HI and C groups in bALP, β-CTx and the bALP/β-CTx ratio, and between exercise groups in bALP. In the second project, only the P group significantly improved the aBMD of the total lumbar spine (+1.28%, trivial ES), some parts of the proximal femur such as the intertrochanteric area (+1.38%, trivial ES), Ward's triangle (+4.66%, small ES), and total hip (+1.03%, trivial ES), with no differences between groups—except between the P and C groups—in intertrochanteric and total hip aBMD after ANCOVA. All the training groups significantly reduced fracture risk, and both the MT and P groups showed positive adaptations ($p \leq 0.05$) in BTMs by increasing OC (MT: +16.37%, moderate ES; P: +24.82%, large ES) and reducing β-CTx (MT: -9.05%, small ES; P: -8.76%, small ES).

Regarding body composition, in the first project, the M group achieved significant decreases in total fat mass (-8.04%) and total body fat percentage (-2.90%) along with a significant increase in total fat-free mass (+2.98%), with small ES in all the parameters. The HI group showed a significant increase (trivial ES) in total fat-free mass (+2.10%) along with a significant decrease in the total body fat percentage (-2.21%), with small ES in both cases. No significant differences between groups were found. After ANCOVA, differences in total fat mass were found between the M and C groups, and differences in total fat-free mass and total body fat percentage were found between the training groups and the C group. In the second project, significant declines in all the training groups were found in WC (MT: -2.75%; P: -2.25%; T: -1.32%), HC (MT: -2.37%; P: -1.97%; T: -0.91%), WHtR (MT: -2.73%; P: -2.26%; T: -1.32%), total fat mass (MT: -4.24%; P: -2.75%; T: -2.44%), and total body fat percentage (MT: -4.53%; P: -3.69%; T: -2.44%), with ES ranging between trivial and small. In addition, the MT and T groups improved ($p \leq 0.05$) the total fat-free mass (MT: +1.52%; T: +1.58%), with trivial ES. Significant differences between the training groups and the C group were found in WC, HC, WHtR, and total body fat percentage.

Regarding neuromuscular strength, in the first project, the HI and M groups significantly improved the strength of the hip abductor (M: +23.71%; HI: +53.28%), hip adductor (M: +15.89%; HI: +23.07%) muscles at 60°/s, while the HI group also increased their strength ($p \leq 0.05$) at 180°/s (hip abductor: +49.78%; hip adductor: +15.52%). The ES ranged between trivial and large. No significant differences were found between the training groups, but there were differences with the C group. The HI and M groups achieved significant increases in knee flexor and extensor muscle strength at both low and high velocities (moderate and large ES), with no significant differences between the training groups. However, both the HI and M groups showed significant differences with the C group in all the knee parameters. The same results were obtained for the upper limbs, where both the HI and M groups showed significant improvements in elbow flexor and extensor muscle strength at both velocities (moderate and large ES). No significant differences were found between the training groups, but there were significant differences between both training groups and the C group in all the parameters. In the second project, after ANOVA or ANCOVA analysis all training modalities significantly improved the neuromuscular strength at the hip, knee, and elbow joints (small to large ES), except the P and MT groups in the knee flexion and elbow flexion at 60°/s, respectively. The P group achieved significant differences from the other exercise modalities in muscle strength at hip abduction and adduction and elbow extension and flexion at 180°/s. Additionally, the T group also showed significant differences from the MT and P groups in elbow extension at low velocities.

Regarding physical function, in the first project, both training groups improved significantly in all the parameters analyzed, with the HI group achieving large ES in 30-secCS (+75.93%), 30sec-AC (+79.08%), TUG (-18.80%), and 6MWT (+10.50%) tests, while the M group achieved large ES in all the tests, apart from moderate ES in 6MWT (+7.93%). No significant differences were found between the training groups, but both training groups

showed significant differences from the C group in all the parameters. In the second project, all the training groups improved all the parameters of physical function analyzed, obtaining mainly moderate and large ES. After ANCOVA, significant differences in training modalities were found in the measure of the power of 5STS between the P group and the rest of the training strategies (moderate ES). Furthermore, significant differences were obtained between the three training modalities and the C group in all the variables.

Conclusions

A progressive elastic resistance training program at a moderate rather than high intensity may be the best strategy for reducing oxidative stress in older women after 16 weeks, while multi-component training—particularly power strength training—is effective in improving oxidative stress and bone turnover rate in older women after 20 weeks of training. In addition, elastic-based resistance training programs at high and moderate intensity effectively improve bone health, body composition, neuromuscular strength, and physical function in older women after 32 weeks of training. Likewise, multi-component, power strength, and high-intensity resistance training are also effective elastic-based strategies for improving the same health parameters in older women after 20 weeks. In the short-term (16 weeks), high-intensity resistance training is the most effective strategy for increasing the bone formation rate in older women, while power strength training modality seems to be the most appropriate for producing muscle power adaptations. At the same time, multi-component training produces the most significant adaptations in body composition. Finally, all the elastic-based exercise interventions analyzed were well-tolerated and safe for older women, as demonstrated by the lack of serious adverse events, the low attrition rate, and the attendance and compliance rates reported in both projects. **Key words:** variable resistance, older adults, high-velocity resistance training, muscle power, bone mineral density, adipose tissue.

VALENCIAN ABSTRACT

Antecedents

L'envelliment de la població mundial és reconegut per l'Organització Mundial de la Salut (OMS) com un problema principal a causa de les discapacitats i comorbilitats relacionades amb aquest procés, sent les dones el gènere més afectat. A causa de la deterioració i les conseqüències associades a l'envelliment, l'activitat física i l'exercici han demostrat ser estratègies eficaces per a reduir l'impacte de l'envelliment. No obstant això, encara es desconeix quin tipus de programa d'entrenament podria ser el més eficaç per a revertir els canvis deleteris relacionats amb l'edat en dones majors. En aquest sentit, el tipus d'intensitat de l'entrenament i la modalitat d'exercici són dos paràmetres clau d'entrenament en la programació de programes d'exercici i, com a tals, podrien induir diferents adaptacions. A més, el tipus de dispositiu d'entrenament també és un factor principal i pot actuar com a barrera o facilitador en la participació dels adults majors en activitats físiques i programes d'exercici. Per tant, els principals objectius de la present tesi doctoral van ser: comparar els efectes d'un programa d'entrenament de resistència elàstica de 32 setmanes a intensitat alta i moderada i les modalitats d'entrenament multi-component, de potència i tradicional de força a alta intensitat amb l'ús de bandes elàstiques durant 20 setmanes en l'estrés oxidatiu, la salut òssia, la composició corporal, la força muscular i funció física en dones majors.

Mètodes

La present tesi doctoral està composta per dos projectes/estudis en els quals van participar voluntàriament dues cohorts diferents de dones majors (primer projecte: 93 subjectes de 60-88 anys [69,93 ± 6,27]; segon projecte: 136 subjectes de 60-82 anys [67,97 ± 4,77]). En el primer projecte, els subjectes van ser assignats aleatòriament a un programa d'entrenament de força progressiu amb bandes elàstiques d'alta intensitat (AI; n = 39),

moderada (M; *n* = 31), o a un grup de control (C; *n* = 23) durant 32 setmanes. En el segon projecte, els participants van ser assignats aleatòriament a un programa d'entrenament multi-component (MT; *n* = 34), potència (P; *n* = 34), tradicional de força d'alta intensitat (T; *n* = 34) o a un grup control (C; *n* = 34) durant 20 setmanes, on la característica comuna entre les tres modalitats d'exercici era l'ús de bandes elàstiques com a material d'entrenament.

En el primer projecte, els grups d'entrenament van realitzar un programa de força progressiu amb bandes elàstiques dues vegades per setmana, compost per tres a quatre sèries de sis (AI) o 15 (M) repeticions, incloent sis exercicis de cos sencer amb una taxa d'esforç percebut de 6-7 (primeres quatre setmanes) i 8-9 (resta de les setmanes) en l'escala OMNI-RES. El grup de control va rebre instruccions de continuar amb la seua vida normal. En el segon projecte el grup P i T van realitzar el mateix entrenament en termes d'exercicis (sis exercicis de cos) i sèries (de tres a quatre sèries per exercici), dues vegades per setmana, usant tots dos bandes elàstiques, però el grup P va desplaçar la càrrega a màxima velocitat en la fase concèntrica mentre que el grup T va utilitzar 2 s per a realitzar la fase concèntrica i 2s per a la fase excèntrica. Així mateix, el grup P va realitzar 12 (en les primeres dues setmanes per a consolidar la tècnica) i 10 (per a la resta del programa) repeticions submàximes en cada sèrie amb un esforç percebut de tres-quatre (molt baix) en l'escala OMNI-RES en la primera repetició, la qual cosa equival al 40-60% d'una repetició màxima (1 RM) (baixa càrrega o baixa intensitat) i mai va sobrepassar el valor de sis al final de les 10 repeticions. El grup T va realitzar sis repeticions submàximas equivalents al 85% d'una 1RM a un valor de sis a set en les primeres quatre setmanes i de huit a nou en les 16 setmanes restants. L'entrenament multi-component va estar compost per exercicis d'equilibri, força, aeròbics, flexibilitat i coordinació en la mateixa sessió i es va realitzar també dues vegades per setmana.

En tots dos estudis es va avaluar l'estrés oxidatiu, la salut òssia, la composició corporal, la força neuromuscular i la funció física. L'estat d'estrés oxidatiu es va avaluar en

productes d'àcid deoxirribonucleic (ADN) (8-oxo- 2-desoxiguanosina [8-oxo-dg] en orina en tots dos projectes), lípids (F2-isoprostans [8-iso-P] en tots dos projectes; malondialdehide [MDA] en el primer projecte), i proteïnes (proteïnes carbonilades en el primer projecte), juntament amb enzims antioxidants (superòxid dismutasa [SOD] i glutatió peroxidasa [GPx] en tots dos projectes; catalasa [CAT] en el segon projecte) i estat redox tiol (glutatió reduït [GSH] , glutatió oxidat [GSSG] , ràtio GSSG/GSH en tots dos projectes; glutatió total i ràtio GSH/GSSG en el segon projecte) . La salut òssia va estar composta per mesures de densitat mineral òssia d'àrea (aDMO) i puntuació T de la columna lumbar (segments L1-L4, L2-L4 i vèrtebres individuals L1, L2, L3, L4, en tots dos projectes), fèmur proximal (coll femoral, trocànter, àrea intertrocantérea, triangle de Ward i maluc total en tots dos projectes) avaluats per absorciometria dual de raigs X (DXA), risc de fractura (probabilitat en 10 anys d'una fractura osteoporòtica major i probabilitat en 10 anys de fractura de maluc) i finalment biomarcadors ossis de formació òssia (propéptid aminoterminal del procolagen tipus I (P1NP) en tots dos projectes, fosfatasa alcalina òssia [FAo] en el primer projecte i osteocalcina (OC) en el segon projecte), reabsorció òssia (forma β-isomeritzada del telopèptid C-terminal del col·lagen tipus I [β-CTx] en tots dos projectes) i relació entre tots dos (FAo/β-CTx en el primer projecte).La composició corporal (la massa corporal total, la massa grassa corporal total, la massa lliure de greix corporal total i el percentatge total de greix corporal) es va mesurar en tots dos projectes per (DXA) mentre que en el segon projecte també es va avaluar el risc cardiovascular a través de mesures antropomètriques (circumferència de cintura [CC], circumferència de maluc [CM], índex cintura-maluc [ICM], índex cintura-altura [ICA]). A més, la força neuromuscular de les extremitats superiors (músculs flexor i extensor del colze) i inferiors (abductor i adductor de maluc juntament amb músculs flexor i extensor de genoll) es va avaluar mitjançant dinamometría isocinètica a baixes (60 °/s) i altes (180 °/s) velocitats en tots dos projectes. Finalment, la funció física es va mesurar usant diverses

proves funcionals i bateries àmpliament utilitzades en la literatura com el test d'alçar-se i asseguera de la cadira durant 30 segons (30seg-AA) i realitzar flexo-extensions de colze durant 30 segons (30seg-FC) per a avaluar la força/resistència de les extremitats inferiors i superiors (usat en tots dos projectes), el test "*timed up and* go" (TUG) per a avaluar l'equilibri dinàmic/agilitat (usat en tots dos projectes), la prova de sis minuts marxa (6MM) per a avaluar la resistència aeròbica (usat en tots dos projectes), el test d'alçar-se i asseure's de la cadira cinc vegades (5AA), pujar escales, la velocitat d'ascensió d'escales (VAE) la i potència d'ascensió d'escales (PAE) per a la força muscular de les extremitats inferiors (utilitzada en el segon projecte) i la prova d'abast funcional (PAF) per a l'equilibri proactiu (utilitzada en el segon projecte).

Les dades es van analitzar a través de l'enfocament d'intenció de tractar (IDT) i anàlisi per protocol (APP) en tots dos projectes. Després d'aplicar les proves de Kolmogorov-Smirnov i Levene per a analitzar la distribució i homogeneïtat de les dades, les dades no distribuïdes normalment es van transformar utilitzant el logaritme natural (log10). Es va utilitzar una anàlisi de variància de dues vies (ANOVA) per a mesures repetides seguides de correccions de Bonferroni per a examinar els efectes de temps, grup i interaccions. A més també es va aplicar una anàlisi de covariància de dues vies (ANCOVA) per a mesures repetides utilitzant els valors basals i l'edat com a covariàncies. També es van calcular les grandàries de l'efecte d de Cohen (GE) i el percentatge delta (Δ%). Les dades es presenten com a mitja ± desviació típica (DT) juntament amb els intervals de confiança (IC) del 95%. La significació estadística es va establir en $p \leq 0,05$. Per a l'anàlisi estadística es va utilitzar el programari comercial SPSS Versió 25.0.

Resultats

Respecte a l'estrés oxidatiu, en el primer projecte, després de 16 setmanes d'entrenament, el grup M va aconseguir descensos significatius en 8-oxo-dg (-21,34%), 8-iso-P (-15,85%) i MDA (-19,12%) amb GE moderats en tots ells, mentre que el grup AI va mostrar augments significatius en 8-oxo-dg (+60,49%; GE gran) i 8-iso-P- P (+24,40%; GE moderat). No es van trobar diferències significatives per temps en les proteïnes carbonilades. Es va trobar una interacció significativa temps × grup en MDA entre els grups M i C. Després d'aplicar l'ANCOVA, es van trobar diferències entre AI i M així com entre els grups AI i C en 8-oxo-dG i entre M vs C en MDA. A més el grup M va mostrar un augment en els nivells de CAT (+5,40%; GE xicotet) ($p \leq 0,05$) mentre que el grup AI va disminuir significativament el GPx (-8,95%; GE moderat) i GSH (-9,31%; GE moderat). En el segon projecte, després de 20 setmanes, tant els grups MT com els P van millorar l'estat d'estrés oxidatiu en disminuir el 8-oxo-dG (MT: -48.56%, GE moderat; P: -65.79%, GE gran) i 8-iso-P (MT: -30,49%, GE moderat; P: -26,98%, GE xicotet). A més el grup MT va incrementar significativament els valors de l'enzim SOD (GE xicotet). Així mateix, es van trobar diferències significatives entre els grups P i C en 8-oxo-dG i entre tots dos grups experimentals i el grup C en SOD. El grup P també va aconseguir canvis positius en l'estat redox tiol ($p \leq 0,05$) (augment en el glutatió total, GSH el ràtio GSSG/GSH i disminució en GSSG). Després d'aplicar l'ANCOVA, el grup MT va mostrar una disminució significativa en GSSG i en el ràtio GSSG/GSH. La GE dels canvis d'estat dels tioles va variar de xicotet a gran.

Quant a la salut òssia, en el primer projecte, després de 32 setmanes tant el grup d'AI com el grup M van aconseguir un augment significatiu de la aDMO de la columna lumbar total (M: +0,89%; AI: +1,12%) amb GE trivial, però només el grup AI va mostrar diferències significatives amb el grup C. En el fèmur proximal, tant el grup AI com el grup M van

augmentar ($p \leq 0,05$) la aDMO del coll femoral (M: +1,57%; AI: +1,39%), triangle de Ward (M: +2,59%; AI: +2,47%), i maluc total (M: +1,13%; AI: +1,21%) mentre que el grup AI també va millorar significativament la aDMO del trocànter (+1,38%). LA GE van ser tots trivials no es van trobar diferències significatives entre els grups. Per un altre comunicat, el risc de fractura osteoporòtica major o de fractura de maluc també es va reduir ($p \leq 0,05$) en tots dos grups. Els canvis en la aDMO es van acompanyar de canvis significatius en els biomarcadors de formació i reabsorció òssia després de 16 setmanes, com va ser el cas de P1NP (M: +11,24%; AI: +8,23%), FAo (AI: + 4,68%), β-CTx (M: -6,65%; AI: -8,07%), i ràtio FAo /β-CTx (M: +13,71%; AI : +9,58%), així com també després de 32 setmanes [P1NP (M: +19,76%; AI : +23,89%), FAo (M: +8,07%; AI: +9,95%), β-CTx (M: -7,24%; AI: -9,80%), i ràtio FAo/β-CTx (M: +20,86%; AI: +19,56%)]. En tots els paràmetres la magnitud dels canvis es va considerar trivial o xicoteta. L'ANCOVA va revelar diferències significatives entre els grups AI i C en FAo, β-CTx i ràtio FAo/ β-CTx, i entre tots dos grups d'exercici en FAo. En el segon projecte, únicament el grup P va millorar significativament la aDMO de la columna lumbar completa (+1,28%, GE trivials) i algunes zones del fèmur proximal, com ara l'àrea intertrocantérea (+ 1,38%, GE trivials), triangle de Ward (+4,66%, GE xicotets) i maluc total (+1,03%, GE trivials), sense diferències entre els grups, excepte entre els grups P i C en l'àrea intertrocantérea i el maluc total després d'aplicar l'ANCOVA. Tots els grups d'entrenament van reduir significativament el risc de fractura i tant els grups MT com a P van mostrar adaptacions positives ($p \leq 0,05$) en els biomarcadors ossis en augmentar la OC (MT: +16.37%, GE moderat; P: +24.82%, GE gran) i reduir el β-CTx (MT: - 9,05%, GE xicotet; P: - 8,76%, GE xicotet).

Quant a la composició corporal, en el primer projecte, el grup M va aconseguir disminucions significatives en la massa grassa total (-8.04%) i en el percentatge de greix corporal total (-2.90%) juntament amb un augment significatiu en la massa lliure de greix

total (+ 2.98%), amb GE xicotets en tots els paràmetres . El grup AI va mostrar un augment significatiu (GE trivial) en la massa lliure de greix total (+2,10%) juntament amb una disminució significativa en el percentatge de greix corporal total (-2,21%) amb GE xicotets en tots dos casos. No es van trobar diferències significatives entre grups. Després l'ANCOVA, es van trobar diferències en la massa grassa total entre els grups M i C, i en la massa lliure de greix total i el percentatge de greix corporal total entre els grups d'entrenament i el grup C. En el segon projecte, es van trobar disminucions significatives en tots els grups de formació en CC (MT: - 2,75%; P: -2,25%; T: -1,32%), CM (MT: -2,37%; P: -1,97%; T : -0,91%), ICA (MT: - 2,73%; P: -2,26%; T: -1,32%), la massa grassa total (MT: -4,24%; P: -2,75%; T: -2.44%), i el percentatge total de greix corporal (MT: -4,53%; P: -3,69%; T: -2,44%), amb GE que van oscil·lar entre trivials i xicotets. A més, els grups MT i T també van millorar ($p \leq 0,05$) la massa lliure de greix total (MT: +1,52%; T: +1,58%) (GE trivial). Es van trobar diferències significatives entre l'els grups d'entrenament i el grup C en CC, CM, ICA i percentatge total de greix corporal.

Quant a la força neuromuscular, en el primer projecte, els grups AI i M van millorar significativament la força dels músculs abductor (M: +23,71%; AI: +53,2 8%) i adductor (M: +15,89%; AI: +23,07%) de maluc a 60 °/s, mentre que el grup AI també va augmentar la força ($p \leq 0,05$) a 180 °/s (abductor de maluc: +49,78%; adductores de maluc: +15,52%). La GE van oscil·lar entre trivials i grans. No es van trobar diferències significatives entre els grups d'entrenament, però si amb el grup C. A més, els grups AI i M van aconseguir augments significatius en la força dels músculs flexor i extensor del genoll tant a velocitats baixes com altes (GE moderats i grans), sense diferències significatives entre els grups d'entrenament . No obstant això, tots dos grups van mostrar diferències significatives amb el grup C en tots els paràmetres del genoll. Similars resultats es van obtindre en les extremitats superiors, on tant el grup AI com el grup M van mostrar millores significatives en la força

dels músculs flexor i extensor del colze a totes dues velocitats (GE moderats i grans). No es van trobar diferències significatives entre els grups d'entrenament, però sí que va haver-hi diferències significatives entre tots dos grups d'entrenament i el grup C en tots els paràmetres. En el segon projecte, després de l'ANOVA o l'ANCOVA, totes les modalitats d'entrenament van millorar significativament la força neuromuscular en les articulacions del maluc, el genoll i colze (GE de xicotets a grans), excepte els grups P i MT en la flexió del genoll i la flexió del colze a 60 °/s, respectivament. El grup P va aconseguir diferències significatives amb la resta de modalitats d'exercici en la força muscular en l'abducció i adducció de maluc així com en l'extensió i flexió del colze a 180°/s. A més, el grup T també va mostrar diferències significatives amb els grups MT i P en la musculatura extensora del colze a baixes velocitats.

Finalment, quant a la funció física, en el primer projecte, tots dos grups d'entrenament van millorar significativament tots els paràmetres analitzats, amb el grup AI aconseguint GE grans en 30seg-AA (+75.93%), 30seg-FC (+79.08%), TUG (-18.80%) i 6MM (+10,50%) mentre que el grup M va obtindre GE grans en totes la proves excepte una GE moderat en el test de 6MM (+7,93%). No es van trobar diferències significatives entre els grups d'entrenament, però tots dos grups d'entrenament van mostrar diferències significatives amb el grup C en tots els paràmetres. En el segon projecte, novament tots els grups d'entrenament van millorar tots els paràmetres de funció física analitzats, obtenint principalment GE moderats i grans. Després de l'ANCOVA, es van trobar diferències significatives entre les modalitats d'entrenament en la mesura de potència de 5AA entre el grup P i la resta d'estratègies d'entrenament (GE moderat). A més, les tres modalitats d'entrenament van obtindre diferències significatives amb el grup C en totes les variables.

Conclusions

El programa d'entrenament de resistència elàstica progressiva a una intensitat moderada en lloc d'alta pot ser una millor estratègia per a reduir l'estrés oxidatiu en dones majors després de 16 setmanes, mentre que l'entrenament multi-component, i especialment el de potència, han demostrat ser efectius per a la millora de l'estrés oxidatiu i la taxa de renovació òssia en les dones majors després de 20 setmanes d'entrenament. Els programes de força amb resistència elàstica realitzats a alta i moderada intensitat són eficaces per a millorar la salut òssia, la composició corporal, la força neuromuscular i la funció física en les persones majors després de 32 setmanes d'entrenament. Així mateix, l'entrenament multi-component, de potència i de força a alta intensitat realitzats amb resistència elàstica també han demostrat ser estratègies efectives per a la millora d'aquests mateixos paràmetres de salut en dones majors després de 20 setmanes. A curt termini (16 setmanes), en entrenament de força d'alta intensitat és l'estratègia més efectiva per a augmentar la taxa de remodelat ossi en les dones majors, mentre que l'entrenament de potència sembla ser la modalitat d'exercici més adequada per a crear adaptacions positives en la potència muscular. Al mateix temps, l'entrenament multi-component produeix els majors canvis en la composició corporal. Finalment, totes les intervencions d'exercici basades en elàstics analitzades en la present tesi doctoral van ser ben tolerades i segures per les dones majors a causa de l'absència d'esdeveniments adversos greus, la baixa taxa de deserció i les taxes d'assistència i compliment informades en tots dos projectes. **Paraules clau:** resistència variable, adults majors, entrenament d'alta velocitat, potència muscular, densitat mineral òssia, teixit adipós.

SPANISH SUMMARY

Debido a la realización de la tesis en una lengua extranjera, a continuación se recoge un resumen más extenso a los anteriormente expuestos en una de las lenguas oficiales del Estado Español y lengua materna del doctorando.

Antecedentes

El envejecimiento de la población mundial es reconocido por la Organización Mundial de la Salud (OMS) como un problema principal debido a las discapacidades y comorbilidades relacionadas con este proceso, siendo las mujeres el género más afectado. Debido al deterioro y las consecuencias asociadas al envejecimiento, la actividad física y el ejercicio han demostrado ser estrategias eficaces para reducir el impacto del envejecimiento. Sin embargo, todavía se desconoce qué tipo de programa de entrenamiento podría ser el más eficaz para revertir los cambios deletéreos relacionados con la edad en mujeres mayores. En este sentido, el tipo de intensidad del entrenamiento y la modalidad de ejercicio son dos parámetros clave de entrenamiento en la programación de programas y, como tales, podrían inducir diferentes adaptaciones. Además, el tipo de dispositivo de entrenamiento también es un factor principal y puede actuar como barrera o facilitador en la participación de los adultos mayores en actividades físicas y programas de ejercicio.

Objetivos

Los objetivos genrales de la presente tesis doctoral fueron:

- Correspondiente al proyecto uno: examinar y comparar los efectos a medio (16 semanas) y a largo plazo de un programa de entrenamiento de fuerza elástica de 32 semanas a intensidad alta y moderada sobre el estrés oxidativo, la salud ósea, la composición corporal, la fuerza muscular y la función física

en mujeres mayores. Este objetivo general se logró mediante varios objetivos específicos.

- Correspondiente al proyecto dos: analizar y comparar los efectos de los programas de entrenamiento multi-componente, de potencia y tradicional de fuerza a alta intensidad utilizando dispositivos de resistencia elástica sobre biomarcadores de estrés oxidativo, salud ósea, riesgo cardiovascular, composición corporal, fuerza muscular y función física en mujeres mayores durante 20 semanas de entrenamiento. Este objetivo general se logró mediante varios objetivos específicos.

Los objetivos específicos pertenecientes al proyecto uno fueron los siguientes:

- 1. Objetivo específico (OE) 1: Investigar los efectos a medio plazo (16 semanas) de la intensidad del entrenamiento (alta vs moderada) en programas de entrenamiento de fuerza con bandas elásticas sobre biomarcadores de estrés oxidativo a través de la evaluación del impacto en el daño del ácido deoxirribonucleico (ADN) (8-oxo-2-desoxiguanosina [8-oxo-dG] en orina), peroxidación de lípidos (F_2-isoprostanos [8-iso-P], malondialdehído [MDA]), oxidación de proteínas (carbonilos de proteínas), estado redox de tiol (glutatión reducido [GSH], glutatión oxidado [GSSG], ratio GSSG/GSH) y enzimas antioxidantes (catalasa [CAT], glutatión peroxidasa [GPx] y superóxido dismutasa [SOD]) en mujeres mayores.

- 2. OE2: Determinar los efectos a medio (16 semanas) y a largo plazo (32 semanas) de la intensidad del entrenamiento (alta vs moderada) en programas de entrenamiento de fuerza que utilizan bandas elásticas sobre la remodelación ósea mediante la evaluación de los biomarcadores de formación ósea

(propéptido aminoterminal del procolágeno tipo I [P1NP], fosfatasa alcalina ósea [FAo]), reabsorción (forma β-isomerizada del telopéptido C-terminal del colágeno tipo I [β-CTx]) y el equilibrio de ambos procesos (relación FAo / β-CTx) en mujeres mayores.

- 3. OE3: Evaluar los efectos a largo plazo (32 semanas) de la intensidad del entrenamiento (alta vs moderada) en los programas de entrenamiento de fuerza que utilizan bandas elásticas sobre la salud ósea mediante la evaluación de la densidad mineral ósea de area (aDMO) y la puntuación T de la columna lumbar (segmentos L1-L4 y L2-L4 y vértebras individuales L1, L2, L3 y L4) y el fémur proximal (cuello femoral, trocánter, intertrocánter, triángulo de Ward y cadera total) junto con 1,25 hydroxyvitamina D (25OHD), sodio (Na), potasio (K), y biomarcadores de cloro (Cl) en mujeres mayores.

- 4. OE4: Determinar los efectos a largo plazo (32 semanas) de la intensidad del entrenamiento (alta frente a moderada) en los programas de entrenamiento de fuerza que utilizan bandas elásticas sobre el riesgo de fractura mediante la evaluación del impacto en la probabilidad de 10 años de una fractura osteoporótica mayor y en la probabilidad a 10 años de una fractura de cadera en mujeres mayores.

- 5. OE5: Analizar los efectos a largo plazo (32 semanas) de la intensidad del entrenamiento (alta vs moderada) en programas de entrenamiento de fuerza que utilizan bandas elásticas sobre la composición corporal mediante la evaluación de la masa corporal total, masa grasa total, masa libre de grasa total, y porcentaje total de masa grasa en mujeres mayores.

- 6. OE6: Investigar los efectos a largo plazo (32 semanas) de la intensidad del entrenamiento (alta frente a moderada) en programas de entrenamiento de fuerza con bandas elásticas sobre la fuerza muscular de las extremidades superiores e inferiores mediante la evaluación de la fuerza isocinética de la flexio-extension de rodilla y codo así como de la abducción y aducción de cadera a 60º/s y 180º/s en mujeres mayores.

- 7. OE7: Determinar los efectos a largo plazo (32 semanas) de la intensidad del entrenamiento (alta vs moderada) en los programas de entrenamiento de fuerza que utilizan bandas elásticas sobre la función física mediante la evaluación del impacto en la fuerza-resistencia de las extremidades superiores (test flexo-extensiones de codo durante 30 segundos [30seg-FC]) y extremidades inferiores (test de levantarse y sentare de la silla durante 30 segundos [30seg-LS]), parámetros de equilibrio dinámico (test de *"time up and go* [TUG]) y resistencia aeróbica (test de seis minutos marcha [6MM]) en mujeres mayores.

- 8. OE8: Evaluar y analizar el estado cognitivo (MMSE), el nivel de las actividades básicas de la vida diaria (ABVDs; índice de Barthel) y actividades instrumentales de la vida diaria (AIVDs; escala de Lawton y Brody), así como datos socioeconómicos, de salud y de estilo de vida generales como posibles variables de confusión.

- 9. OE9: Identificar las diferencias en los parámetros mencionados en OE1 a OE7 al final de la intervención en función de la intensidad de entrenamiento empleada.

- 10. OE10: Determinar la efectividad y seguridad de los programas de entrenamiento de fuerza a intensidad alta y moderada intensidad supervisados

y progresivos realizados con bandas elásticas a través de la evaluación de las tasas de asistencia, cumplimiento y eventos adversos reportados por las mujeres mayores participantes.

Los objetivos específicos pertenecientes al proyecto dos fueron los siguientes:

- 1.OE1: Comparar los efectos de la modalidad de entrenamiento (multi-componente vs entrenamiento de potencia) en un período de intervención de 20 semanas utilizando resistencia elástica sobre biomarcadores de estrés oxidativo mediante la evaluación del impacto en el daño del ADN (8-oxo-dG en orina), peroxidación de lípidos (8-iso-P), estado redox del tiol (proporciones de glutatión total, GSH, GSSG, GSSG GSH y GSH/GSSG) y enzimas antioxidantes (GPx y SOD) en mujeres mayores.

- 2. OE2: Determinar los efectos de la modalidad de entrenamiento (multi-componente vs entrenamiento de fuerza) en un período de intervención de 20 semanas utilizando resistencia elástica sobre la remodelación ósea mediante la evaluación de biomarcadores de formación ósea (osteocalcina [OC]) y resorción ósea (β- CTx) en mujeres mayores.

- 3. OE3: Evaluar los efectos de la modalidad de entrenamiento (multi-componente, de potencia o entrenamiento tradicional de fuerza a alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica sobre la salud ósea mediante la evaluación de aDMO y puntuación T de la columna lumbar (segmentos L1-L4 y L2-L4 y vértebras individuales L1, L2, L3 y L4) y el fémur proximal (cuello femoral, trocánter, intertrocánter, triángulo de Ward y cadera total) en mujeres mayores.

- 4. OE4: Determinar los efectos de la modalidad de entrenamiento (multi-componente, de potencia o entrenamiento traditional de fuerza a alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica sobre el riesgo de fractura mediante la evaluación del impacto en los parámetros de probabilidad de fractura osteoporótica mayor y probabilidad de fractura de cadera en 10 años en mujeres mayores

- 5. OE5: Analizar los efectos de la modalidad de entrenamiento (multi-componente, de potencia o entrenamiento traditional de fuerza a alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica sobre el riesgo cardiovascular mediante evaluación de la circunferencia de la cintura (CC). , circunferencia de la cadera (CCA), índice cintura-cadera (ICCA) e índicecintura-altura (ICA) en mujeres mayores.

- 6. OE6: Investigar los efectos de la modalidad de entrenamiento (multicomponente, de potencia o entrenamiento de tradicional de fuerza a alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica sobre la composición corporal a través de la evaluación de la masa corporal total, total masa grasa, masa libre de grasa total y porcentaje total de masa grasa en mujeres mayores.

- 7. OE7: Determinar los efectos de la modalidad de entrenamiento (multicomponente, de potencia o entrenamiento tradicional de fuerza de alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica sobre la fuerza muscular de los miembros superiores e inferiores mediante la evaluación de la fuerza isocinética de la flexo-extension de rodilla

y codo así como la abducción y aducción de la cadera a 60º/sy 180º/s en mujeres mayores.

- 8. OE8: Evaluar los efectos de la modalidad de entrenamiento (multicomponente, de potencia o entrenamiento tradicional de fuerza de a alta intensidad) en un período de intervención de 20 semanas utilizando resistencia elástica en la función física mediante la evaluación del impacto en la fuerza-resistencia de las extremidades superiores (30seg-FC) e inferiores (30seg-LS), potencia de las extremidades inferiores (test de levantarse y sentarse de la silla cinco veces [5SLS] y prueba cronometrada de subir escaleras), equilibrio proactivo (test de alcance funcional [PAF]) y dinámico (TUG), así como la resistencia aeróbica (6MM) en mujeres mayores.

- 9. OE9: Evaluar y analizar el estado cognitivo (MMSE), nutricional (registro de dieta de 3 días), síntomas de ansiedad (escala general de severidad y deterioro de la ansiedad [Overall anxiety severity and impairment scale, OASIS]), síntomas de depresión (escala general de severidad y deterioro de la depresión [Overall depression severity and impairment scale, ODSIS]) ; el nivel de actividad física (Cuestionario Global de Actividad Física [GPAQ]), las ABVDs (índice de Barthel) y las AIVDs (escala de Lawton y Brody); y los datos socioeconómicos, de salud y de estilo de vida generales como posibles variables de confusión.

- 10. OE10: Identificar las diferencias en los parámetros mencionados de OE1 a OE8 al final de la intervención según la modalidad de entrenamiento empleada.

- 11. OE11: Determinar la eficacia y seguridad de los programas de entrenamiento multi-componente, de potencia y tradicional de fuerza a alta intensidad supervisados y progrevivos tradicionales realizados con resistencia elástica a través de la evaluación de las tasas de asistencia, cumplimiento y eventos adversos reportados por las mujeres mayores participantes.

Metodología

La presente tesis doctoral está compuesta por dos proyectos/estudios en los que participaron voluntariamente dos cohortes diferentes de mujeres mayores (primer proyecto: 93 sujetos de 60-88 años [69,93 ± 6,27]; segundo proyecto: 136 sujetos de 60-82 años [67,97 ± 4,77]). En el primer proyecto, los sujetos fueron asignados aleatoriamente a un programa de entrenamiento de fuerza progresivo con bandas elásticas de alta intensidad (AI; *n* = 39), moderada (M; *n* = 31), o a un grupo de control (C; *n* = 23) durante 32 semanas. En el segundo proyecto, los participantes fueron asignados aleatoriamente a un programa de entrenamiento multi-componente (MT; *n* = 34), potencia (P; *n* = 34), tradicional de fuerza a de alta intensidad (T; *n* = 34) o a un grupo control (C; *n* = 34) durante 20 semanas, donde la característica común entre las tres modalidades de ejercicio era el uso de bandas elásticas como material de entrenamiento.

En el primer proyecto, los grupos de entrenamiento realizaron un programa de fuerza progresivo con bandas elásticas dos veces por semana, compuesto por tres a cuatro series de seis (AI) o 15 (M) repeticiones, incluyendo seis ejercicios de cuerpo entero con una tasa de esfuerzo percibido de 6-7 (primeras cuatro semanas) y 8-9 (resto de las semanas) en la escala OMNI-RES. El grupo de control recibió instrucciones de continuar con su vida normal. En el segundo proyecto el grupo P y T realizaron el mismo entrenamiento en términos de ejercicios (seis ejercicios de cuerpo) y series (de tres a cuatro series por ejercicio), dos veces por

semana, usando ambos bandas elásticas, pero el grupo P desplazó la carga a máxima velocidad en la fase concéntrica mientras que el grupo T utilizó 2 s para realizar la fase concéntrica y 2s para la fase excéntrica. Asimismo, el grupo P realizó 12 (en las primeras dos semanas para consolidar la técnica) y 10 (para el resto del programa) repeticiones submáximas en cada serie con un esfuerzo percibido de tres-cuatro (muy bajo) en la escala OMNI-RES en la primera repetición, lo que equivale al 40-60% una repetición máxima (1 RM) (baja carga o baja intensidad) y nunca sobrepasó el valor de seis al final de las 10 repeticiones. El grupo T realizó seis repeticiones submáximas equivalentes al 85% de una 1RM a un valor de seis a siete en las primeras cuatro semanas y de ocho a nueve en las 16 semanas restantes. El entrenamiento multi-componente estuvo compuesto por ejercicios de equilibrio, fuerza, aeróbicos, flexibilidad y coordinación en la misma sesión y se realizó también dos veces por semana.

En ambos estudios se evaluó el estrés oxidativo, la salud ósea, la composición corporal, la fuerza neuromuscular y la función física. El estado de estrés oxidativo se evaluó en productos de ADN (8-oxo-dG en orina en ambos proyectos), lípidos (8-iso-P en ambos proyectos; MDA en el primer proyecto), y proteínas (proteínas carboniladas en el primer proyecto), junto con enzimas antioxidantes (SOD y GPx en ambos proyectos; CAT en el segundo proyecto) y estado redox tiol (GSH, GSSG, ratio GSSG/GSH en ambos proyectos; glutatión total y ratio GSH/GSSG en el segundo proyecto) . La salud ósea estuvo compuesta por medidas aDMO y puntuación T de la columna lumbar (segmentos L1-L4, L2-L4 y vértebras individuales L1, L2, L3, L4, en ambos proyectos), fémur proximal (cuello femoral, trocánter, área intertrocantérea , triángulo de Ward y cadera total en ambos proyectos) evaluados por absorciometría dual de rayos X (DXA), riesgo de fractura (probabilidad en 10 años de una fractura osteoporótica mayor y probabilidad en 10 años de fractura de cadera) y finalmente biomarcadores óseos de formación ósea (P1NP en ambos

proyectos, FAo en el primer proyecto y OC en el segundo proyecto), reabsorción ósea (β-CTx en ambos proyectos) y relación entre ambos (FAo/β- CTx en el primer proyecto).La composición corporal (la masa corporal total, la masa grasa corporal total, la masa libre de grasa corporal total y el porcentaje total de grasa corporal) se midió en ambos proyectos por DXA mientras que en el segundo proyecto también se evaluó el riesgo cardiovascular a través de medidas antropométricas (CC, CCA, ICCA, ICA). Además, la fuerza neuromuscular de las extremidades superiores (músculos flexores y extensores del codo) e inferiores (abductores y aductores de cadera junto con músculos flexores y extensores de rodilla) se evaluó mediante dinamometría isocinética a bajas (60 °/s) y altas (180 °/s) velocidades en ambos proyectos. Finalmente, la función física se midió usando varias pruebas funcionales y baterías ampliamente utilizadas en la literatura como los tests 30seg-LS y 30seg-FC para evaluar la fuerza/resistencia de las extremidades inferiores y superiores (usado en ambos proyectos), el tes TUG para evaluar el equilibrio dinámico/agilidad (usado en ambos proyectos), la prueba de 6MM para evaluar la resistencia aeróbica (usado en ambos proyectos), el test 5SLS, subir escaleras, la velocidad de ascensión de escaleras (VAE) y la potencia de ascensión de escaleras (PAE) para la fuerza muscular de las extremidades inferiores (utilizada en el segundo proyecto), así como la PAF para el equilibrio proactivo (utilizada en el segundo proyecto).

Los datos se analizaron a través del enfoque de intención de tratar (IDT) y análisis por protocolo (APP) en ambos proyectos. Después de aplicar las pruebas de Kolmogorov-Smirnov y Levene para analizar la distribución y homogeneidad de los datos, los datos no distribuidos normalmente se transformaron utilizando el logaritmo natural (log10). Se utilizó un análisis de varianza de dos vías (ANOVA) para medidas repetidas seguidas de correcciones de Bonferroni para examinar los efectos de tiempo, grupo e interacciones. Además también se aplicó un análisis de covarianza de dos vías (ANCOVA) para medidas

repetidas utilizando los valores basales y la edad como covarianzas. También se calcularon los tamaños del efecto d de Cohen (TE) y el porcentaje delta (Δ%). Los datos se presentan como media ± desviación típica (DT) junto con los intervalos de confianza (IC) del 95%. La significación estadística se estableció en $p \leq 0,05$. Para el análisis estadístico se utilizó el software comercial SPSS Versión 25.0.

Resultados

Respecto al estrés oxidativo, en el primer proyecto, tras 16 semanas de entrenamiento, el grupo M logró descensos significativos en 8-oxo-dG (-21,34%), 8-iso-P (-15,85%) y MDA (-19,12%) con TE moderados en todos ellos, mientras que el grupo AI mostró aumentos significativos en 8-oxo-dG (+60,49%; TE grande) y 8-iso-P-P (+24,40%; TE moderado). No se encontraron diferencias significativas por tiempo en las proteínas carboniladas. Se encontró una interacción significativa tiempo × grupo en MDA entre los grupos M y C. Después de aplicar el ANCOVA, se encontraron diferencias entre AI y M así como entre los grupos AI y C en 8-oxo-dG y entre M vs C en MDA. Además el grupo M mostró un aumento en los niveles de CAT (+5,40%; TE pequeño) ($p \leq 0,05$) mientras que el grupo AI disminuyó significativamente el GPx (-8,95%; TE moderado) y GSH (-9,31%; TE moderado). En el segundo proyecto, después de 20 semanas, tanto los grupos MT como los P mejoraron el estado de estrés oxidativo al disminuir el 8-oxo-dG (MT: -48.56%, TE moderado; P: -65.79% , TE grande) y 8-iso-P (MT: -30,49%, TE moderado; P: -26,98% , TE pequeño). Además el grupo MT incrementó significativamente los valores de la enzima SOD (TE pequeño). Así mismo, se encontraron diferencias significativas entre los grupos P y C en 8-oxo-dG y entre ambos grupos experimentales y el grupo C en SOD. El grupo P también logró cambios positivos en el estado redox tiol ($p \leq 0,05$) (aumento en el glutatión total, GSH el ratio GSSG/GSH y disminución en GSSG). Después de aplicar la ANCOVA, el grupo MT mostró una

disminución significativa en GSSG y en el ratio GSSG/GSH. El TE de los cambios de estado de los tioles varió de pequeño a grande.

En cuanto a la salud ósea, en el primer proyecto, después de 32 semanas tanto el grupo de AI como el grupo M lograron un aumento significativo de la aDMO de la columna lumbar total (M: +0,89%; AI: +1,12%) con TE trivial, pero solo el grupo AI mostró diferencias significativas con el grupo C. En el fémur proximal, tanto el grupo AI como el grupo M aumentaron ($p \leq 0,05$) la aDMO del cuello femoral (M: +1,57%; AI: +1,39%), triángulo de Ward (M: +2,59%; AI: +2,47%), y cadera total (M: +1,13%; AI: +1,21%) mientras que el grupo AI también mejoró significativamente la aDMO del trocánter (+1,38%). Los TE fueron todos triviales no se encontraron diferencias significativas entre los grupos. Por otro parte, el riesgo de fractura de osteoporótica mayor o de fractura de cadera también se redujo ($p \leq 0,05$) en ambos grupos. Los cambios en la aDMO se acompañaron de cambios significativos en los biomarcadores de formación y reabsorción ósea después de 16 semanas, como fue el caso de P1NP (M: +11,24%; AI: +8,23%), FAo (AI: + 4,68%), β- CTx (M: -6,65%; AI: -8,07%), y ratio FAo /β-CTx (M: +13,71%; AI : +9,58%) , así como también después de 32 semanas [P1NP (M: +19,76%; AI : +23,89%), FAo (M: +8,07%; AI: +9,95%), β- CTx (M: -7,24%; AI: -9,80%), y ratio FAo/β-CTx (M: +20,86 %; AI: +19,56%)] . En todos los parámetros la magnitud de los cambios se consideró trivial o pequeña. El ANCOVA reveló diferencias significativas entre los grupos AI y C en FAo, β-CTx y ratio FAo/ β-CTx, y entre ambos grupos de ejercicio en FAo. En el segundo proyecto, únicamente el grupo P mejoró significativamente la aDMO de la columna lumbar completa (+1,28%, TE triviales) y algunas zonas del fémur proximal, tales como el área intertrocantérea (+ 1,38%, TE triviales), triángulo de Ward (+4,66%, TE pequeños) y cadera total (+1,03%, TE triviales), sin diferencias entre los grupos, excepto entre los grupos P y C en el área intertrocantérea y la cadera total después de aplicar el ANCOVA.

Todos los grupos de entrenamiento redujeron significativamente el riesgo de fractura y tanto los grupos MT como P mostraron adaptaciones positivas ($p \leq 0,05$) en los biomarcadores óseos al aumentar la OC (MT: +16.37%, TE moderado; P: +24.82%, TE grande) y reducir el β- CTx (MT: - 9,05%, TE pequeño; P: - 8,76%, TE pequeño).

En cuanto a la composición corporal, en el primer proyecto, el grupo M logró disminuciones significativas en la masa grasa total (-8.04%) y en el porcentaje de grasa corporal total (-2.90%) junto con un aumento significativo en la masa libre de grasa total (+ 2.98%), con TE pequeños en todos los parámetros. El grupo AI mostró un aumento significativo (TE trivial) en la masa libre de grasa total (+2,10%) junto con una disminución significativa en el porcentaje de grasa corporal total (-2,21%) con TE pequeños en ambos casos . No se encontraron diferencias significativas entre grupos. Después del ANCOVA, se encontraron diferencias en la masa grasa total entre los grupos M y C, y en la masa libre de grasa total y el porcentaje de grasa corporal total entre los grupos de entrenamiento y el grupo C. En el segundo proyecto, se encontraron disminuciones significativas en todos los grupos de formación en CC (MT: - 2,75%; P: -2,25%; T: -1,32%), CCA (MT: -2,37%; P: -1,97%; T : -0,91%), ICA (MT: - 2,73 %; P: -2,26%; T: -1,32%), la masa grasa total (MT: -4,24%; P: - 2,75%; T: -2.44%), y el porcentaje total de grasa corporal (MT: -4,53%; P: -3,69%; T: - 2,44%), con TE que oscilaron entre triviales y pequeños. Además, los grupos MT y T también mejoraron ($p \leq 0,05$) la masa libre de grasa total (MT: +1,52%; T: +1,58%) (TE trivial). Se encontraron diferencias significativas entre la los grupos de entrenamiento y el grupo C en CC, CCA, ICA y porcentaje total de grasa corporal.

En cuanto a la fuerza neuromuscular, en el primer proyecto, los grupos AI y M mejoraron significativamente la fuerza de los músculos abductores (M: +23,71%; AI: +53,2 8%) y adductores (M: +15,89%; AI: +23,07%) de cadera a 60 °/s, mientras que el grupo AI también aumentó la fuerza ($p \leq 0,05$) a 180 °/s (abductores de cadera: +49,78%;

adductores de cadera: +15,52%). Los TE oscilaron entre triviales y grandes. No se encontraron diferencias significativas entre los grupos de entrenamiento, pero si con el grupo C. Además, los grupos AI y M lograron aumentos significativos en la fuerza de los músculos flexores y extensores de la rodilla tanto a velocidades bajas como altas (TE moderados y grandes), sin diferencias significativas entre los grupos de entrenamiento. Sin embargo, ambos grupos mostraron diferencias significativas con el grupo C en todos los parámetros de la rodilla. Similares resultados se obtuvieron en las extremidades superiores, donde tanto el grupo AI como el grupo M mostraron mejoras significativas en la fuerza de los músculos flexores y extensores del codo a ambas velocidades (TE moderados y grandes). No se encontraron diferencias significativas entre los grupos de entrenamiento, pero sí hubo diferencias significativas entre ambos grupos de entrenamiento y el grupo C en todos los parámetros. En el segundo proyecto, después del ANOVA o ANCOVA, todas las modalidades de entrenamiento mejoraron significativamente la fuerza neuromuscular en las articulaciones de la cadera, la rodilla y codo (TE de pequeños a grandes), excepto los grupos P y MT en la flexión de la rodilla y la flexión del codo a 60 °/s, respectivamente. El grupo P logró diferencias significativas con el resto de modalidades de ejercicio en la fuerza muscular en la abducción y adducción de cadera así como en la extensión y flexión del codo a 180°/s. Además, el grupo T también mostró diferencias significativas con los grupos MT y P en la musculatura extensora del codo a bajas velocidades.

Finalmente, en cuanto a la función física, en el primer proyecto, ambos grupos de entrenamiento mejoraron significativamente todos los parámetros analizados, con el grupo AI logrando TE grandes en 30seg-LS (+75.93%), 30seg-FC (+79.08%), TUG (-18.80%) y 6MM (+10,50%) mientras que el grupo M obtuvo TE grandes en todas la pruebas excepto un TE moderado en el test de 6MM (+ 7,93%). No se encontraron diferencias significativas entre los grupos de entrenamiento, pero ambos grupos de entrenamiento mostraron diferencias

significativas con el grupo C en todos los parámetros. En el segundo proyecto, nuevamente todos los grupos de entrenamiento mejoraron todos los parámetros de función física analizados, obteniendo principalmente TE moderados y grandes. Después del ANCOVA, se encontraron diferencias significativas entre las modalidades de entrenamiento en la medida de potencia de 5SLS entre el grupo P y el resto de estrategias de entrenamiento (TE moderado). Además, las tres modalidades de entrenamiento obtuvieron diferencias significativas con el grupo C en todas las variables.

Conclusiones

El programa de entrenamiento de resistencia elástica progresiva a una intensidad moderada en lugar de alta puede ser una mejor estrategia para reducir el estrés oxidativo en mujeres mayores después de 16 semanas, mientras que el entrenamiento multi-componente, y especialmente el de potencia, han demostrado ser efectivos para la mejora del estrés oxidativo y la tasa de renovación ósea en las mujeres mayores después de 20 semanas de entrenamiento. Los programas de fuerza con resistencia elástica realizados a alta y moderada intensidad son eficaces para mejorar la salud ósea, la composición corporal, la fuerza neuromuscular y la función física en las personas mayores después de 32 semanas de entrenamiento. Así mismo, el entrenamiento multi-componente, de potencia y de fuerza a alta intensidad realizados con resistencia elástica también han demostrado ser estrategias efectivas para la mejora de estos mismos parámetros de salud en mujeres mayores después de 20 semanas. A corto plazo (16 semanas), en entrenamiento de fuerza de alta intensidad es la estrategia más efectiva para aumentar la tasa de remodelado óseo en las mujeres mayores, mientras que el entrenamiento de potencia parece ser la modalidad de ejercicio más adecuada para crear adaptaciones positivas en la potencia muscular. Al mismo tiempo, el entrenamiento multi-componente produce los mayores cambios en la composición corporal. Finalmente, todas las intervenciones de ejercicio basadas en elásticos analizadas en la presente tesis

doctoral fueron bien toleradas y seguras por las mujeres mayores debido a la ausencia de eventos adversos graves, la baja tasa de deserción y las tasas de asistencia y cumplimiento informadas en ambos proyectos.

Palabras clave: resistencia variable, adultos mayores, entrenamiento de alta velocidad, potencia muscular, densidad mineral ósea, tejido adiposo.

LIST OF ABBREVIATIONS

Abbreviations are defined at first mention and used consistently thereafter:

•OH	Hydroxyl
α-CTx	α-isomerized form of CTx
β-CTx	β-isomerized form of CTx
1RM	One repetition maximum
2D	Two-dimensional
25OHD	1,25 hydroxyvitamin D
3D	Three-dimensional
30sec-AC	30 seconds arm curl
30sec-CS	30 seconds chair stand test
30seg-AA	Test d'alçar-se i asseguera de la cadira durant 30 segons
30seg-FC	Test de realizar flexo-extensiones durante 30 segundos
30seg-LS	Test de levantarse y sentarse de la silla durante 30 segundos
4-HNE	4-hydroxynonenal
5AA	Test d'alçar-se i asseure's de la cadira cinc vegades
5SLS	Test de sentarse y levantarse de la silla cinco veces
5STS	Five times sit to stand test
6MM	Prueba de seis minutos marcha
6MWT	Six minute walking test
8-iso-P	F2-isoprostanes
8-oxo-dG	8-oxo-2-deoxyguanosine
%1RM	Percentage of the 1 RM
AACE	American Association of Clinical Endocrinologists
aBMD	Areal bone mineral density
ACh	Acetylcholine
ACSM	American College of Sports Medicine

ADLs Activities of daily living

aDMO Densidad mineral ósea de área

AHA American Heart Association

AI Alta intensidad

ALM Appendicular lean mass

ALP Total alkaline phosphatase

ANCOVA Analysis of covariance

ANOVA Analysis of variance

APP Análisis por protocolo

ASM Appendicular skeletal mass

ATP Adenosine triphosphate

BADLs Basic activities of daily living

bALP Bone-specific isoform of alkaline phosphatase

BIA Bioelectric impedance analysis

BMD Cone mineral density

BMI Body mass index

BMC Bone mineral content

BPM Beats per minute

BSP Bone sialoprotein

BTMs Bone turnover markers

C Control group

CC Circunferencia de cintura

CAT Catalase

CCA Circunferencia de cadera

CG Control group

CGs Control groups

CHO Carbohydrates

CIs	Confidence intervals
Cl	Chlorine
CLIA	Chemiluminescent immunoassay
CM	Circumferència de maluc
CoM	Body's centre of mass
CONSORT	Consolidated Standards of Reporting Trials
COPD	Chronic obstructive pulmonary disease
CSA	Cross-sectional area
CTSK	Cathepsin K
CTSL	Cathepsin L
CTX-I	C-terminal telopeptide of type I collagen
CV	Coefficient of variance
DDK-1	Dickkopf-related protein 1
DNA	Deoxyribonucleic acid
DPD	Deoxypyridinoline
DT	Desviación típica
DXA	Dual energy X-ray absorptiometry
EC	Electrochemical detection
ECLIA	Electrochemiluminescence immunoassay
EDTA	Ethylenediaminetetraacetic acid
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
ES	Effect size
EWGSOP	The European Working Group on Sarcopenia in Older People
FAo	Fosfatasa alcalina ósea
FeSOD	Iron SOD
FISABIO	Fundación para Fomento de Investigación Sanitaria y Biomédica

FRAX	Fracture risk assessment tool
FRT	Functional reach test
F-V	Force-velocity
GDP	Gross domestic product
GE	Grandària del effecte
GHYL	Galactosyl hydroxylysine
GGHYL	Glucosylgalactosyl-hydroxylysine
GLA	Gamma-carboxyglutamic acid
GPAQ	Global Physical Activity Questionnaire
GPx	Glutathione peroxidase
GSH	Reduced glutathione
GSSG	Oxidized glutathione
GUG	Get-Up and Go Test
H1-11	Hypothesis one to eleven
H_2O_2	Hydrogen peroxide
H_2O	Water
HC	Hip circumference
HI	High-intensity resistance training
HIIT	High-intensity interval training
HLys	Hydroxylysine
HO_2•	Hydroperoxyl
HSCs	Haemopoietic stem cells
HYP	Hydroxyproline
IADLs	Instrumental activities of daily living
IC	Intervalo de confianza
ICC	Intraclass correlation coefficient
ICA	Índice cintura-altura

ICCA	Índice cintura-cadera
ICM	Índex cintura-malic
IDT	Intención de tratar
IMRA	Immunoradiometric assay
INE	Instituto Nacional de Estadística
IOF	International Osteoporosis Foundation
IPAQ	International Physical Activity Questionnaire
ISCD	International Society for Clinical Densitometry
ITT	Intention-To-Treat analysis
K	Potassium
M	Moderate-intensity resistance training
MACOP	Municipal Activity Centers for Older People
MCIDs	Minimum clinically important differences
MDA	Malonaldehyde
MDC	Minimal detectable changes
MES	Minimum effective strain
METs	Metabolic equivalent tasks
MHR	Maximal heart rate
MMSE	Mini mental state examination
MRI	Magnetic resonance imaging
MSCs	Mesenchymal stem cells.
MT	Multi-component training
mtROS	Mitocondrial reactive oxigen species
MVIC	Maximal voluntary isometric contraction
N	Newton
Na	Sodium
NADPH	Nicotinamide adenine dinucleotide phosphate

NAMS	North American Menopause Society
NAS	National Academic of Science
NBHA	National Bone Health Alliance
NCSA	National Strength and Conditioning Association
nDNA	Nuclear DNA
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institutes of Health
NO_2•	Dioxide nitric
NO•	Nitric oxide
NOF	National Osteoporosis Foundation
NTX-I	Amino- (N-) terminal cross-linking
O_2	Oxygen
O_2•−	Superoxide radical
OADR	Old-age dependency ratio
OASIS	Overall anxiety severity and impairment scale
OC	Osteocalcin
ODSIS	Overall depression severity and impairment scale
OE	Objetivo específico
OH•	Hydroxyl radical
OMNI-RES	OMNI resistance exercise scale
OMS	Organización Mundial de la Salud
OPG	Osteoprotegerin
P	Power strength training
P1CP	Procollagen type 1 C-terminal propeptide
P1NP	Procollagen type I N propeptide
PAE	Potencia de ascension de escaleras

PAF Prueba de alcance funcional

PBMCs Peripheral blood mononuclear cells

PPA Per protocol analysis

pQCT Peripheral quantitative computed tomography

PTH Parathyroid Hormone

PUFAs Polyunsaturated fatty acids

P-V Power-Velocity

PYD Pyridinoline

QCT Quantitative computed tomography

QUS Quantitative ultrasound

R Ratio

RANK Receptor Activator of Nuclear factor-κB

RANKL RANK ligand

RCT Randomized controlled trial

RCTs Randomized controlled trials

RDA Recommended dietary allowance

Redox Redox reduction-oxidation

RFD Rate of force development

RIA Radioimmunoassay

RiR Repetitions in reserve

RIs Reference intervals

RISE Resistance Intensity Scale for Exercise

RM Repetition maximum

RNS Reactive nitrogen species

RoI Region of interest

ROM Range of motion

RONS Reactive oxygen and nitrogen species

ROS	Reactive oxygen species
RPE	Rate of perceived exertion
SCP	Stair-climbing power
SCS	Stair-climbing speed
SD	Standard deviation
SFT	Senior fitness test
SLM	Skeletal lean mass
SMD	Standard mean difference
SMM	Skeletal muscle mass
SO1-10	Specific objective one to ten
SOD	Superoxide dismutase
SOD1	Copper-zinc SOD
SOD2	Manganese SOD
SOD3	Extracellular SOD isoenzyme
SPPB	Short Physical Performance Battery
sRPE	Session RPE
T	Traditional high-intensity resistance training
TE	Tamaño del efecto
TRACP5b	Isoform 5b of tartrate-resistant acid phosphatase
TUG	Time Up & Go test
UN	United Nations
US	United States
USA	Unites States of America
X-ray	Single- energy x-ray absorptiometry
VO_2max	Maximal oxygen consumption
VO_2peak	Peak oxygen consumption
VAE	Velocidad de ascensión de escaleras

W	Watts
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio
WHtR	Waist-to-height ratio
WMD	Weighted mean differences

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CHAPTER I

Introduction

Population aging is recognized as a global phenomenon and a global issue, one of the four global demographic "megatrends" (Cesari et al., 2015). The number of people aged over 65 years has increased considerably in recent years. In 2019, one in 11 people worldwide were over 65, representing 10% of the global population, but the projections indicate that this rate could reach one in six people by 2050, representing 21.8% of the population (United Nations [UN], 2019). In Spain, this phenomenon is still more significant, as it is predicted that by 2050 the country will be the only one in Europe to remain among the 10 countries with the largest increase in the share of older people (UN, 2019). Currently, one in five Spanish people (19.4%) are over the age of 65 (Instituto Nacional de Estadística [INE] 2019), which represents almost 9 million individuals. According to the INE projection for 2018–2068 (INE, 2018), in 2068 there could be more than 14 million older people, representing 29.4% of the total population. However, the demographics relating to aging differ according to gender, with women comprising more than 55% of the global population aged 65 or over, and more than 60% among the population aged 80 or over (UN, 2019). This phenomenon is called the "feminization of old age" (Abellán et al., 2019). It is particularly noticeable in Spain, not only in terms of a larger population of older women, but also in the fact that women are often responsible for taking care of other older adults in the family.

During the 20th century, one of the scientific community's main objectives was to discover and modify the processes that increase life expectancy (Borrás et al., 2011), but in the last two decades the focus has changed. Currently, it is not only the quantity of life that is important, but the quality (Hansen & Kennedy, 2016). Extending lifespan without improving healthspan could have negative consequences, resulting in longer periods living with disabilities and comorbidities. This constitutes a high risk of older adults suffering a higher prevalence of aging-related diseases (Olshansky, 2018). The process of aging has been linked with degenerative processes in multiple systems, and thus with several non-communicable

chronic diseases. For example, it has been suggested that chronic oxidative stress associated with old age plays a primary or secondary role in the development of more than 100 acute and chronic human pathological processes (Dalle-Donne et al., 2006; Fisher-Wellman & Bloomer, 2009; Kalogeris et al., 2014; Valko et al., 2007). Furthermore, older adults are at a significantly increased risk of suffering osteopenia, osteoporosis, and osteoporotic fracture compared to other age groups due to the greater loss of trabecular and cortical bone after the age of 50 (Riggs & Melton, 1992). Furthermore, aging is associated with a marked decline in skeletal muscle mass (Cruz-Jentoft et al., 2019), which can lead to the pathological condition of sarcopenia, along with an age-related increase in adipose tissue and a redistribution of fat mass from peripheral to central body areas (Droyvold et al., 2006; Hunter, Gower & Kane, 2010; Schutz et al., 2002; Wilson & Kannel, 2002). This leads to increased cardiovascular risk due to the presence of the metabolic disease conditions of obesity or being overweight (O'Leary et al., 2006). Moreover, age-related declines in muscle strength and power in the upper and lower limbs have been well documented (Goodpaster et al., 2006). It is well-known that the reduction in older adults' capacity to generate muscle force—which relates to muscle power—is strongly linked to physical function impairments (da Rosa Orssatto, Moura et al., 2018). Thus, the consequences of aging also include the decline of physical function or mobility and the inability to perform some of the basic activities of daily living (BADLs) and the instrumental activities of daily living (IADLs), such as chair-standing, walking, and stair-climbing.

It is noteworthy that women show lower levels of bone mineral density (BMD) than men of a similar age—women lose on average ~50% of their trabecular bone tissue and ~30% of their cortical bone, while men lose 30% and 20%, respectively (Riggs & Melton, 1992). The same pattern is seen with skeletal muscle mass (Jankowski et al., 2008; Valentine et al., 2009), muscle strength (Boudard et al., 2011), and muscle power (Reid et al., 2012).

The increase in adiposity is also greater in older females than in older males (Vincent et al., 2010; Tseng et al., 2014). All these factors can negatively impact physical function and place older women at a greater risk of disability than men. Furthermore, these negative changes always occur at an earlier age in women than in men due to the estrogen withdrawal during menopause. Consequently, women tend to live longer with disability than men and, at the same time, tend to suffer to a greater extent with conditions such as arthritis, obesity, osteoporosis, sarcopenia, and frailty, which present more comorbidities related to physical disability. In Spain, the number of years lived in poor health or with a disability was 12.2 years in women and 9.7 years in men in 2017 (Kyu et al., 2018). This situation generates a high economic cost for health systems faced with preventing or treating age-related chronic diseases and dependency situations, and the impact falls particularly hard on healthcare systems in countries such as Spain, which have high numbers of older adults.

Due to age-associated declines in health and the consequences of aging, older people need to maintain their health and wellbeing to facilitate continued independent living, societal participation, and quality of life. Disability and the loss of independence are not inevitable consequences of aging (Cadore et al., 2014). Engaging in physical activity and exercise activities is considered one of the most beneficial factors of a modern lifestyle and is seen as an indispensable element of good health (Simioni et al., 2018). Physical activity and exercise in later life have several proven benefits for health, including the maintenance and possible improvement of physical components such as cardiovascular function, muscle strength, muscle power, muscle mass, physical function, balance, posture, stability, body composition, and flexibility (Sun, Norman, While, 2013). The mental and psychosocial benefits of physical activity and exercise have also been demonstrated (Windle et al., 2010). Furthermore, physical activity is a cornerstone in the primary prevention of at least 35 chronic conditions (Booth et al., 2011).

There is strong evidence that resistance exercise training, when combined with general physical activity and exercise, provides multiple and unique benefits for older adults' health, regardless of age (Fragala et al., 2019; Romo-Perez et al., 2011), reducing the incidence of age-related conditions that reduce the quality of life in this population (Lavin et al. 2019). It is well documented that resistance training, in its different types, can partially reverse losses in muscle strength, muscle mass, and muscle power by maintaining or increasing them (Fragala et al., 2019; Hunter et al., 2004; Lavin et al., 2019; Liu & Latham, 2009). However, resistance training is recommended for older adults not only for its benefits at the neuromuscular level, but also for its positive effects in maintaining functional independence and improving body composition, BMD, cognitive function, self-confidence, and health-related quality of life (Fragala et al., 2019; Liu & Latham, 2009). Furthermore, there is a growing body of evidence for the effectiveness of resistance training in preventing and treating many chronic illnesses (Lange et al., 2008), reducing the risk factors for diabetes, osteoporosis, and colon cancer among others (Chodzko-Zajko et al., 2009).

These demographic changes and consequences of aging bring challenges for national strategies in healthcare and social services. Although the prevalence of disability rates worldwide is concerning, the incidence of disability for older adults who engage in resistance or aerobic exercise is only 37.1%, compared to a 52.5% incidence in non-exercisers (Penninx et al., 2001). This is because most of the factors underlying impairments in physical function are modifiable with exercise. As such, and according to the benefits demonstrated by the evidence previously mentioned, governments around the world and international organizations have designed physical activity guidelines to provide clear and evidence-based recommendations to encourage older adults to engage in physical activities. Initially, most national public health physical activity recommendations emphasized aerobic exercise (Blair et al. 2004; Oja & Titze 2011), although current exercise recommendations for older adults

consistently advocate strength training (Romo-Pérez et al., 2011). The 2020 WHO global recommendation for older adults proposes that muscle-strengthening activities involving the major muscle groups should be performed at least twice a week (WHO, 2010a). The American College of Sports Medicine (ACSM) makes the same recommendations and stresses that a combination of endurance and strength training activities is more effective than either form of training in isolation (Chodzko-Zajko et al., 2009).

Because of the cumulative effect of different factors throughout life, regardless of genetic and other predisposing factors, leading a healthy lifestyle is particularly important for older people seeking to minimize the risk of premature death and maximize their chances of an active, healthy, and independent life (Burton , Farrier et al., 2017; Knoops et al., 2004). However, despite the impressive benefits of regular physical activity and exercise for older adults, this group has been identified as having one of the lowest physical activity rates in society (Berk et al., 2006; Wister & Wanless, 2007). The situation for older women is of particular concern because women have significantly lower physical activity levels than men at all ages (Laird et al., 2014), but this is particularly evident at older ages (DiPietro et al., 2001). Unfortunately, most older adults do not meet the general physical activity recommendations of a minimum of 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity exercise per week, and even fewer achieve the two recommended weekly sessions of strength training (Jefferis et al., 2014; Kohn et al., 2015). This means that they do not engage in sufficient physical activity to promote health benefits (Sun, Norman & White, 2013). It has been estimated that 60%–75% of older people worldwide do not exercise at the recommended levels, with approximately 25% in this age group participating in regular exercise (Hallal et al., 2012; Nied & Frankin, 2002) and only 12% meeting the recommended levels of aerobic and muscle-strengthening physical activity

(Kohn et al., 2015). In Spain, 80% of older adults are physically inactive, and only 17.2% of older women meet the physical activity recommendations.

The fact that so few older people meet the strength-training recommendations is of particular concern. Aging involves a reduction in all types of physical activity participation, but the most significant reduction occurs in muscle-strengthening activities (Gray et al., 2018). Studies have shown that fewer than 15% of older people participate in resistance training twice a week, which is the minimum recommended frequency (Bennie et al., 2016; Merom et al., 2012). Furthermore, reflecting the general levels of physical activity, fewer older women than men reported engaging in resistance training (Strain et al., 2016), with around 10% or even less meeting the recommended levels (Centers for Disease Control and Prevention, 2006; Humphries et al., 2010). As a consequence of these low physical activity rates, physical inactivity has become the fourth leading risk factor for non-communicable diseases (Hallal et al., 2012) and the fourth leading cause of death worldwide (Forwood, 2013), and is therefore considered to be a pandemic.

Several barriers limit older adults' participation in physical activity and exercise, particularly in resistance training programs (Burton, Farrier et al., 2017). One aspect regularly reported in the literature is the nature and suitability of training equipment, because older adults perceive it not only as a barrier to engaging in resistance training programs but also as a reason for ceasing participation in a resistance training program (Burton, Farrier et al., 2017; Burton, Hill et al., 2017). Furthermore, the exercise equipment has been commonly identified as a negative aspect of resistance training programs by those older adults who participate in one (Burton, Farrier et al., 2017; Burton, Hill et al., 2017). Hence, it seems that along with others barriers, the suitability, availability, and comfortability of the resistance training device used is a crucial factor in encouraging or limiting older adults' participation in resistance training programs.

Resistance machines and free weights are currently considered the gold standard exercise devices for producing muscle strength adaptations through resistance training (de Oliveira et al., 2016). They are the most common and traditional devices used in resistance training programs due to their demonstrated positive effects (category A) on strength, power, body composition, physical function, and other health-related parameters across different populations (Chodzko-Zajko et al., 2009; Kwak et al., 2016; Liao et al., 2016; Winters-Stone & Snow, 2006). However, despite the widespread use of these devices, they often require special facilities or involve high cost, which can limit access to them (Colado & Triplett, 2008). Furthermore, some individuals fear using free weights and resistance machines because these are commonly associated with an increased perception of injuries or high physical demands (Jakobsen et al., 2013). It is estimated that 50% of the individuals who perform resistance training with machines abandon exercise practice during the first year, mainly due to logistical difficulties and financial cost (Dishman et al., 2014).

However, despite the widespread use of this kind of equipment for resistance training protocols in scientific, rehabilitation, and sport settings, several studies have investigated the effects of elastic resistance training in the elderly. This is because elastic bands are a more portable, user-friendly, and less-expensive alternative to conventional resistance training, allowing greater adherence and accessibility to a fitness program and producing similar results (Colado, Mena et al., 2020; Damush & Damus, 1999; de Alencar Silva et al., 2020; de Oliveira et al., 2016; Fritz et al., 2018; Gargallo et al., 2018; Lopes et al., 2019; Ribeiro et al., 2009). Colado and colleagues (Colado, Mena et al., 2020) pointed out in their systematic review involving adults of all ages that elastic resistance training programs are effective in improving muscle strength, physical function, and other health-related variables across the lifespan. Elastic resistance training tools, categorized as variable resistance tools, are not only useful because of their easy handling and low cost, but also because the load/resistance

produced by them varies throughout the range of motion (ROM) of the resistance exercise prescribed (Wernborn et al., 2007). These variable elastic characteristics allow some advantages compared with the isotonic load, such as the possibility of maintaining a high velocity and acceleration throughout the ROM, (Frost et al., 2010; Wallace et al., 2006) and the possibility of overcoming the weakest part of the resistance training, known as the "sticking point". The elastic bands are therefore considered an effective and valid variable resistance device that can increase adherence to resistance training in older adults, as they are an easily available, low cost, and safe tool that can be used in different settings such as gyms, hospitals, medical clinics, long-term institutions, and even the subject's home (de Alencar Silva et al., 2020).

Together with the type of training device chosen, the training intensity applied in resistance training interventions and the type of training modality prescribed are two key training parameters that can increase training program adherence and improve the health of older adults. The proper manipulation and administration of training intensity are crucial in maximizing the potential benefits and adaptations of resistance training protocols (Fisher et al., 2011, 2013). Traditionally, intensity in resistance training is defined as the training load. Nevertheless, using load alone as a description of intensity in resistance training programs is not accurate enough. Intensity in resistance training also has to be representative of the degree of effort involved during a specific resistance exercise (Steele, 2014; Winett et al., 2019). Therefore, intensity in resistance training should be understood as synonymous with both load and effort and defined as the level of effort applied to a given load (Fisher & Smith, 2012).

To produce desirable training adaptations in older adults through resistance training, world-leading organizations in exercise research have recommended moderate-to-high intensities in the range of 60% to 80% 1RM (Chodzko-Zajko et al., 2009; Fragala et al.,

2019; Peterson & Gordon, 2011). Several meta-analyses have supported these recommendations by comparing resistance training interventions at different intensities and showing greater gains for higher intensities (loads) (Peterson et al., 2010; Steib et al., 2010; Silva et al., 2014). However, several studies have tried to change this classic notion that only high intensity produces greater adaptations in older adults (Schuenke, Herman & Staron 2012; Burd et al., 2013; Schoenfeld, 2013a). These studies have demonstrated that the problem lies in focusing only on the load as an indicator of intensity, leaving effort out of the equation, or in prescribing moderate-to-high loads but with low levels of effort. In fact, when resistance training interventions are matched for mechanical work or effort, the improvements are similar between intensities (Léger et al., 2006; Alegre et al., 2015). However, it is unknown whether these intensity-dependent effects could occur in older women when resistance training is performed with elastic bands. It is also unknown whether this behavior occurs equally in any health-related parameter, or if it differs between different health indicators such as oxidative stress, bone health, body composition, strength, or physical function.

The low participation rates and broad health benefits of physical activity—and particularly resistance training—underscore the need for an evidence-based identification of the most suitable, simple, attractive, and safe physical activities and training modalities to encourage older adults to be more active. Many studies have examined the effects of different exercise modalities, trying to identify which kind of training strategy should be prescribed to older adults based on their greater benefits over different health-related parameters (Borde et al., 2015; Byrne et al., 2016; Fragala et al., 2019). Regarding training intensity, the proper selection of the training modality is a critical factor in maximizing target adaptations in older adults. The training strategy selected is a crucial factor in maximizing the performance for given individuals and groups. Alternatives have emerged that could equal or even better the

effects of strength training, at least in regard to specific components of health. Among the different training modalities that exist, multi-component training and power strength training are paramount, not only due to their reported benefits in older adults, but also their characteristics, high applicability, and safety. Multi-component training is characterized by the inclusion of different physical components such as strength, aerobics, balance, or flexibility within the same session, while the main characteristic of power strength training is the displacement of the load at high velocities (with the maximum intention of movement). Both modalities are effective exercise strategies for improving health in older adults, especially for improving balance in the case of multi-component training, and improving muscle power in the case of power strength training (Bangsbo et al., 2019; Beaudart et al., 2019; Byrne et al., 2016). However, their efficacy in other highly relevant parameters such as oxidative stress, bone health, and body composition has hardly been studied. Similarly, despite evidence of their effects on improving strength and functionality in older adults, no studies to date have analyzed the effects of these exercise modalities in older women.

It would be of practical interest to compare the effects of the three modalities that appear to have the most significant impact in improving the health of the elderly, namely high-intensity resistance training, multi-component training, and power strength training. Such a comparison could determine which approaches are the most effective, and in which areas. It is also possible that all of them produce positive adaptations due to different metabolic and physiological processes, and they could thus be used interchangeably to improve the health of older adults.

In this context, the present PhD dissertation aims to analyze the effects of training intensity (high vs moderate) in elastic-based resistance protocols and to compare the effects of the type of exercise modality (high-intensity, multi-component, and power using elastic bands) on oxidative stress parameters, bone health, body composition, neuromuscular

strength, and physical function in older women. The study seeks to determine the optimal training intensity, and ascertain which type of training modality is more effective in elastic-based training interventions in older women.

This PhD dissertation consists of 13 chapters. Chapter one is the introduction. Chapter two, the literature review, is composed of nine sections that analyze the following: 1) the aging process; 2) the relationship between aging and exercise; 3) variable resistance, particularly with regard to elastic-based interventions; 4) the training intensity and its control and prescription methods; 5) the resistance exercise, multi-component, and power strength training modalities; 6) oxidative stress; 7) body composition in terms of bone, muscle, and adipose tissues; 8) neuromuscular strength; and 9) the physical functioning in older adults. In this way, first will be detailed the independent variables or those aspects inherent to the sample population and the training program (sections one to five). The second part then focuses on the dependent variables or parameters analyzed in this thesis (sections six to nine). The literature review discusses these factors in detail to arrive at a better understanding of the subject and to underpin the rest of the thesis.

In the sections referring to the parameters analyzed, the same script is followed, initially detailing the physiological characteristics, types and classification of these parameters in order to later explain the various pathological conditions, the influence of aging on these conditions, the measurement methods, and the positive effects of resistance, elastic resistance, multi-component, and power strength training. At the end of the literature review chapter, the factors that have led to the realization of this PhD dissertation are provided as a justification. Chapters three and four detail the objectives, hypotheses, and methodology relating to the two projects that constitute the thesis. The statistical analysis section is described for both studies in a single section. Chapter five presents the results and discussion, displayed together to facilitate the reading and understanding of the text. In Chapters six to

eight, the project's strengths and limitations are presented, along with the study's practical implications and the future perspectives. In Chapter nine the conclusions of the present PhD dissertation are detailed. In Chapter ten a summary of the key findings is presented. Chapter eleven is the references. Supplementary material and Appendices (Chapters twelve and thirteen) are placed at the end of the dissertation to enable readers to consult the complementarymaterial.

CHAPTER II
Literature Review

II.I. AGING

II.I.I. Conceptualization of aging

A. Aging and senescence

There are countless theories as to why and how we age, but the definition of aging remains uncertain. Scientists and philosophers throughout history have been captivated by the topic of aging, having explored it for over 5,000 years – from prehistory into the scientific era (Mulley et al., 2012).

In fact, in ancient Greece, Plato (428-347BC) argued that those who lived longer reached the deepest philosophical understanding of mortal life, which led to the desire to understand eternal ideas and truths (Baars, 2012): "for wisdom and assured true conviction, a man is fortunate if he acquires them even on the verge of old age" (Cary et al., 1852). More recently, in the throes of the industrial revolution, we find probably one of the most accurate depictions of the human perception of aging, which comes from the hand of Giacomo Leopardi (1798-1837): "Old age is the supreme evil, because it deprives us of all pleasures, leaving us only the appetite for them, and it brings with it all sufferings. Nevertheless, we fear death, and we desire old age" (Leopardi et al., 1905).

This interest in learning more about the aging process has continued from the ancient Greece to the modern day. In 1909, the medical doctor Ignatz Leo Nascher was the first to use the word "Geriatrics" to describe the medicine of old age, his term derived from "*geronte*," or the group of men over the age of 60 years who ran the legislative council (*gerousia*) in Athens (Morley et al., 2004). Years later, the study of aging *per se* (not the clinical conditions of aging, or "geriatrics") would be a branch of science called "gerontology" (i.e., the study of the biological, behavioral, and social sciences of old age; Mulley et al., 2012).

However, despite the efforts of the research community during the last century to define the concept of aging, the term has multiple interpretations and remains a hotly contested matter. According to Kirkwood (2005) and Spirduso (2005), in its broadest sense, "aging" refers to the changes that occur during an organism's lifespan, although the rate at which these changes take place varies widely between individuals. Consequently, at the base of this definition there are innocuous changes, such as graying hair, which are not necessarily deleterious, alongside changes that lead to an increased risk of disability, disease, or death. To differentiate between these change processes, gerontologists tend to use a term more precise than "aging" to refer to the progressive deterioration of bodily functions over time: "senescence" (Dollemore, 2002). In this dissertation, however, we will use the more inclusive term "aging," due to its extensive use in the literature.

During recent decades, four postulates have characterized the aging process, and these were established in 1985 by the American gerontologist Bernard L. Strehler (1985):

- Universal: each phenomenon associated with aging must occur to a lesser or greater extent in all individuals of the same species.
- Intrinsic: the causes that lead to aging must be of endogenous origin, not depending on external factors or environmental origin.
- Progressive: the changes that lead to aging occur gradually throughout life.
- Deleterious: the events related to the aging process are harmful.

Although the process of aging is intrinsic, as Anton and colleagues note (Anton et al., 2005), the phenotype is the end result of the interaction between the genotype and the external factors (Figure 1). It is this phenomenon that will allow us to modify the aging processes – for example, through physical exercise, as in the case presented in this dissertation.

Figure 1. *Phenotype equation.*

[Phenotype]=[genotype]+[(diet, lifestyle **(physical activity, exercise)** and environment)]

Note. Extracted and adapted from "Can we delay aging? The biology and science of aging" (p. 527), by Anton et al., 2005, *Annals of the New York Academy of Sciences, 1057*(1).

B. "Older adults" and "elderly"

Terms such as "older people," "elders," and "the elderly" are commonly used among the general population, with the latter term usually reserved for those aged 65 years or older, while "elders" and "older people" often include people in their 50s and older. However, the definitions of "aging," "old age," and "older adult" differ between countries and socioeconomic classes (Spirduso et al., 2005). In most countries, demographers, insurance companies, and employers set an age of 65 years, while in others the limit is 55 years. In contrast, gerontologists have established 75 years as "old age" (Gill, 2002).

A simple way of describing older adults involves the use of the chronological age threshold to demarcate old age in relation to decades of life: sexagenarians (60-69), septuagenarians (70-79), octogenarians (80-89), nonagenarians (90-99), and so on (Skelton & Dinan-Young, 2008), or subclassification as "young-old" (e.g. 60-73 years [Toraman, 2005], 56-65 years [Sculthorpe et al., 2017], 60-69 years [Verrusio et al., 2016], or >70 years [(Toraman, 2005)]).

However, despite the use of these sub-divisions, the heterogeneity between the health statuses of older people remains considerable (Lowsky et al., 2013). Moreover, the use of any chronological age threshold is limited by the assumption that biological and chronological ages are synonymous. Accordingly, any definition of an older adult is likely to be imperfect. The same arises with the term "elderly," because this implies a uniformity that may hide the considerable differences between the wide range of ages, inter-individual differences in the rate of aging, and the prevalence of chronic diseases.

As we can see, these terms have typically been defined on the basis of chronological age alone. For example, the World Health Organization (WHO) has accepted an age of 65 years as its definition of an older adult in a developed country, while in developing regions (e.g., Africa), the same organization defines old age as 50 years and above (Kowal & Dowd, 2002). The United Nations (UN; 2012), in contrast, categorizes older adults as all those aged 60 and above, not distinguishing between regions.

However, although biological and physical changes appear to be an unavoidable consequence of aging and, of course, of age, these changes do not occur in a linear progression and are only loosely correlated with chronological age (Steves et al., 2012). The roles assigned to older people and the loss of such roles – as well as the socially constructed meanings of age – may contribute to the definition of old age (Kowal & Dowd, 2002). For example, in most developed countries, the age of retirement – which is usually around 60 or 65 years – is often said to be the beginning of old age (WHO, 2015). It should be noted, however, that aging represents a complex interplay between biological and social factors, which are inextricably linked (Anton et al., 2015). It could be the case that people with functional impairments tend to reduce their levels of participation in social and leisure activities. Therefore, the definition of an "older adult" requires consideration of more than chronological age alone.

Taking into account data from the National Health Interview Survey that show a significant decline among adults aged 50-64 years in mobility-related physical functions (Martin et al., 2010), along with the collected theoretical framework, this dissertation considers "older adults" to be those aged 60 years and above.

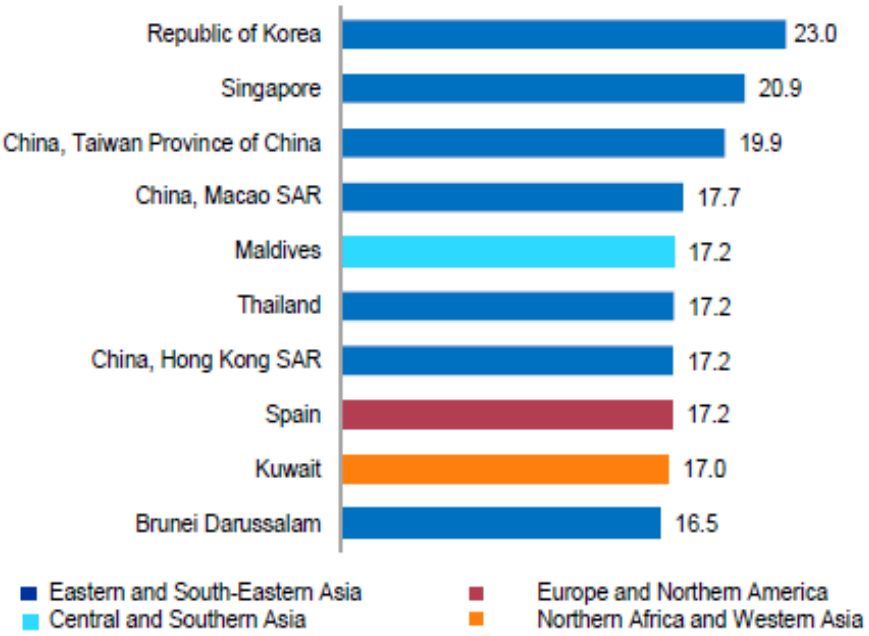
II.I.II. Aging population

A. Aging demography

According to World Population Prospects 2019 (UN, 2019), by 2050, 1 in 6 people in the world will be above the age of 65 years – up from 1 in 11 in 2019. In percentages, the proportion of individuals around the world aged ≥ 60 years will increase from 10% in 2000 to 21.8% in 2050 and 31.2% in 2100 (Lutz et al., 2008), with the highest increments in developing regions, such as Western Asia (+226%) and Saharan Africa (+218%); while, in developed areas such as Europe, the projected increase is relatively small (+48%) due to the population already being significantly older. Spain will be the only country in Europe among the 10 countries with the largest increase in its share of older people by 2050 (UN, 2019; Figure 2).

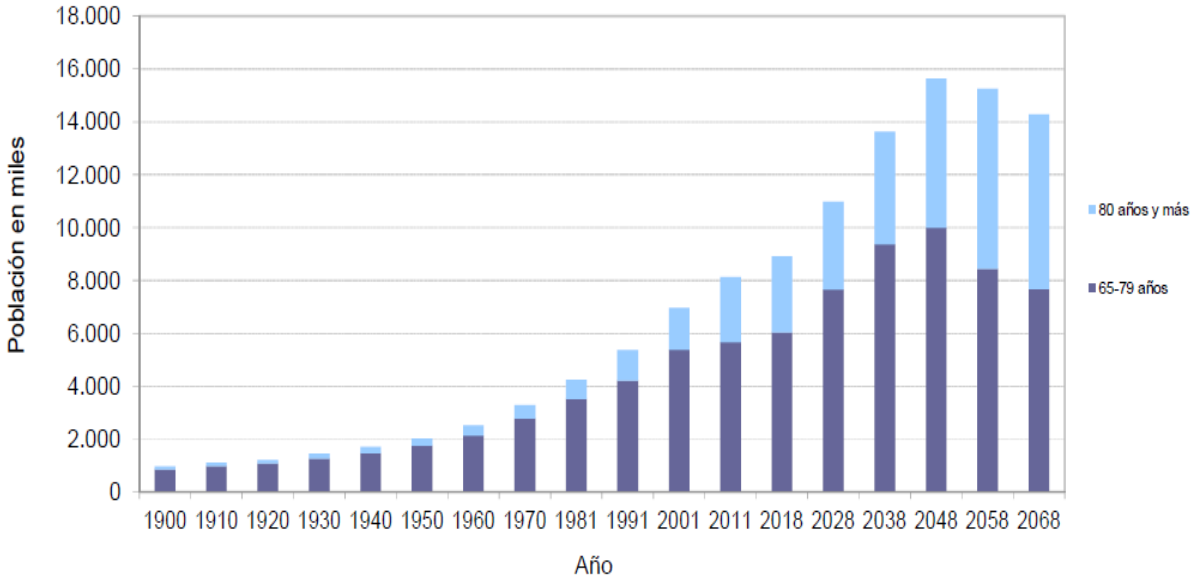
Although the overall global population is aging, the process is regionally heterogeneous. In Spain, in 2001, older adults (those aged 65 years and older) outnumbered children aged 0 to 14 years. In 2019, one in five Spanish people (19.4%) were over the age of 65 years (Instituto Nacional de Estadística, [INE], 2019), amounting to almost 9 million of the total Spanish population (46 million), with more than 6% aged over 80 years. According to the INE projection (2018-2018; INE, 2018), in 2068, there could be more than 14 million older people, comprising 29.4% of the total population (Figure 3).

Figure 2. *Countries or areas with the largest percentage point increase in the share of older persons aged 65 years or over between 2019 and 2050.*



Note. Extracted from "World Population Prospects 2019: highlights", by UN, 2019, *Department of Economic and Social Affairs, Population Division*

Figure 3. *Evolution of the Spanish population of 65 years and over.*



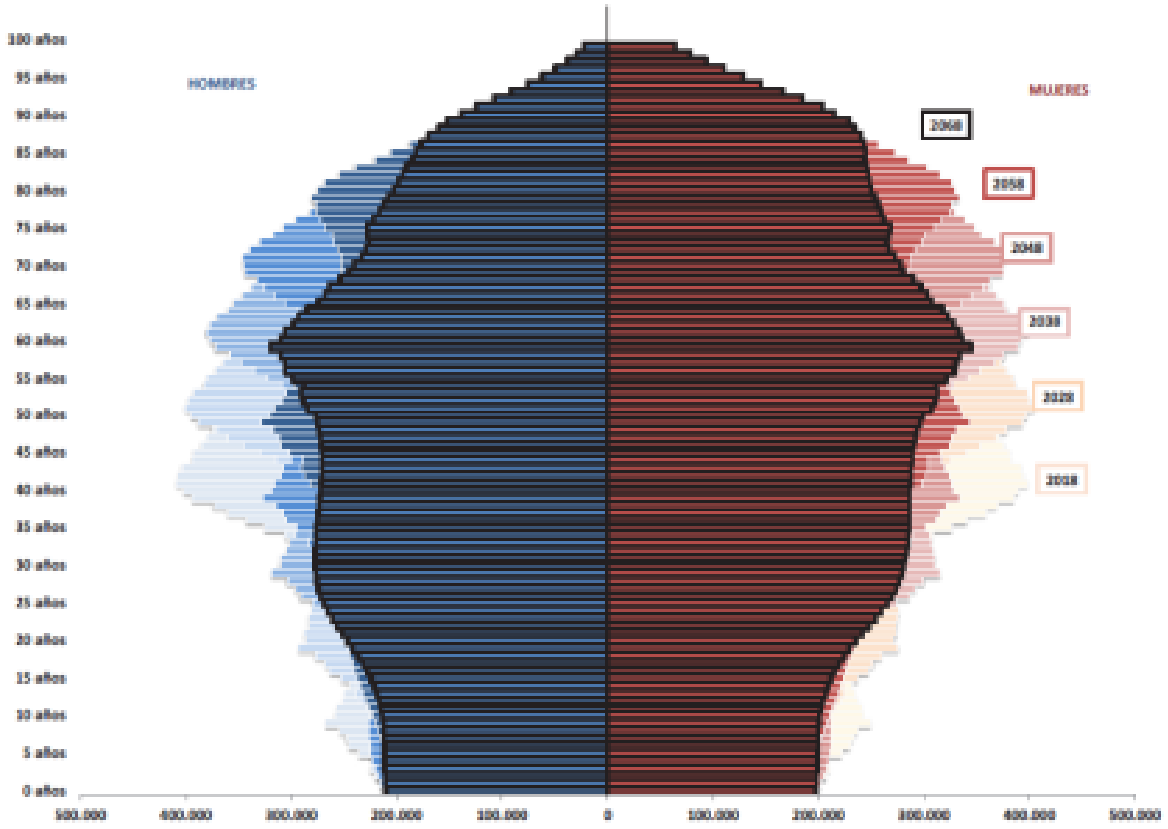
Note. Extracted from "Un perfil de las personas mayores en España, 2019. Indicadores estadísticos básicos", by Abellán et al., 2019, *Informes Envejecimiento en red*, (22).

The reasons for this increase in longevity are manifold, but they include public-health interventions, improvements in health care, education, significant fertility decline, and the arrival of the "baby boomer" generation in their old age (Lee & Zhou, 2017; Murphy, 2017; Preston & Stokes, 2012; Salomon et al., 2012).

In terms of gender, projections indicate that, in 2050, women will comprise 54% of the global population aged 65 and over, while the female proportion of the total population aged 80 years or over is projected to decline slightly to 59% from 61% in 2019 (UN, 2019). In Spain, an analysis of the pyramid population structure by gender reveals that the aging demographic includes more females than males, and this heterogeneity becomes greater with increasing age (Figure 4; Abellán et al., 2019). This phenomenon is called the "feminization of old age" (Abellán et al., 2019). Here, "feminization" describes not only the disproportionate number of older women in the population, but also the tendency to assign to women the responsibility for the care of the elderly within the family.

Finally, it is necessary to highlight that, in 2018, the older population (>65 years) of Comunitat Valenciana, where the research presented in this thesis was carried out, was 19.1% of the total, the same value as the nationwide average for that year (Abellán et al., 2019), with more older women than men (20.9% vs 16.6%).

Figure 4. *Population projections by sex and age.*



Note. Extracted from "Un perfil de las personas mayores en España, 2019. Indicadores estadísticos básicos", by Abellán et al., 2019, *Informes Envejecimiento en red*, (22).

B. Lifespan and healthspan

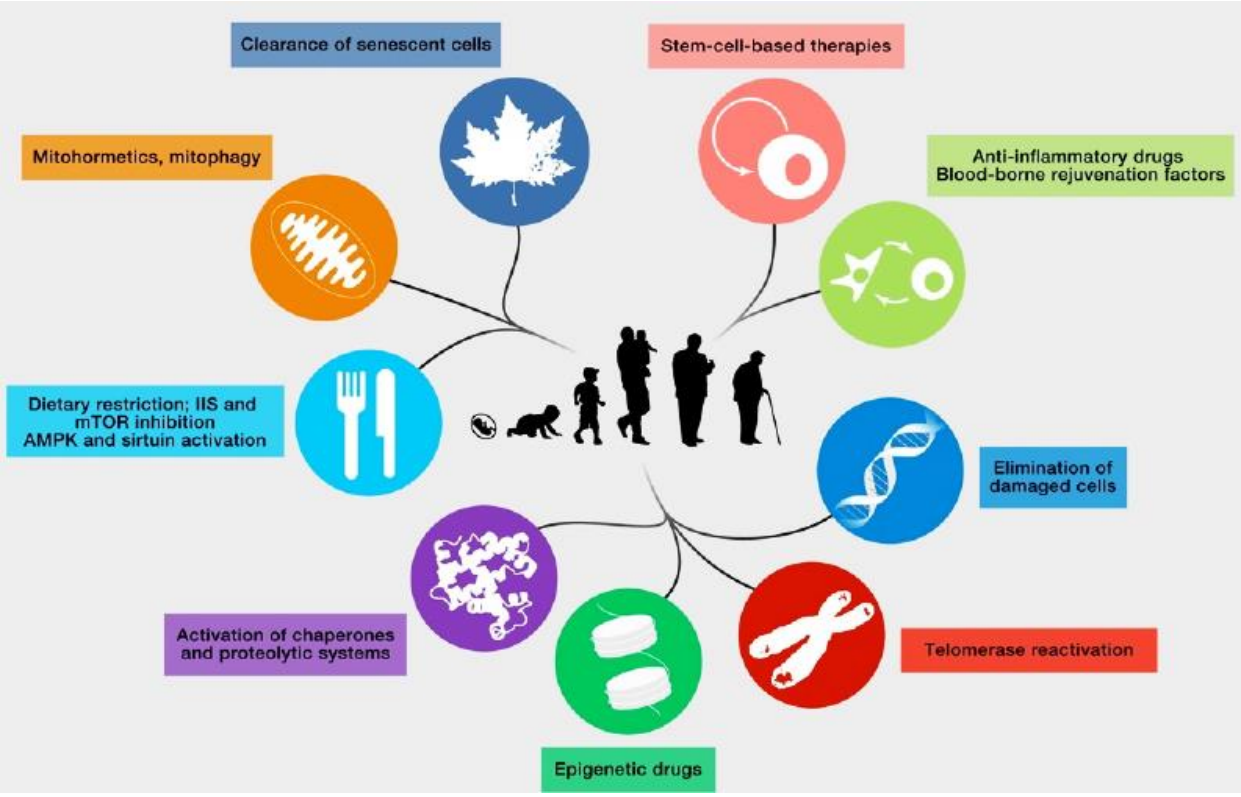
Throughout most of the world, life expectancy at birth improved incredibly during the last century, markedly so in developed regions. In 1990-1995 and 2015-2020, the global average life expectancy at birth increased by 7.7 years (12%), and it is projected to increase by an additional 4.5 years (6%) in 2015-2020 and 2045-2050 (UN, 2019). At the global level, women tend to live longer than men by an average of 4.8 years (6.1 years in Europe and North America). In Spain, the average lifespan in 1900 was around 30-35 years; and, in 2017, it was about 85.7 years for women and 80.4 years for men (Abellán et al., 2019; García-Valles et al., 2013).

An even more important indicator than life expectancy at birth is life expectancy at age 65, which reflects the average number of additional years a 65-year-old person would live if subjected to the age-specific mortality risks of a given period throughout the remainder of his or her life. Globally, a person aged 65 could expect to live an additional 17 years in 2015-2020 and an additional 19 years by 2045-2050 (UN, 2019). In Spain, this indicator also increased in 2017, giving one of the highest lifespans at 65 in the world, with an additional 19.1 years for men and 23.0 for women (Abellán et al., 2019). These increments in longevity have occurred for multiple reasons, the most relevant being the improvements in public health care systems (prevention of disease), public health interventions, education, and nutrition (Lee & Zhou, 2017; Murphy, 2017; Preston & Stokes, 2012).

During the 20th century, one of the main objectives of the scientific community was to discover and modify the processes that increase life expectancy (Borrás et al., 2011; Matheu et al., 2007); but in the last two decades, the focus has changed. Today, both quantity and quality are considered important (Hansen & Kennedy, 2016). Extending the lifespan without taking care to also improve the healthspan can have negative consequences, resulting in a long period (years) living with disabilities and comorbidities that put the older population at a higher risk of suffering aging-related diseases (Olshansky, 2018). Figure 5 illustrates several therapeutic strategies that might prolong human healthspan (López-Otín et al., 2013).

Accordingly, the heathy life expectancy indicator adds a new dimension to the measure of life by also including quality. The measure is usually taken from general data on chronic morbidity and self-perceived health. In this case, one finds that in Spain, after the age of 65 years, 53.7% of men will live with good health, in contrast to just 44% of women (Abellán et al., 2019). As we can see, although female life expectancy is, on average, four to six years longer than that of males, longevity does not necessarily equate to better quality of life.

Figure 5. *Therapeutic strategies that might prolong human healthspan.*



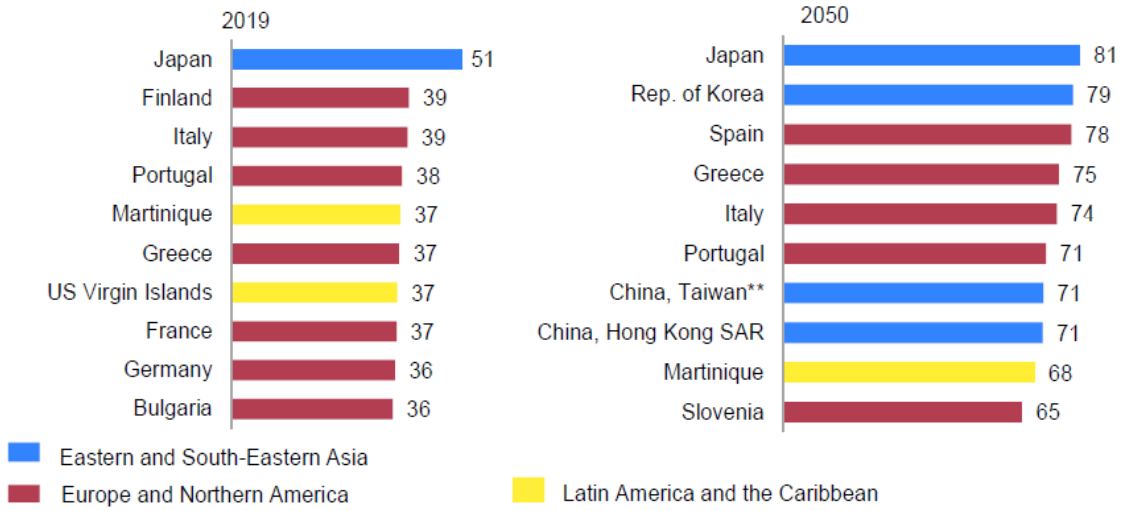
Note. The nine hallmarks of aging are shown together with those interventions that account with a proof of principle in mice. Reproduced from "The hallmarks of aging" (p.1195), by López-Otín et al., 2013, *Cell*, *153*(6).

C. Cost of population aging

Population aging is recognized as a global phenomenon (Cesari et al., 2015; Lloyd-Sherlock, 2000; Shrestha, 2000), being one of the four global demographic "megatrends" (along with population growth, international migration, and urbanization) seen to have lasting impacts on sustainable development (UN, 2019). While earlier concepts have focused on demographic data and different life expectancies, it is necessary to show the impact of aging structure and the aging process on the economy, as these would be among the main reasons for prevention programs such as physical training activities to improve health in this population and decrease the economic impact on the health and public pension systems.

There are different measures with which to examine the relationship between population age structures and economic systems. The old-age dependency ratio (OADR) is the most common, and this is defined as the number of old-age dependents (people aged 65 years or over) per 100 people of working age (aged 20 to 64 years). This metric is often used as a proxy for the economic dependency of the older population (UN, 2019). Since the 1990s, the OADR has continuously increased across all regions, due to decline in fertility and increase in longevity, but the speed of this increment varies between countries. According to the projections of the UN (2019), Spain will have the third highest OADR of any country in the world by 2050, with 79, while the European OADR will have reached 49 (Figure 6).

Figure 6. *Countries or areas with the highest old-age dependency ratio (65+ / 20-64), 2019 and 2050.*



Note. Extracted from "World Population Prospects 2019: highlights", by UN, 2019, *Department of Economic and Social Affairs, Population Division.*

As we can see, population aging will put increased financial pressure on old-age support systems, especially in Spain, where public transfer represents the primary method of financing the retirement of older people. Currently, more than 60% of the total income of the older person comes from public transfer, which is one of the highest rates in the world (UN, 2019). Indeed, the economic cost of the pension system in Spain currently represents 10% of the gross domestic product (GDP), and it is expected to have doubled by 2050 (INE, 2019).

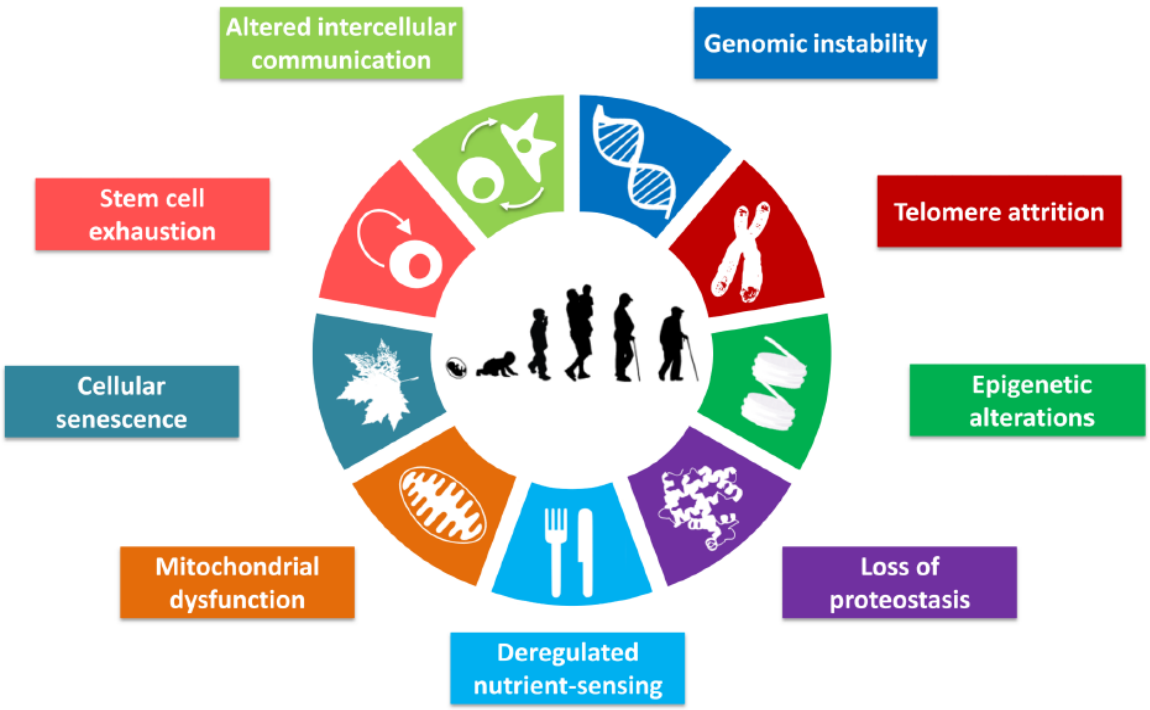
This phenomenon is a major challenge for public health-care sectors in relation to the sustainability of their welfare states, particularly in the European Union, and more specifically, in Spain (Ahn et al., 2005; Blanco Moreno, 2013). Although the statistics indicate that modern medicine has successfully attenuated mortality, this has not been accompanied by a parallel reduction in morbidity, with a consequent increase in public health expenditure (Breyer et al., 2010). Such costs are not limited to those associated with medication and treatment, but also include disability support and care home accommodation (Breyer et al., 2010; Jacobzone, 2000).

Spain currently spends 6% of its GDP on public healthcare annually, and its health expenditure is expected to grow to between 6.4% and 8.8% of its GDP by 2060, growth of more than 2% in 35 years, with the effect of its aging demographic and – to use the terms of economists – the associated "cost of death" and "end-of-life-costs" – responsible for 25% of this increase (Blanco-Moreno, 2013). Ideally, the best outcome for population aging is morbidity compression (i.e., gains in life expectancy and good health, or living in good health for more years than are gained in life expectancy), with the rise in life expectancy being maintained and accompanied by decreased morbidity. This would relieve the financial stress on the government and enhance quality of life. One potential strategy to facilitate morbidity compression is to increase and promote physical activity programs for older people

II.I.III. Biological aging process

In recent decades, the field of aging research has undergone a significant advancement, gaining crucial insights into the processes and underlying molecular mechanisms of aging. However, the mechanisms responsible for the aging process are difficult to define and harder to prove (Dodig, 2019). Scientists, through technological progress, have focused on the detection of the molecular and biological mechanisms associated with aging. In 2013, López-Otín and colleagues proposed nine "Hallmarks of Aging" (Figure 7) in an attempt to identify and classify the cellular and molecular characteristics of aging in mammals (Lopez-Otín et al., 2013).

Figure 7. *The Hallmarks of Aging.*

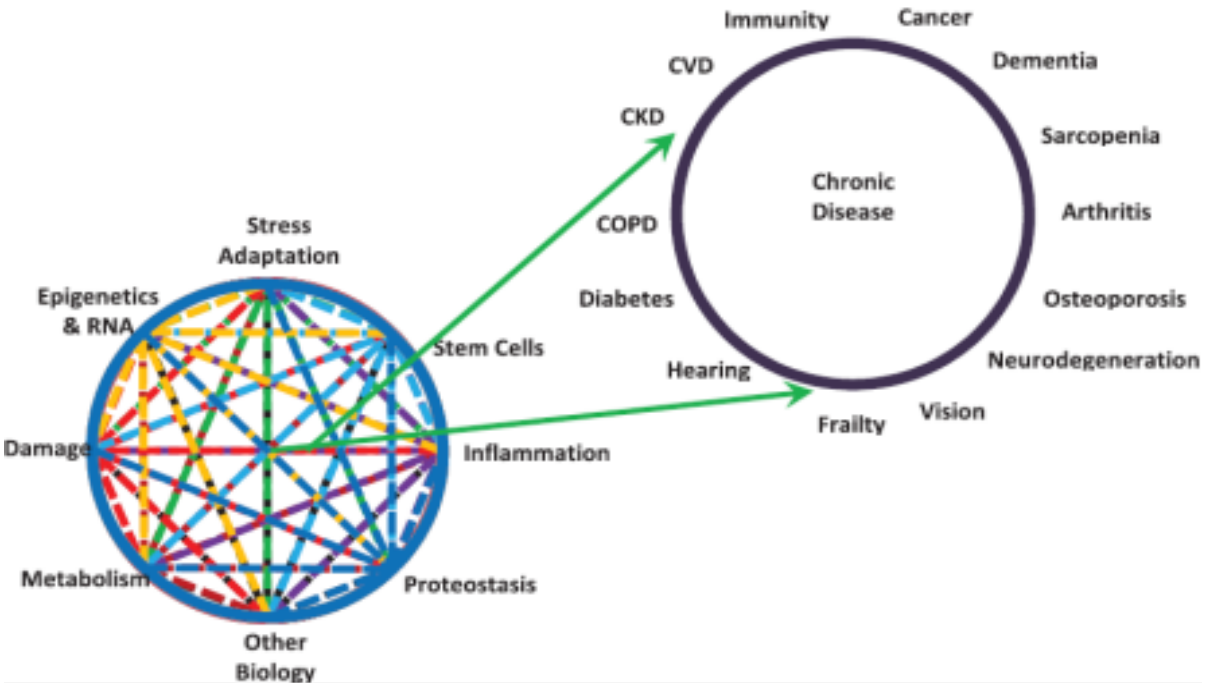


Note. The scheme enumerates the nine hallmarks of aging. Reproduced from "The hallmarks of aging", (p.1208), by López-Otín et al., 2013, *Cell, 153*(6).

These nine hallmarks can be grouped into three categories (Lopez-Otín et al., 2013). Primary hallmarks (genomic instability, telomere attrition, epigenetic alterations, and loss of proteostasis) all cause damage to cellular functions and progressively hasten aging. Antagonistic hallmarks (deregulated nutrient sensing, mitochondrial dysfunction, and cellular senescence) respond to such damage, but their effects depend on their intensity. For example, the senescence process (i.e., cell degeneration and death) protects the organism at low levels, but in excess can promote aging. Finally, integrative hallmarks (stem cell exhaustion and altered intercellular communication) are the result of a clinical phenotype that ultimately contributes to the clinical effects of aging as seen in organ decline and reduced function. Notably, several of the proposed hallmarks are typical of other related disease processes (Aunan, 2016). Very recently, Lopez-Otín and Kroemer have also published the "Hallmarks of Health" (López-Otín & Kroemer, 2020).

New understanding of the mechanisms of the aging process launched the era of geroscience, which strives to uncover how the molecular, cellular, and systemic degenerative processes of aging affect the etiologies of chronic disease, with the objective of finding and developing novel multi-disease preventative and therapeutic approaches (Buch et al., 2014; Kennedy et al., 2014). In this context, the trans National Institute of Health (NIH) Geroscience Interest Group propose "the seven pillars of aging," or the mechanisms that intersect aging and chronic disease pathways: inflammation, adaptation to stress, epigenetics, metabolism, macromolecular damage, proteostasis, and stem cells and regeneration (Figure 8; Buch et al., 2014). However, our current understanding of the hallmarks of the aging process is likely to change in the future, with advances in our knowledge and the appearance of new technologies (Fulop et al., 2018).

Figure 8. *The Seven Pillars of Geroscence and health progress*.



Note. Reproduced from "Advances in Geroscience: Impact on Healthspan and Chronic Disease", (p. S2), by Burch et al., 2014, *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 69*(Suppl_1).

These available data suggest that single target interventions may not be fully effective unless they interface across other interconnected pathways. In older adults, multiple chronic diseases such as sarcopenia, dynapenia, osteoporosis, and obesity share common risk factors of little physical activity, loss of muscle mass, and insufficient protein nutrition, suggesting crosstalk between frailty, disability, and diverse disease pathways (Buch et al., 2014).

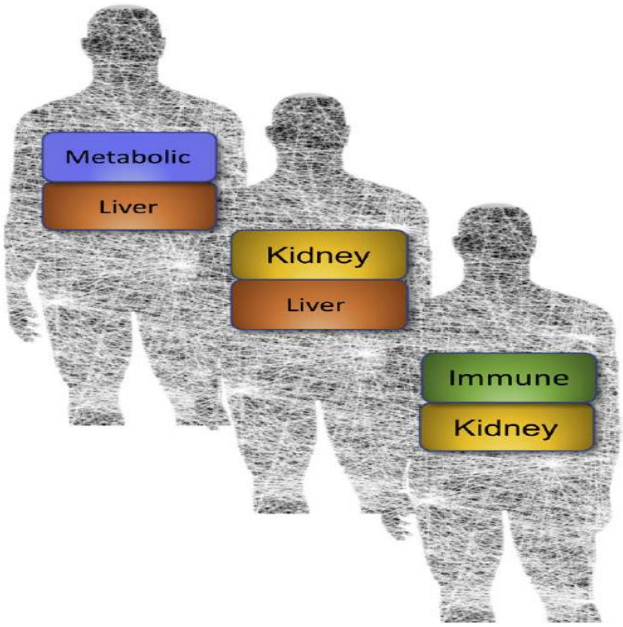
Given the undesirable physical consequences of aging, strategies for both prevention and treatment are necessary for the health and well-being of older adults. In addition, it is noted that some contributors to the aging process, such as muscle disuse, are preventable and reversible, and their improvement will improve other risk factors by the mechanism of the previously mentioned interconnected pathways.

II.I.IV. Types of aging

Although scientists identify associations between chronological and biological age, many studies have demonstrated that tissues, cells, and organisms with identical chronological age can exhibit significant differences in rate of biological decline. There are various possible reasons for this, such as the "epigenetic clock" (Horvath, 2013) and the existence of different types of molecular phenotypes (Earls et al., 2019; Tasaki et al., 2018; Zierer et al., 2016), which Ahadi et al. (2020) describe as "ageotypes."

According to Ahadi et al (2020), there are key molecules and microbes that vary dramatically between individuals in an age-dependent manner, showing different aging trajectories. They define the four "ageotypes" as liver, kidney, immune, and metabolic. The same individual might even show different aging trajectories if one phenotype – or "ageotype" – exhibits signs of accelerated aging, while another shows a minimal rate. However, the ageotypes are not mutually exclusive and, for example, a metabolic ager could also be a liver ager (Figure 9).

Figure 9. *Example of Ageotypes*.



Note. Reproduced from "Ageotypes: Distinct Biomolecular Trajectories in Human Aging", (p. 2), by Piening et al., 2020, *Trends in Pharmacological Sciences, 41*(5).

Other authors have also sought to classify aging. One of the most interesting classifications comes from Holloszy (2000), who describes two types of aging: primary and secondary. Primary aging involves "an inevitable deterioration of cellular structure and function independent of disease and environment" (Holloszy, 2000) and depends essentially on oxidative stress and the metabolic rate (Broskey et al., 2019). Secondary aging is "caused by diseases and environmental factors such as smoking and exposure to ultraviolet radiation" (Holloszy, 2000).

While a reduction in primary aging is reflected in an increase in maximal lifespan, the reduction of secondary aging modifies life expectancy but not maximum lifespan. There is no effective treatment to reverse primary aging in humans (Booth et al., 2011) because it is attributed to genetic factors. However, physical exercise and caloric restriction are strategies that attenuate secondary aging, as low physical activity and overeating are social behaviors that produce substantial dysfunction in all the systems, especially in the metabolic pathway (Broskey et al., 2019). In a recent review, Broskey and colleagues (2019) suggest that caloric restriction has a significant impact on even primary aging by improving mitochondrial function and reducing oxidative stress, while more research on the impact of physical exercise is necessary, as no consistent data were found.

This particular research gap is one of the justifications for the projects presented in this dissertation, as a key aim is to show the effects of physical exercise on oxidative stress in older women, as this is a major factor in primary aging.

II.I.V. Aging theories

While many theories have been proposed to explain the phenomenon of aging (specifically, why and how we age), none has yet been able to fully explain the mechanisms that drive the fundamental process(es) of aging (Slijepcevic, 2008). In 1990, Medvedev (1990) published a key review that attempted to rationally classify the numerous theories of aging, and this highlighted more than 300 different theories.

The vast amount of research conducted in relation to aging and aging-related processes makes it almost impossible to give a complete overview of the theories that have been put forth. However, most can be classified into three categories: programmed, error/damage, and combined (Costa et al., 2016; Semsei, 2000).

Programmed theories, also referred to as "active" or "adaptive" aging theories, are based on the idea of biological clocks or "aging clocks" that govern the schedule of the lifespan, as a limited lifespan results in evolutionary benefits (Goldsmith, 2012; Jin, 2010; Weinert & Timiras, 2003).

The "error" or "damage" theories are based on the idea of accumulation damage as a spontaneous, entropy-driven process; hence, aging cannot be programmed. As such, the kinetics of this biological damage can be genetically and environmentally modulated, as we observe in the wide range of lifespans currently seen between individuals and regions (Aledo & Blanco, 2015; da Costa et al., 2016; Weinert & Timiras, 2003). One of the most prevalent and important theories in this "damage" group is the free radical theory hypothesized by Harman (1981), which suggests that oxidative damage signaled by reactive oxygen species (ROS) during oxygen pathway metabolism leads to the cumulative deoxyribonucleic acid (DNA), lipid, and protein damage that is observed over a lifetime and more accentuated in old age (Freitas et al., 2013; Piedrafita et al., 2015; Thanan et al., 2014).

Finally, combined theories contain elements from both of the previous groups. Current knowledge provides support for this group, also called "network or integrative theories," because aging is best described as a multi-factorial process involving complex interactions between biological, molecular, and environment mechanisms (Weinert & Timiras, 2003, Kirkwood & Kowald, 1997). However, there are still some theories, such as evolutionary theories, that do not accept the evolution of phenotypic plasticity, or the ability of a single genotype to produce different phenotypes in response to changes in the environment – such as nutrition, infection, predation, and physical stresses (Flatt et al., 2013).

Such classifications are subjective, taken from the researchers' points of view, and others theory categorizations have been suggested; for example, Baltes et al. (2012) propose psychology, biology, and sociology theories; de Magalhães (2005) mechanistic theories; Viña et al. (2007) genetic mutation, cellular waste accumulation, and wear and tear theories; and Weinert and Timiras (2003) evolutionary, molecular, cellular and system theories.

However, many of these theories agree that the underlying cause of aging is the accumulation of molecular damage in the DNA, lipid, and protein molecules, originated principally by ROS (Sergiev et al., 2015). This PhD dissertation partially focuses on the free radical theory of aging and the effect of exercise training on oxidative stress damage in some biomarkers of DNA, lipid, and protein ROS.

A. The free radical theory of aging

As shown in the previous section, many theories seek to explain the phenomenon of aging, but one of the most prominent of these is the free radical theory proposed by Denham Harman (1956), though the idea of free radicals as toxic agents was first suggested by Gerschman et al. (1954). Harman (1956) states that, "aging and the degenerative diseases

associated with it are attributed basically to the deleterious side attacks of free radicals on cell constituents and on the connected tissues."

The free radical theory of aging has been adjusted many times since Harman first proposed it; and it was later shown that the accumulation of oxidative damage is dependent on more than free radicals alone, and all oxidizing agents or oxidants – such as hydrogen peroxide and hypochlorous acid – react with biomolecules in the same way. These are, together with oxygen radicals, known as ROS. In light of this, some authors have renamed the theory, from "the free radical theory" to "the oxidative stress theory of aging" (Hagen, 2003; Harman, 1972; Stadtman, 2004). This theory was later expanded by Miquel and colleagues (1980) to become the "mitochondrial free radical theory of aging," highlighting that the mitochondria are the main source of the ROS production that causes age-related damage and organ dysfunction (Harman, 1972).

In its strictest sense, in the free radical theory of aging and its later modifications, lifespan is primarily dependent on the reduction of oxidative stress, by the reduction of ROS, the increase of antioxidant defenses, or a combination of both (Beckman & Ames, 1998; Salmon et al., 2010).

However, although the free radical theory of aging appeared to have been established, recent evidence has provoked a reevaluation of the theory. One of the main reasons for this has been the new findings about ROS. Although ROS are usually considered to be damaging compounds, and there is evidence to support the role of ROS in aging, studies have confirmed that these play an important role in multiple cellular functions (Ray et al., 2012; Sena & Chandel, 2012).

ROS, including in mitochondria, are not necessarily detrimental. In fact, it is generally accepted that a gradual increase in cellular levels of ROS is, under normal conditions, well-

handled by several antioxidant systems, which are beneficial for responding to various physiological signals (Hekimi et al., 2011). For instance, ROS can play a positive role in extending lifespan under stress conditions (Lee et al., 2007) and "healthy" levels of accumulation of ROS promote the formation and activation of the osteoclasts needed to remodel the skeleton (Garret et al., 1990). In fact, ROS stimulate physiological adaptations to physical exercise (Viña et al., 2013). Hence, current evidence focuses more on the intensity of the ROS response, not on the ROS *per se*, as low levels of these may induce an adaptive response that ultimately leads to the general improvement of systemic defense mechanisms, a concept termed "mitochondrial hormesis" or "mitohormesis" (Kawagishi & Finkel, 2014; Ristow, 2014). In this sense, aging may be the result of a deregulation of the ROS signaling pathways and not of the reactive species themselves (Sethe & de Magalhães, 2014).

Another "update" to the original free radical theory in recent years has been in relation to the other part of the theory: the antioxidant system. One major experimental deduction from this theory is that antioxidants should curtail the effect of ROS in aging and general health. However, multiple studies have demonstrated that this conclusion is not always right (Fortmann et al., 2013; Grodstein et al., 2013; Higashida et al., 2011), at least in terms of exogenous antioxidants. Some meta-analyses have demonstrated that people who take antioxidant supplementation do not have any extra protection against age-associated diseases or greater life expectancy, when compared with placebo groups (Bjelakovic et al., 2004, 2007; Fortmann et al., 2013; Grodstein et al., 2013; Lin et al., 2013).

In an attempt to unify the evidence in favor of and against the free radical theory of aging, Viña and colleagues propose a modified version: "the cell signaling disruption theory of aging" (Viña et al., 2013). This theory postulates that free radicals fail to act as useful signals for the regulation of cell metabolism, altering homoeostatic capacity and decreasing the "resilience" of the cells and their ability to tolerate stresses (Viña et al., 2013).

Furthermore, the same authors suggest that oxidative stress could be more involved in the development of age-associated frailty than in aging itself (Viña, 2019), postulating a new adaptation of the free radical theory of aging known as "the free radical theory of frailty" (Viña et al., 2018).

The specific concepts and terms related to the free radical theory of aging are explained in more detail in Section II.VI.

II.II. AGING AND EXERCISE

II.II.I. Exercise terminology clarification

Terms such as "physical activity," "exercise," "fitness training," "training," and "physical fitness" are often confused with one another and sometimes wrongly used interchangeably (Caspersen et al., 1985; Paoli & Bianco, 2012). So that readers can easily understand these terms as they appear in this document, the basic concepts of physical activity, exercise, and fitness training will be defined in the following paragraphs.

According to Caspersen et al. (1985), the U.S. Centers for Disease Control and Prevention (CDC; 2011), and the ACSM (Whaley et al., 2006), physical activity can be defined as any bodily movement produced by skeletal muscle contraction that results in energy expenditure above an individual's resting level. Physical activity is considered to encompass both activities of daily living (ADLs), such as transportation and household tasks, and leisure-time activities such as exercise and sports (Ashe et al., 2007). "Exercise" is a similar but more restrictive concept, defined as planned, structured, organized, or repetitive physical activity intended to maintain or enhance one or more components of physical fitness or a specific health outcome (Caspersen et al., 1985; CDC, 2011; Horlick et al., 2004). In contrast, exercise training or fitness training is defined as a psycho-pedagogical process that seeks to improve performance in terms of physical (endurance, strength, balance, flexibility, coordination), psychological (cognitive function), and biological (metabolic, cardiovascular, neurological, neuromusculoskeletal) components through the development of conditional, motor, and informational factors in accordance with scientific and empirical knowledge (Legaz-Arrese, 2013).

These definitions are of great importance, as the projects comprising the present PhD dissertation concern the effects of different training modalities and exercise interventions on several health-related parameters among older women.

II.II.II. Benefits of physical activity and resistance training in elderly population

A. Benefits of physical activity and general exercise for older adults

Physical exercise activities are considered to be among the most beneficial lifestyle characteristics, recognized today as indispensable for good health (Simioni et al., 2018). Although this recognition of the strong and positive association between exercise and health seems relatively recent, the earliest records of the promotion of exercise for health come from ancient China in 2,500 BC (Hardman & Stensel, 2003).

The current messages about the benefits of being active began to spread at the end of the 20th century, when WHO (1996) published a paper on the physiological, psychological, and social benefits of practicing regular physical activity. Three decades later, the accumulated evidence supports the role of physical activity and exercise in ameliorating age-related health declines. Physical activity and exercise in later life has several proven benefits for health, including improvements in or at least maintenance of cardiovascular function, muscle strength, muscle power, muscle mass, physical function, balance, postural, stability, body composition, and flexibility, among other functions (Canadian Society for Exercise Physiology, 2011; Sun, Norman & White, 2013).

In addition, physical activity and exercise has been demonstrated to have mental and psychosocial benefits for cognitive function, sense of general well-being, anxiety, depression and stress symptoms, self-esteem, self-efficacy, intergenerational relationships, and social integration, and more (WHO, 1996; Hurley et al., 2003; Windle et al., 2010; Blake et al., 2009; Herring, et al., Dishman, 2010). In fact, a strong dose-response relationship has been established, with higher levels of physical activity associated with greater health benefits and symptom relief (Jebb & Moore, 1999).

Both programmed and (to a lesser degree) non-programmed physical exercises have been reported to be therapeutic, both during adulthood and among aging populations, as they can reduce the risk of numerous non-communicable chronic diseases and they have a medicinal role in relation to multiple conditions, including cardiovascular diseases (hypertension, coronary heart disease, heart failure, cerebral apoplexy, and claudication intermittent); metabolic diseases (obesity, hyperlipidemia, metabolic syndrome, polycystic ovarian syndrome, type 2 diabetes, and type 1 diabetes); musculoskeletal disorders (osteoarthritis, osteoporosis, back pain, and rheumatoid arthritis); neurological diseases (dementia, Parkinson's disease, and multiple sclerosis); pulmonary diseases (chronic obstructive pulmonary disease, asthma, and cystic fibrosis); psychiatric diseases (depression, anxiety, stress, and schizophrenia); and cancer (Petersen & Saltin, 2015). In addition, physical activity represents a cornerstone in the primary prevention of at least 35 chronic conditions (Booth et al., 2011). Regular exercise alleviates the negative effects of free radicals and reduces the risk of all-cause mortality (Hupin et al., 2015; Simioni et al., 2018; Warburton et al., 2006, Wen et al., 2011).

B. Benefits of resistance training for older adults

There is strong evidence that resistance exercise training has multiple unique benefits for older adults' health, regardless of age (Fragala et al., 2019; Romo-Pérez et al., 2011), reducing the incidence of the age-related conditions that deteriorate quality of life in this population (Lavin et al. 2019). It is well documented that resistance training, in its different forms, can partially reverse losses in muscle strength, mass, and power by maintaining or increasing muscle (Fragala et al., 2019; Hunter et al., 2004; Lavin et al., 2019; Liu & Latham, 2009). In fact, resistance training is the most widely recognized strategy for combatting age-related muscle atrophy, or sarcopenia, and neuromuscular impairments associated with physical function, or dynapenia (Lavin et al. 2019; Romo-Pérez et al., 2011).

Furthermore, resistance training is not recommended for the elderly population only for its benefits at the neuromuscular level, but also for its positive effects in reducing difficulties with performing daily tasks; maintaining functional independence; enhancing energy expenditure; and improving body composition, bone mineral density (BMD), cognitive function, self-confidence, and health-related quality of life (Bean et al., 2009; Fragala et al., 2019; Hanson et al., 2009; Hunter et al., 2004; Leite et al., 2010; Liu & Latham, 2009). Resistance training can also enhance many physical function parameters, such as aerobic capacity, balance, coordination, gait speed, and agility (Chodzko-Zajko et al., 2009). Furthermore, there is a growing body of evidence for the value of resistance training in the prevention and treatment of a number of chronic illnesses (Lange et al., 2008), reducing the risk factors for diabetes, osteoporosis, and colon cancer, among other conditions (Chodzko-Zajko et al., 2009). Moreover, resistance training can reduce the signs and symptoms of chronic illnesses such as arthritis, diabetes, and depression (Liu & Latham, 2009), as well as reducing the risk of falling among older adults (Gillespie et al., 2012; Lloyd et al., 2008, Lloyd et al., 2009).

Based on the aforementioned evidence, it is clear that a health strategy of promoting physical activity and resistance exercise among older populations is of the utmost importance for reducing the morbidity and mortality associated with insufficient physical activity in this population, which are an important public health issue (Nelson et al., 2007).

II.II.III. Current physical activity and exercise guidelines for older adults

Due to age-associated decline, it is particularly important for older people to maintain their health and well-being to facilitate continued independent living, societal participation, and quality of life, as disability and a loss of independence are not inevitable consequences of aging (Cadore et al., 2014). In addition, with life expectancy increasing and the older populations around the world growing, it is important to stay as healthy as possible for as

long as one can to avoid the need for ongoing health and care services or hospitalization. As such, physical activity guidelines around the world are designed to provide clear and evidence-based recommendations to encourage older adults to engage in physical activity to decrease rates of chronic disease and promote functional independence. In the following sections, the current international guidelines regarding physical activity and resistance training for older adults will be examined.

A. Physical activity and general exercise recommendations for older adults

Many governments around the world have produced physical activity guidelines for children, adults, and older adults. Since the first publication of the ACSM "Position Stand on Physical Activity and Exercise for Older Adults" and the U.S. government's "Physical Activity Guidelines for Americans" emphasized the need for national guidelines to promote appropriate physical activity levels (Romo-Pérez et al., 2011), several countries have developed their own recommendations, based primarily on the recommendations of the WHO (Canada [Tremblay et al., 2011a, 2011b]; the United States [Nelson et al., 2007; Haskell et al., 2007]; Australia [Hordern et al., 2012; Sims et al., 2009]; Japan [Ohta et al., 1999]; the United Kingdom (British Heart Foundation, 2008; Bull & the Expert Working, 2010]; South Africa [Department of Health South Africa, 2000]; Spain [Ministry of Health, Social Services and Equality, 2015]; Finland [Bennie et al., 2017]). Furthermore, in Europe, the European Union has strongly advised its member states to adopt a series of recommendations to promote physical activity as a major public health strategy (Romo-Pérez et al., 2011). In Spain, the national recommendations were implemented in 2015 and are based on global recommendations set by the WHO (2010a), the CDC (2015), and the ACSM (1995) in the United States.

In Spain, the national recommendations for physical activity and the reduction of sedentarism, elaborated by the Ministry of Health, Social Services, and Equality (2015), state that older adults should aim to be active daily and that, over a week, an individual should perform a minimum of 150 minutes (30 minutes, five days per week) of moderate-intensity aerobic physical activity (3-6 metabolic equivalent of tasks [METs]) or 75 minutes (25 minutes, three days per week) of vigorous-intensity activity (> 6 METs) per week (Ainsworth et al., 2000) and at least two sessions should include resistance training (8-12 repetitions for each muscle group). Flexibility and balance activities are also recommended, but an exact dosage is not specified. For additional health benefits, individuals may increase their moderate-intensity aerobic physical activity to more than 150 minutes or do more than 75 minutes of vigorous-intensity aerobic physical activity or an equivalent combination of moderate- and vigorous-intensity activity throughout the week.

These guidelines are similar to those endorsed by the ACSM (Haskell et al., 2007; Nelson et al., 2007) and the WHO (2010a), which suggest that adults aged > 65 years should aim to perform 30 minutes of physical activity in sessions of 10 minutes or more, at least five days per week, as well as three sessions of balance activities and two or more of muscle strength activities per week (WHO, 2010a). However, these recommendations may have become obsolete, as the WHO has very recently published new guidelines on physical activity and sedentary behavior (WHO, 2020). The updates to the 2010 guidelines include an increase in the amount of recommended physical activity. Currently, for older adults, the WHO recommends a minimum of 150-300 minutes of moderate-intensity aerobic physical activity per week, or at least 75-150 minutes of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity activity throughout the week. In addition, individuals should, on two or more days a week, do muscle-strengthening activities of moderate or greater intensity that involve all major muscle groups. For additional

health benefits, individuals may increase their moderate-intensity aerobic physical activity to more than 300 minutes or do more than 150 minutes of vigorous-intensity aerobic physical activity or an equivalent combination of moderate- and vigorous-intensity activity throughout the week. In addition, to help reduce the detrimental health effects of high levels of sedentary behavior, all older adults should aim to do more than the recommended levels of moderate- to vigorous-intensity physical activity. Finally, the WHO recommendations also indicate that, as part of their weekly physical activity, older adults should do varied multi-component physical activity that emphasizes functional balance and strength training at moderate or greater intensity on three or more days a week, thereby enhancing functional capacity and preventing falls. For people living with chronic conditions or disabilities (e.g., e.g., those with hypertension or type 2 diabetes and cancer survivors), the recommendations are the same.

Along with the general physical activity guidelines, specific recommendations prescribe exercise for certain pathologies, such as sarcopenia and osteoporosis (Chodzko-Zajko et al., 2009; Law et al., 2016). For instance, the WHO, the ACSM, the National Osteoporosis Foundation (NOF), and the NIH have issued exercise recommendations to promote bone health and to prevent and treat osteoporosis (Chodzko-Zajko et al., 2009; Cosman et al., 2014; Kohrt et al., 2004; NIH, 2000; WHO, 2010a). In summary, recommendations include aerobic exercise training, such as walking (low-intensity weight bearing activity); higher-intensity bone loading activities, such as walking with weighted vests, jogging, stair-climbing and -descending, and brisk walking; and high-intensity resistance exercise training, which appears to be effective in counteracting age-related declines in BMD, especially in postmenopausal women (Chodzko- Zajko et al. 2009; Nelson et al. 2007).

B. Specific resistance training recommendations for older adults

Currently, exercise recommendations for older adults consistently advocate for strength training. However, since the mid-1970s, most national public-health physical activity recommendations have primarily promoted aerobic exercise (Blair et al. 2004; Oja & Titze, 2011). Only in the last two decades have national public health agencies and departments added recommendations for muscle-strengthening activities to their physical activity recommendations (Chodzko-Zajko et al., 2009; WHO, 2010a). The WHO, the ACSM, and multiple national bodies now include resistance training in their recommended physical activity guidelines, particularly those for older people (Romo-Pérez et al., 2011). The 2020 WHO global recommendation for elderly populations suggests that muscle-strengthening activities involving major muscle groups should be done at least twice a week (WHO, 2010a). The ACSM recommends the same dose and stresses that a combination of endurance and strength-training activities is more effective than either form of training in isolation (Chodzko-Zajko et al., 2009).

The vast majority of the guidelines suggest that, among older adults, resistance training should be performed at least twice a week, on alternate days, starting with a rate of two or three days per week and including the major muscle groups (e.g., gluteus, quadriceps, hamstrings, dorsal, pectoral, biceps and triceps; Romo-Pérez et al., 2011). Nevertheless, there are some discrepancies regarding volume and intensity. Romo-Pérez et al. (2011) conducted a review of the resistance training guidelines published around the world and found evidence that the following are the most common: a) muscular strength exercises, 2-3 times per week on alternate days; b) resistance exercises focused on the main muscular groups; c) 2-3 sets of eight repetitions for each exercise; and d) an intensity of approximately 40% to begin, increasing as appropriate, with intensities of between 60% to 80% 1 repetition maximum (RM) to stimulate a greater increase in muscle strength.

It is also important to note that key training principles of overload, specificity, and progression must be followed, while the selection should predominantly include multi-joint exercises (Chodzko-Zajko et al., 2009). In addition, the delayed onset of muscle soreness should also be considered when working with older adults, as increasing aches and pains with age can be compounded by the added stress of resistance training.

II.II.IV. Sedentary lifestyles in the elderly population

A. Physical activity levels in later life

Due to the cumulative effect of various factors that arise throughout one's life – in addition to genetic and other predisposing issues – a healthy lifestyle is vital for older people to minimize their risk of premature death and maximize their chances of active, healthy, and independent aging (Burton, Farrier et al., 2017; Knoops et al., 2004). However, despite the substantial benefits of regular physical activity and exercise for older adults, physical-activity engagement tends to decline with age (Statistics Canada, 2015). As people age, there is a tendency to reduce the amount of exercise they undertake (Burton, Farrier et al., 2017). It has been recognized that older adults are usually less active than young adults (Hallal et al., 2012), while people older than 70 to 80 years are typically less active than individuals of 60 to 69 years in all domains of physical activity (Milanovic et al., 2013). Since the 1980s, research has firmly established that, as people age, their participation in physical activity and exercise decreases (Curtis et al., 2000; McPherson, 1984; McPherson & Kozlik, 1980), with advancing age being associated with a decline in the total volume and intensity of physical activity and an increase in sedentary time (Raffaerty et al., 2002; Schoenborn & Adams, 2010). Older adults have one of the lowest rates of physical activity in society (Berk et al., 2006; Wister & Wanless, 2007). The situation of older women is especially serious, as their levels of physical activity are significantly lower than those of men. This is true at all ages (Laird et al., 2014) and particularly evident at older ages (DiPietro et al., 2001), as women's

physical activity levels continuously decrease as their age increases (Kim et al., 1999). Hence, older women are less likely to engage in physical activity than older men (Schiller et al., 2014; U.S. Department of Health and Human Services, 2014).

It should be noted here that "sedentary behavior" and "physical inactivity" are different concepts: the former describes behaviors in which the energy used is less than 1.5 METs, such as being in a sitting or lying position, watching television or driving (Sedentary Behavior Research Network, 2012). A MET corresponds to 3.5 mL/min/kg and it is the amount of oxygen necessary for the maintenance of the metabolic functions of the body for one minute, when the individual is at sitting and at rest (Subirats-Bayego et al., 2012). In contrast, "physical inactivity" describes the failure to reach the minimum recommended levels of physical activity (Lee et al., 2012). Thus, many people are physically active, while engaging in high levels of sedentary behavior. Unfortunately, most older adults do not meet the general physical activity recommendations of a minimum of 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous intensity per week, and even fewer achieve the two recommended weekly sessions of strength training (Jefferis et al., 2014; Kohn et al., 2015). Therefore, they do not engage in a sufficient volume of physical activity to promote health benefits (Sun, Norman & White, 2013). It has been estimated that, worldwide, 60% to 75% of older people do not do the recommended levels of exercise, with just 25% in this age group participating in regular exercise (Hallal et al., 2012; Nied & Frankin, 2002) and only 12% achieving the recommended levels of aerobic and muscle-strengthening physical activity (Kohn et al., 2015). For instance, 80% of older people in North America (Colley et al., 2011; Troiano et al., 2008), 75% in Australia (Australian Bureau of Statistics, 2015), 62% in Canada (National Advisory Council on Aging, 2006), 69% in Finland (Bennie et al., 2017), and 68% in England (Health Survey for England, 2012)

do not engage in the recommended levels of physical activity and are thus considered "physically inactive."

In Spain, the rates of physical inactivity are similar to those found elsewhere. Based on data from the European Health Survey in Spain, executed by the INE and the Ministry of Health, Social Services and Equality, Latorre-Román et al. (2018) report that 80% of Spanish older adults are physically inactive, with just 17.2% of older women and 24.2% of older men adhering to the physical-activity recommendations. Likewise, in the last National Health Survey performed in Spain in 2017 (Ministry of Health, Consumption and Social Welfare, 2017), rates of physical inactivity reached 69.7% for older men and 81.6% for older women. In addition, the prevalence of sedentary behavior at 65 years was 40% among older women and 32% among men; while at 75 years, these rates increased to 76.2% for women and 58.7% for men (Ministry of Health, Consumption and Social Welfare, 2017).

As a consequence of these low rates, physical inactivity has become the fourth leading risk factor for non-communicable diseases (Hallal et al., 2012) and the fourth leading cause of death worldwide (Forwood, 2013), effectively a pandemic. According to the WHO (2008), up to 80% of cardiovascular and metabolic diseases – including heart disease, stroke, type 2 diabetes, obesity, and over a third of cancers – could be prevented by eliminating lifestyle risk factors such as physical inactivity (WHO, 2008). Decreasing levels of physical activity lead to impairments in strength, balance, and endurance and a decline in the ability to maintain independence in ADLs (Burton, Farrier et al., 2017). In addition, a sedentary lifestyle increases the risk of mortality (Martínez-Gomez et al., 2016; Zakkoyya et al., 2017), and older adults who are both sedentary and physically inactive have a higher risk of mortality (Warburton & Bredin, 2016).

In summary, it seems that, globally, only 20% to 30% of older adults achieve the recommended levels of physical activity, with similarly low rates in almost all developed countries (WHO, 2008). Older adults – and especially older women – are not meeting the physical activity guidelines. However, participation in regular physical activity is critical for older adults to ensure health and functional independence into later life. Thus, the promotion of physical activity among the elderly populations is paramount for public health. Researchers should focus on women when promoting and facilitating long-term maintenance of physical activity and exercise programs, especially as – paradoxically – this gender has the longest life expectancy.

B. Compliance with resistance training recommendations among older adults

The WHO and multiple other national agencies specifically include resistance training among their recommended physical activities, particularly in the guidelines for older people (Australian Government Department of Health, 2014; WHO, 2015). This is due to the substantial benefits of resistance training for preventing and addressing age-related physical decline (Chodzko-Zajko et al., 2009; Fragala et al., 2019; Steib et al., 2010). However, there are age-related reductions in all types of physical activity participation, with the greatest reduction occurring in muscle-strengthening activities (Gray et al., 2018), and older people are less likely than their younger counterparts to engage in resistance training or aerobic exercise (Humphries et al., 2011; Mayer et al., 2011; Pettigrew et al., 2017). Studies have shown that less than 15% of older people participate in resistance training at least twice a week, which is the minimum recommended frequency (Bennie et al., 2016; Merom et al., 2012). In fact, the proportion of older people participating in the recommended amount of resistance training is even lower in most developed countries. For instance, in Finland, only 11% of adults aged 65-74 years report meeting the recommendations (Bennie et al., 2016). Likewise, in Australia, it is estimated that just 8% meet the strength-training guidelines

(Bennie et al., 2016; Pettigrew et al., 2017). In the United States, only 8.7% of older adults (75 years of age) participate in muscle-strengthening activities during their leisure time (National Center for Health Statistics, 2015; Peterson, Zhang, Duchowny et al., 2016). Similar rates have also been reported in the United Kingdom (Health and Social Care Information Centre, 2012), Germany (Mayer et al., 2011), and Japan (Harada et al., 2008). To date, no data are available on the prevalence of strength training in the elderly Spanish population.

Moreover, as with the overall levels of physical activity, the percentage of older women who report engaging in resistance training is lower than that of older men (Strain et al., 2016). For instance, only 10.7% of older women in the United States meet the resistance training recommendations, compared to 14.1% of older males and 20.1% of women aged 18-24 years (CDC, 2006). In Scotland, only 16% of women aged 55-64 years perform two sessions of muscle-strengthening activities per week, compared with 19% of males, and this decreases to 14% for women aged 65-74 years and to 4% for women aged over 75 years (Strain et al., 2016). Worryingly, the population data in many other countries corroborate these findings (Bennie et al., 2020; National Center for Health Statistics, 2015; Humphries et al., 2010).

In summary, despite the benefits of strength training, older adults – and especially older women – are not meeting the resistance training guidelines. Therefore, there is a strong potential to increase participation in resistance training among older adults and thereby improve health and reduce age-related illnesses in this population. However, to increase the participation of the elderly in muscle-strengthening activities, researchers should focus their attention on barriers to and facilitators of physical activity and resistance training and study alternative training strategies to improve muscular fitness and physical function.

II.II.V. Barriers and facilitators of physical activity and resistance training in older adults

Due to the low participation rates of older adults in physical activities and resistance training, it is vital for researchers to identify and understand the factors that could encourage older people to meet the recommendations, both for general physical activity and resistance training specifically (Burton, Farrier et al., 2017; Burton, Hill et al., 2017). In the sections that follow, relevant barriers and facilitators that have been found to limit or motivate participation in physical activity among older adults will be described.

A. Barriers and facilitators of physical activity and exercise in general in older adults

There are a number of barriers that limit older adults' participation in physical activity and exercise. These can be classified into four groups: physical, psychological, social, and environmental (Burton, Farrier et al., 2017). The main barriers to physical activity, as reported by older people, are physical. These include poor health status, physical pain, pain associated with health problems, painful joints, shortness of breath, fatigue, health concerns, injury, and illness (Baert et al., 2011). Poor health is probably the most frequently cited barrier to participation in physical activity and exercise (Booth et al., 1997; Newsom & Kemps, 2007), along with pain (Burton, Farrier et al., 2017; Cohen-Mansfield et al., 2003) and fatigue (Ananian et al., 2008). Interestingly, physical barriers are reported to a greater extent by older women, with 52% of women and just 33% of men identifying poor health as the main barrier (Cohen-Mansfield et al., 2003). Back and knee pain are cited as substantial barriers for women, but not for men (Clark, 1999). The four most common psychological barriers reported in the literature are negative affect (no motivation, feelings of embarrassment), negative experiences, fear of injury or falling, and lack of self-efficacy (which is defined as the belief in one's ability to perform a particular behavior or specific

task, such as physical activity or exercise, despite negative experiences or obstacles; Boyette et al., 2002; Mathews et al., 2010; Schutzer & Graves, 2004).

Along with the physical and psychological barriers, social factors have also been reported in the literature as significant barriers to older adults' participation in physical activity and exercise (Hill et al., 2011). These social factors include the absence of another person to exercise with; the desire to feel safe while exercising; not knowing anyone doing any exercise; being unsure of what to do; and a lack of support from family, friends, and health-care providers (Baert et al., 2011; Hill et al., 2011). Another important social barrier, especially in Western cultures, is a form of agism that means youthfulness is associated with health and aging is seen as inevitably a time of dependence, inactivity, and loss of health (Bowd, 2003; Butler, 2005; Nelson, 2002; Palmore, 1999). These negative agist stereotypes negatively affect older adults' physical-activity-related attitudes and behaviors, as well as the meaning and value older people place on physical activity in later life (Emile et al., 2014; Henwood et al., 2011; Wurm et al., 2010). Older adults state that they feel "too old" to exercise, when there is no age limit on the ability to exercise. This feeling is more common among older women than among men (Booth et al., 2002). Many older women have been socialized to perceive physical activity as too difficult and risky for them in later life, and they believe it will cause muscle and joint pain, injuries, or diseases such as heart attacks (Grant, 2001).

Finally, older adults' participation in physical activity and exercise has been found to be limited by several environmental barriers, including limited access to appropriate facilities, financial concerns (low socioeconomic status), high cost of the activities, lack of time, geographical location (rural vs urban), unsupportive physical environments, neighborhood conditions, transportation challenges (sidewalk conditions, and lack of means of transport), safety issues, places to participate, weather conditions (rain, cold or hot

temperatures), and lack of programs and equipment (Boyette et al., 2002; Mathews et al., 2010; Rasinaho et al., 2007; Shutzer & Graves, 2004; Trost et al., 2002; Wilcox et al., 2005). Exercise-program-related factors that influence participation include intensity, time, format, location, affordability, equipment, and structure (with group-based programs preferred to individual alternatives; Hong et al., 2008; Van Uffelen et al., 2012).

In addition to the barriers that limit older adults' participation in physical activity, there are also several factors that promote engagement. These facilitators can be classified into the same four categories as the barriers. The findings from the literature reveal that older adults usually engage in physical activity to maintain their health and body's functioning, to slow down body decline, to manage health concerns, to alleviate or improve physical symptoms (pain, discomfort, fatigue), to feel better physically, and to become more physically active (Ashe et al., 2009; Bailey et al., 2016; Evans & Sleap, 2012; Hofmeier et al., 2016; Hudson et al., 2015; Kluge et al., 2012). These physical facilitators are common among both older men and women. For older adults, psychological factors are also an important source of motivation for engagement in physical activity or exercise. Psychological facilitators such as improved self-confidence and self-efficacy, the desire for fun, the development of positive attitudes towards the aging body and one's health, and personal enjoyment and pleasure are some of the factors commonly reported by older women and men (Evans & Sleap, 2012; Wilcox et al., 2005).

The social and environmental facilitators of participation in physical activity and exercise are comparable to the social and environmental barriers. For example, health-care providers such as physical therapists, sport scientists, and trainers who encourage participation in physical activity and exercise among older adults have been shown to be a fundamental motivator, especially for older women (Wilcox et al., 2005). In addition, someone to exercise with and with whom to build interpersonal relationships are also key

social motivators (Devereux-Fitzgerald et al., 2016; Kosteli et al., 2016; Wilcox, et al., 2005). The literature on environmental facilitators indicates that suitable environments, places for activity, good weather, safe neighborhoods, good transportation, low-cost facilities, specific and well-designed exercise programs, and exercise equipment are important motivators of participation for older adults (Rasinaho et al., 2006; Wilcox, et al., 2005).

B. Barriers and facilitators of resistance training in older adults

A number of studies have explored facilitators of and barriers to participation in resistance-training programs, in an attempt to increase participation rates among older people, many of whom do not participate in muscle-strengthening activities (Burton et al., 2016; Burton, Hill et al., 2017; Henwood et al., 2011). Reported barriers to participation include health issues (e.g., arthritis, back pain, heart problems, recent surgery), poor health, pain, fatigue, lack of time, lack of social support, cost of the activities, lack of facilities, lack of willpower, safety, fear, and a preference for other types of exercise (Burton et al., 2016; Burton, Farirer et al., 2017; Burton, Hill et al. 2017; Pettigrew et al., 2018). Pain, injury and illness (or the fear of incurring the same), and a feeling of being too old are the barriers most commonly cited to participation in resistance training (Burton et al., 2016). Previous studies have also found that older people commonly report disliking resistance activities and simply not being interested in this kind of training (Burton et al., 2016).

Traditional resistance training requires appropriate facilities and specialized equipment, and research into older people's perceptions of strength training in sports centers has identified various barriers in relation to these requirements, including lack of accessibility; program and equipment costs; intimidating environments; inadequate instruction; limited access to equipment; and the type of exercise devices and equipment offered, such as free weights and machines (Andreasson et al., 2016; Bethancourt et al., 2014; Burton, Farrier et al., 2017; Burton, Hill et al., 2017). The last of these factors is especially

important – namely, the suitability of the resistance equipment – because older adults perceive this as not only a barrier to engagement in resistance-training programs, but also as a reason for ceasing participation altogether. The three most commonly reported reasons for leaving a program are illness, holidays, and the unsuitability of the program (Burton, Farrier et al., 2017; Burton, Hill et al., 2017). In addition, exercise equipment is commonly identified as a negative aspect of resistance-training programs even by those older adults who participate in them (Burton, Farrier et al., 2017; Burton, Hill et al., 2017). Therefore, it seems that, along with other barriers, the suitability, availability, and comfort of the resistance-training devices are key to encouraging or limiting the participation of older adults in such programs.

Turning to gender, previous research has identified differences between older women and men in terms of the barriers to their participation in resistance-training programs. Older women report pain, a lack of time, the cost of the activities, the class times being unavailable or unsuitable, and the lack of an exercise partner as the main barriers to participation (Booth et al., 2002; Burton et al., 2016). From older men, the reasons most commonly given for not participating in resistance exercises include pain, lack of interest, feeling too old, and ongoing injury or illness (Burton et al., 2016).

The factors influencing older people's participation in strength training are similar to those reported previously for physical activity and general exercise. The most commonly identified facilitators of older adult participation in resistance training are the desire to feel good physically and mentally, to feel fit, to prevent falls, for enjoyment, to increase self-efficacy, to prevent deterioration and disability, to have better concentration, to be more independent, to maintain weight, to prevent injuries and illness, to be social, to feel strong, to maintain physical capabilities (including balance, mobility, strength, endurance), and to feel energized and "good" (Burton et al., 2016; Burton, Farrier et al., 2017; Burton, Hill et al.,

2017; Henwood et al., 2011; Kekäläinen et al., 2018; Sims-Gould et al., 2012). Health professionals' advice and other medical reasons are also strong motivators for older people to take up resistance training (Burton et al., 2016).

The evidence suggests that, for older adults, engaging in physical activities and exercise or resistance-training programs is not easy, due to multiple limiting factors. Exploring and addressing the combination of personal, socio-cultural, and environmental factors that underly patients' behavior is crucial for increasing participation in physical activity and resistance exercises in this population. In this sense, the large body of evidence extolling the physical, mental, and social health benefits of being physically active can also be used to promote resistance training in the elderly population. Furthermore, it is the responsibility of trainers and physical therapists to educate the older individuals to increase their knowledge and awareness of the risks of physical inactivity and the benefits of physical activity, while avoiding the agism and negative stereotypes that promote frailty and passive behaviors in this population.

Finally, the low participation rates and broad health benefits of physical activity generally – and resistance training in particular – underscore the need to identify the most evidence-based, suitable, simple, attractive, and safe physical activities and training modality approaches to encourage older adults to be more active. In this sense, resistance-training programs or other training modalities that either do not require special, expensive equipment or which only require easily administrable and cost-effective equipment (e.g., elastic bands) – and which can be performed at the practitioner's convenience (e.g., in sports centers, at home, outdoors) – may facilitate to the greater participation of older people in resistance-training programs and other beneficial training modalities and physical activities.

II.III. VARIABLE RESISTANCE

II.III.I. Definition, types, benefits and how it works

Critical for ensuring adequate stimuli when performing resistance exercises is the choice of training equipment and devices, as this plays a significant role in the adaptations associated with training (Kraemer et al., 1998). Today, there are two main types of resistance-exercise devices, which differ in response to how the load or resistance they offer behaves throughout the range of motion (ROM). The best known are the "isotonic" or "isoinertial" devices, such as free weights and resistance machines, excluding isokinetic machines (Abernethy et al., 1995). These devices offer a constant resistance during the entire ROM, with a constant mass whose resistive torque modulates dependent upon the joint angle (Abbodarda et al., 2016). Less well-known and less frequently used than the former are "variable-resistance devices." Unlike the isotonic or isoinertial exercise equipment, variable-resistance devices are characterized by producing a varying load or resistance throughout the ROM (Fleck & Kraemer, 1997; Wernborn et al., 2007). This type of device includes elastic bands, chains, and some machines that allow for variation in the velocity of load displacement and its magnitude. When these types of devices are used in a strength-training program, it can be named as variable-resistance training or elastic- or chain-resistance training, depending on the specific device used.

Variable-resistance training has been used in powerlifting for decades (Joy et al., 2016); but more recently, it has become an important component of strength and conditioning programs to improve health in special populations (Anderson et al., 2008; Bellar et al., 2011; de Alencar Silva et al., 2020; de Oliveira et al., 2017; Ebben et al., 2002; Fritz et al., 2018; Gargallo et al., 2018; Israetel et al., 2010; Stevenson et al., 2010; Wallace et al., 2006). The main goal of using variable-resistance devices is to closely match the resistance with the strength of the subject throughout the ROM (Grimby, 1992). Due to its characteristics, the

resistance directed against the target muscle or muscle groups can be varied over the range of the resistance-exercise movement (Aboodarda, George et al., 2011; García-Lopez et al., 2014). Therefore, the variable-resistance training devices provoke neuromuscular adaptations due to the high variation of stimuli they produce during the ROM, improving the different expressions of strength during the motion (Baker & Newton, 2009; Joy et al., 2013).

Chains and elastic bands can be used in strength programs in different ways. They can be used as the main training devices to perform the different resistance exercises programmed or in combination with isotonic or isoinertial devices (fixed loads), as they are attached to barbells or disks (Soria-Gila et al., 2015). Variable resistance, mainly elastic bands, can also be used for assistance with certain movements and situations; for instance, one can place the elastic band below the barbell, rather than above it, when performing a back squat. It is important to note that variable resistance has numerous advantages compared to conventional weight training performed with isotonic or isoinertial devices. It has been demonstrated that variable resistance can improve the recruitment of motor units, coordination between antagonist and synergist muscles, and the rate of force development (RFD), while limiting the reduction in force at the sticking point or region (Soria-Gila et al., 2015).

Overcoming the most challenging part of the resistance training, known as the "sticking point," is probably one of the most common uses of this type of device by sport scientists, trainers, and physical therapists. The sticking point or sticking region refers to the ROM area (usually 35% to 45% of the ROM; van den Tillar & Etterna, 2010) with the highest mechanical disadvantage due to biomechanical factors, where the muscle groups involved cannot meet the demands of the exercise when working with loads higher than 80% of 1 RM (Elliot et al., 1989) and therefore, a marked loss of speed occurs. Variable resistance reduces the mechanical disadvantage of the sticking point by offering lower resistance in this less-efficient region and higher loads in the most-efficient movement ranges, ultimately

producing greater absolute external load (Anderson et la., 2008; Elliot et al., 1989). When strength training is performed at high intensities by older adults, this advantage can be crucial for provoking greater adaptation and lower effort perception and fatigue.

The other main advantage that variable resistance has, compared with isotonic load, is the possibility of maintaining a high velocity and acceleration throughout the ROM, or at least for a greater range (Berning et al., 2008; Coker et al., 2006; Frost et al., 2010; Wallace et al., 2006). Since free weights and resistance machines always exert the same load during the ROM, it is necessary to apply greater force during the initial phase of the movement, producing an acceleration of mass; and to generate a deceleration phase at the middle-end of the movement, it is necessary to stop applying force, or even to apply force in the opposite direction to the movement. Thus, unlike variable resistance, this kind of training device does not permit the maintenance of an acceleration phase during most of the ROM. However, with variable resistance, individuals can accelerate more quickly and reach a faster speed sooner, as well as accelerating for a longer time, because the bands or chains continue to add resistance as the movement occurs. The higher speed and longer acceleration phase that occur with the same percentage of 1 RM when using variable-resistance devices could be especially valuable for strength-training programs based on high-velocity contractions, such as high-velocity resistance training, as this can lead to greater power and strength gains at high speeds.

Finally, it is important to note that, with variable-resistance devices, the greatest workload is generated at the end of the ROM, when the agonist muscles are shorter, due to a steady load increase being produced throughout the trajectory of the movement; whereas with "fixed-load" devices, the greatest workload is generated at the beginning of the concentric phase (Ghigiarelli et al., 2009; Gonzalez-Badillo & Sanchez-Medina, 2010).

II.III.II. Elastic bands

Different types of variable resistance equipment can be used during strength-training interventions, the most common being the elastic resistance devices and chains. The elastic devices – including elastic bands, rubber bands, and tubing (sport cords, bungee cords and surgical tubing) – are portable, low-cost, easy-to-maintain training devices, widely used in sport and therapeutic settings for multipurpose physical training and primarily to develop muscle strength and power (Abbodarda et al., 2016; Andersen et al., 2010; Colado et al., 2010; Colado, Mena et al., 2020; Hintermeister et al., 1998; Hostler et al., 2001; Jakobsen et al., 2013; Page & Ellenbecker, 2003). Of all elastic resistance devices, the elastic bands are the most traditional and best known. They are made with latex to favor their elastic deformation properties.

It is necessary to note that the load patterns of elastic bands and chains, when used as variable resistance devices, are different. It seems that both increase the load when lifted in a linear fashion. Nevertheless, elastic bands exhibit a curvilinear length-load relationship, increasing resistance in a curvilinear manner, whereas chains display a much simpler linear relationship because of their different physical and mechanical properties (Frost et al., 2010; McMaster et al., 2009; 2010).

When elastic bands are used, sufficient force and acceleration is needed in the early stage and throughout the ROM to overcome the elastic recoil and complete the movement (Frost et al., 2020). Thus, elastic bands act by increasing tension when the stretch-length of the band increases. When an elastic material is stretched, the amount of resistance in the material is proportional to the deformation of its initial length. In the elastic-band-deformation curve, the greater the extent of the elongation, the greater the tension force generated. In other words, the more the band is stretched, the higher its resistance to stretch becomes. However, unlike elastic bands, chains act by adding mass, with the load exerted by

them being proportional to the height reached by the chain from the ground (Frost et al., 2010).

Some authors have criticized the use of elastic bands as a resistance-training device, stating that they are not as effective as conventional training devices because elastic resistance provides a linear increase in resistance – and primarily at the end of the ROM (Anderson et al., 2008; Hostler et al., 2001). However, previous studies have demonstrated that, despite providing an increasing resistance load, elastic bands offer a curvilinear length-load relationship, similar to the "bell-shaped" muscle length-tension curve generated by the muscles throughout the ROM in many human movements (Aboodarda et al., 2013; Hughes et al., 1999; Rassier et al., 1999; Simoneau et al., 2001).

In the case of elastic bands, since they act by deformation of its structures, the resistance they offer is determined by three factors: the coefficient of elasticity (constant), the amount of elastic material (cross-sectional area [CSA]), and the percentage change in length (Theraband, 2009):

$$F = k * CSA * \Delta L$$

Where "F" is the resistance/force generated by the elastic band; "k" remains constant; "CSA" is the cross-sectional area of the elastic band; and "ΔL" is the variation of the length of the elastic band at rest. The percentage of the change in length with respect to rest (% ΔL) is calculated using the following formula (Thera-Band, 2009): % ΔL = [(Final length - length at rest) / length at rest] * 100. Consequently, if the elastic band increases its length or CSA, the resistance will increase proportionally, following Hooke's Law, which states that the resistance or load increases in proportion to the elongation. The different band colors indicate the different thicknesses of the CSA, which increase the levels of resistance. From one color to the next, there is an increase in resistance of approximately 20% to 30% when it is

stretched up to twice its length at rest (Page & Ellenbecker, 2005). This allows the subject to regulate by themselves the resistance of the elastic band, selecting the color, grip width, and RPE based on the validated OMNI-RES for elastic bands (Colado, Garcia-Masso, Triplett et al., 2012), according to the objective of the training program or session established.

Therefore, elastic bands are considered a good and valid variable resistance device to increase adherence to resistance training among older adults. They are an easily available, low-cost, and safe tool that can be used in different settings, including gyms, hospitals, medical clinics, long-term institutions, and even the subject's home (de Alencar Silva et al., 2020).

II.III.III. Elastic resistance training[1]

Resistance machines and free weights are currently considered the gold standard in exercise devices for producing muscle-strength adaptations through resistance training (de Oliveira et al., 2016). They are the most common traditional devices used for resistance-training programs, due to their widely demonstrated positive effects on strength, power, body composition, physical function, and other health-related parameters for different populations (Kwak et al., 2016; Liao et al., 2016; Winters-Stone & Snow, 2006). However, despite the widespread use of these conventional devices, they are often costly and require special facilities, which can limit access (Colado & Triplett, 2008). Furthermore, some individuals may be anxious about using free weights and machines, as they are commonly perceived to be associated with an increase of injuries or high physical demands (Jakobsen et al., 2013). In fact, it is estimated that 50% of individuals who begin resistance training programs with

[1] Related publication: Colado, J.C., Smolkay, R., Calatayud, J., Gargallo, P., Flández, J., & Page, P. (2020). Effects of strength training with variable elastic resistance across the lifespan: a systematic review. (Efectos del entrenamiento de la fuerza con resistencia variable elástica a lo largo de la vida: una revisión sistemática). *Cultura, Ciencia y Deporte, 15*(44), 147-164. http://dx.doi.org/10.12800/ccd.v15i44.1458

machines cease the exercise practice during the first year, usually due to logistical difficulties and financial costs (Dishman et al., 2014).

In contrast, variable resistance training with elastic bands – also known as "elastic resistance training," "elastic-based resistance training," "elastic tubing-based resistance training," "elastic strength training," and "strength training with elastic band or tubing" – provides a more portable, user-friendly, and cheaper alternative to conventional resistance training, allowing greater adherence and accessibility, and providing similar results for different populations (Colado, Mena et al., 2020; Lopes et al., 2019). The use of this training modality became popular in the 1980s and has been increasing in recent years. Historically, the first elastic resistance exercises were used for rehabilitation in hospital settings; but, with the time, this strategy was also introduced into fitness and sports settings to improve the general health status of different populations (Page & Ellenbecker, 2003; Shaw et al., 2015), including healthy populations (Colado et al., 2010). In fact, the literature provides evidence for the benefits of elastic resistance training for different types of musculoskeletal conditions, including low levels of strength, poor balance, limited ROM, and pain impairments (Aboodarda et al., 2012; Brandt et al., 2013; Serner et al., 2014; Sundstrup et al., 2014). Evidence suggests that elastic resistance training can improve muscle strength, muscle power, body composition, functional capacity, and quality of life (Calatayud et al., 2015; Colado et al., 2010; Ramos et al., 2014; Suchomel et al., 2018). Colado and colleagues (Colado, Mena et al., 2020) recently conducted a systematic review and conclude that elastic resistance training programs are effective for improving muscle strength, physical function, and other health-related variables across the lifespan.

Finally, several studies have demonstrated that elastic resistance training provides similar prime mover, antagonist, stabilizer, and assistant mover muscle activation to conventional isotonic resistance training (Aboodarda et al., 2016), with no significant

difference in electromyographic activity level during exercises using elastic bands or conventional devices (Aboodarda, George et al., 2011, Aboodarda, Shariff et al., 2011, 2013; Borreani et al., 2014; Ebben & Jensen, 2002; Jakobsen et al., 2013). In addition, evidence suggests that resistance training with elastic devices provides similar strength gains when compared to resistance training performed with conventional devices in different populations (Ghigiarelli et al., 2009; Lopes et al., 2019; Lubans et al., 2010).

It should be noted that, in the rest of this PhD dissertation, "elastic resistance training," "elastic-based resistance training," and "resistance training with elastic band" will be used interchangeably. In addition, the effects of this training modality on the different parameters analyzed are described with more detail in each of its sections.

A. Elastic resistance training in older adults[2]

Particularly important are the effects of elastic resistance training in older adults, as the characteristics of the material (low cost, easy handing, high portability, and accessible) favor adherence to resistance training and other exercise training modalities in this

[2] Related publications:

1.Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877.

2.Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30.

3.Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High- and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise* (In Press).

4.Fritz, N. B., Juesas, Á., Gargallo, P., Calatayud, J., Fernández-Garrido, J., Rogers, M. E., & Colado, J. C. (2018). Positive effects of a short-term intense elastic resistance training program on body composition and physical functioning in overweight older women. *Biological Research for Nursing, 20*(3), 321-334. https://doi.org/10.1177/1099800418757676

population. Due to the nature of this PhD dissertation, a brief review of the literature on the effectiveness of this modality in older adults is presented in the following lines.

Currently, the guidelines on resistance training for older adults recommend the use of free weights and weight or pneumatic machines for developing and maintaining musculoskeletal fitness (Chodzko-Zajko et al., 2009; Garber et al., 2011). There is strong evidence (category A) for the positive effects of free-weight and machine exercises for improving muscle strength, power, and physical function in healthy adults and older adults (Chodzko-Zajko et al., 2009). However, despite this kind of equipment being commonly used for resistance training protocols in scientific, rehabilitation, and sports settings, a wide range of studies have investigated the effects of elastic resistance training in the elderly due to the higher accessibility and portability of the elastic bands, compared to conventional resistance devices (Damush & Damus, 1999; de Alencar Silva et al., 2020; de Oliveira et al., 2016; Flández et al., 2020; Fritz et al., 2018, 2021; Gargallo et al., 2018; Ribeiro et al., 2009). Since the first randomized controlled trial (RCT) by Topp et al. (1996), which was conducted in healthy community dwelling for older adults and demonstrated the positive effects of a 16-week elastic resistance training program for muscle strength and gait speed, most studies have corroborated the effectiveness of this training strategy for increasing isometric, isotonic, and isokinetic muscle strength in community-based, institutionalized, and healthy older adults (Damush & Damush, 1999; Dancewicz et al., 2003; Fritz et al., 2018; Gargallo et al., 2018, Ribeiro et al., 2009; Webber & Porter, 2010b; Woo et al., 2007).

From the first study in 1996, research into the effectivity of elastic resistance training in older adults has increased rapidly. Various articles, systematic reviews, and meta-analyses have concluded that elastic resistance training can provide both strength and functional improvements among both adults (de Oliveira et al., 2016) and elderly participants (Colado, Mena et al., 2020; Martins et al., 2013; Santos Silva et al., 2019), suggesting that elastic

resistance may have benefits for a variety of age groups (Colado, Mena et al., 2020; Martins et al., 2013; Thiebaud et al., 2014). However, these studies report a lack of high-quality interventions, due to small sample sizes, short duration, and the absence of quantitative methods used to control the intensity of the elastic bands (Colado, Mena et al., 2020; Martins et al., 2013).

In summary, despite the positive effects of the elastic resistance training reported in different systems, further studies of a higher quality are needed to analyze this type of training strategy in the medium- to long-term (i.e., more than 16 weeks), with a larger number of subjects, using a valid method to control the intensity of the training devices, and comparing the elastic resistance training with other training modalities. The two projects included in this PhD dissertation were partially designed based on these needs.

II.IV. TRAINING INTENSITY IN RESISTANCE TRAINING

II.IV.I. Intensity: definition and levels

Resistance training has been widely demonstrated as an efficient training method for improving health and performance across different populations (Fisher et al., 2011; Fragala et al., 2019; Ratamess et al., 2009; Westcott, 2012). The increase in lean mass, muscle strength, muscle power, and functional capacities, along with the decrease in fat mass and improvements in quality of life, among other effects, are some of the benefits generated by the resistance-training method and previously reported by researchers (Fragala et al., 2019). However, the proper manipulation of resistance training parameters is crucial for maximizing the potential benefits and adaptations generated by this training method (Fisher et al., 2011, 2013). Of all the training parameters, intensity is the key to maximizing performance and health improvements. Its correct manipulation and administration are essential for producing the target adaptations and results previously established for a given individual or group (Folland & Williams, 2007).

Unlike in the area of aerobic or cardiovascular exercise, where intensity is generally considered to represent the effort required by the body (Fisher & Smith, 2012), in resistance training, there is a misuse of the term "intensity" due to difficulties in defining it (Fisher & Smith, 2012). Several publications have attempted to offer clarification on the definition of the term (Fisher et al., 2011; Fisher & Smith, 2012; Steele 2014). Some authors defend the use of the term "intensity" to indicate "effort" (Fisher & Smith, 2012), while some consider it to be synonymous with "load" (Sakamoto et al., 2012), and others argue that the use of "intensity" to refer to "load" is inappropriate in the resistance-training context (Boring, 1945).

Classically, "intensity" in resistance training is defined as the training load, given in percentage or absolute value, relative to maximal dynamic or static strength (i.e., 1 RM or

maximal voluntary isometric contraction; Balady et al., 2002; Chodzko-Zajko et al., 2009). This approach is the most common, where "intensity" refers to the amount of load or resistance, often described as the number of repetitions and sets performed for a given load (Howley, 2001; Hurst et al., 2017). However, the use of "load" as a description of intensity in resistance training programs is not accurate, as previous research has shown that maximal repetition ranges at relative loads can vary considerably between individuals (Hoeger et al., 1990; Shimano et al., 2006). This is because this approach does not take into account the effort put forth during resistance exercise. For instance, two individuals performing the same number of repetitions at the same relative load are probably not working at the same intensity because the exercise effort of both subjects is likely to differ. Based on this view that intensity is equal to load, and taking the example proposed by Steele (2014), if two individuals have a 1 RM of 100 kg, the subject who performs one easy repetition with a load of 80 kg (80% of 1 RM) is training more intensely than the other person who performs a hard set of repetitions until muscle failure with 79 kg (79% of 1 RM), but this is clearly not so.

Based upon these considerations, it is concluded that this long-standing paradigm is not correct (Morton et al., 2016). Instead, intensity in resistance training must be representative of the degree of effort exerted during a specific resistance exercise (Steele, 2014; Winett et al., 2019). As with load in terms of 1 RM, the most accurate control of effort is only possible when the individual trains to muscle failure, which means that the last repetition performed is in good form (Hoeger et al., 1990; Shimano et al., 2006; Peterson, Zhang, Choksi et al., 2016). In practice, this approach means that a set of repetitions of light-to-moderate resistance in terms of load performed with a high degree of effort is similar in intensity and can provide comparable stimulus to a set of repetitions of high load and low effort (Winett et al., 2019).

The Oxford English Dictionary (2012) defines "intensity" as the degree or magnitude of a measurable characteristic or variable; and as pointed out Steele (2014) in relation to the appropriate use of this term in the resistance-training research field, it seems that "intensity" could best be used to describe the degree of both load and effort, since intensity concerns the magnitude or degree of some measurable quantity. Thus, in resistance training, it could be more appropriate to refer to "intensity of load" or "intensity of effort," since load can be measured by the percentage of 1 RM or maximal voluntary isometric contraction, whereas exercise effort can be assessed through RPE scales. Therefore, intensity in resistance training must be understand as synonymous with both "load" and "effort" and simply defined as the level of effort applied to a given load (Fisher & Smith, 2012).

In addition, it is important to note that there are no consistent and standardized criteria in the literature to define the different levels of intensity in resistance training (Raymond et al., 2013). Some authors (e.g., Peterson & Gordon, 2010) have classified resistance training intensity into low (≤ 60% RM), low/moderate (60-69% 1 RM), moderate-high (70-79% 1 RM) and high intensity (≥ 80% 1 RM), while others define loads of ≥ 70% 1 RM as high intensity, 50-70% 1 RM as moderate intensity, and ≤ 50% as low intensity (Beneka et al., 2005; Lavin et al., 2019; Raymond et al., 2013).

In all the classifications reported to date, only the load component is taken into account. For the present PhD dissertation, the first classification is followed as a reference, and perceived effort is reported to show an appropriate use of intensity in the resistance-training interventions and exercise interventions with resistance exercises prescribed.

II.IV.II. Quantification and control methods of intensity in resistance training

A. Load-based "traditional" methods

Control of intensity is a fundamental factor in strength and conditioning and sports science practice, and it is essential to ensure the safety and efficacy of the exercise protocols in any context (athletic, recreational, and therapeutic; Bautista, Chirosa, Chirosa et al., 2014; Robertson, 2004). Therefore, the quantification and control of intensity by researchers, coaches, and physical therapists in relationship to training goals (such as increasing muscle strength, power, physical function, and muscle mass) is essential for an accurate and individualized exercise prescription (Wernborn et al., 2007), as well as for improving health and reducing morbidity and mortality in populations with pathologies (Pedersen & Saltin, 2015).

Traditionally, to quantify the intensity of resistance training exercises, external indices relating to load have been used. These include 1 RM; a specific percentage of 1 RM (Fleck, 1999); a number of repetitions per set, where a specific RM target or target zone is used, such as 10 RM or 6-8 RM (Wernborn et al., 2007); the total number of sets and repetitions per exercise (Bird et al., 2005; Fleck, 1999); and the rest between sets (Miranda et al., 2009; Senna et al., 2008). The 1 RM, defined as the largest amount of weight lifted once using correct technique, is the most commonly used descriptor of resistance-training intensity and the main reference used to prescribe the load during resistance training programs (Hass et al., 2001; Ratamess et al., 2009). Along with the 1 RM, the intensity of resistance training is often estimated based on the percentage of the 1 RM or by prescribing the maximum number of repetitions that can be performed with a given submaximal weight, such as 10 RM – which refers to a weight that can be lifted 10 times, but no more (González-Badillo et al., 2011). Some studies have established an RM continuum that associates the percentage of 1 RM with the number of repetitions to failure. As advantages, these methods eliminate the need to

assess the direct 1 RM and can be used to prescribe resistance training programs for different individuals at the same time, the loads being later transformed into absolute values for each person (González-Badillo et al., 2011). In addition, expression of intensity as a percentage or submaximal repetitions of 1 RM can also be used to reflect the evolution of the training load (González-Badillo et al., 2011). Furthermore, it may be argued that research has shown these methods to be safe, even among older populations, for controlling, quantifying, and prescribing intensity in resistance training interventions (Hass et al., 2001; Braith & Beck, 2008).

However, the direct determination of 1 RM and the expression of intensity in relative load (percentage of 1 RM or number of repetitions of 1 RM) have some potential disadvantages worth noting that make neither of these methods entirely appropriate for precise monitoring of real intensity in resistance training sessions. For instance, the number of repetitions at the same given percentage of 1 RM differs inter-individually between trained and untrained/novice participants, due to training status (Hoeger et al., 1987, 1990; Hurst et al., 2019; Sales et al., 2013; Shimano et al., 2006), and intra-individually because of the muscle groups (Robertson et al., 2003) and type of exercises trained (Eches et al., 2013; Hoeger et al., 1990; Shimano et al., 2006), with the number of repetitions reached in single-joint exercises being smaller than that in multi-joint exercises for the same relative load (Eches et al., 2013). Studies have also shown that the obtained 1 RM value is often not the subject's true maximum and the specific evaluation of the 1 RM one day may be susceptible to change by numerous physiological and psychological factors. As a result, subsequent training loads could be lighter or heavier than intended. In addition, it is a time-consuming procedure and impractical for large groups (Marcos-Pardo, González-Hernández et al., 2019), and even less so for older populations, as older adults require 8-9 sessions for consistency in the measurement of the 1 RM of the lower limbs (Marcos-Pardo, González-Hernández et al.,

2019). Furthermore, 1 RM value can change quite rapidly as a consequence of training and thus requires constant evaluation to guarantee that the intensity is adjusted in response to the evolution of the individual's performance (Dos Santos et al., 2020). Ultimately, these methods are purely a representation of absolute and relative load, rather than the relative intensity of the participant, and they are highly influenced by the numerous factors described above. This means that the 1 RM of a person for a given resistance exercise cannot enable an accurate prediction of the number of repetitions this subject could perform at any given percentage of 1 RM, let alone be transferred across other individuals or groups of muscles and exercises.

B. Velocity-based methods

Owing to the lack of practical application of these methodologies, researchers have sought easier methodologies to quantify control intensity in the resistance-training context. The monitoring of movement velocity of each repetition has been proposed as an alternative to prescribing and quantifying the training load, and this has been shown to be a good indicator of the intensity of resistance exercises (Kawamori & Haff, 2004; Kawamori & Newton, 2006; Row et al., 2012; Sánchez-Medina et al., 2010). The popularity of this method has increased notably in the last decade, with the appearance of new tools such as the portable linear position transducer, mobile applications, and video analysis that allows the measurement of exercise velocity of individuals and small groups (Conceicao et al., 2016; Moss et al., 2003; Richardson, Duncan, Jimenez, Juris et al., 2018). These new devices have, in most cases, replaced the isokinetic dynamometers, which, unfortunately, is not an ideal or common training scenario. From the use of this methodology, with velocity as an indicator of intensity, two main applications can be identified.

First, movement velocity can be used to estimate the 1 RM. Previous studies have identified a strong and linear relationship between the percentage of 1 RM and movement

velocity in a variety of resistance training exercises for the upper and lower limbs, such as bench press, leg press, deadlift, squat, and bench pull (Sánchez-Medina et al., 2014; Helms et al., 2017; García-Ramos et al., 2018b, 2019; Pérez-Castilla et al., 2018), especially when they are performed using a Smith machine instead of free-weights (Banyard et al., 2017; Hughes et al., 2018). This application is especially interesting for older adults, as it raises the possibility of determining the 1 RM without the need to perform a lift with the maximal load, which is discouraged for vulnerable populations. However, most studies to date have been conducted in young, healthy individuals (Torrejon et al., 2018; Balsalobre-Fernández et al., 2018; Pérez-Castilla et al., 2019). The study by Marcos-Pardo, González-Hernández et al. (2019) is the only one to investigate the relationship between movement velocity and relative load (percentage of 1 RM) during bench press and leg press exercises by older adults, specifically, older women. The authors found that movement velocity could be useful for prescribing loads during resistance training for older women, but they also note that the movement velocity associated with submaximal loads (below 1 RM) was significantly lower for older women in both exercises, compared to young and healthy individuals (Marcos-Pardo, González-Hernández et al., 2019). For example, with the bench press, the movement velocity associated with 50% of 1 RM was 0.48 m/s^{-1}, whereas the same velocity was equivalent to a load of 78% of 1 RM in the young individuals (Sánchez-Medina et al. 2014). The same was true of the leg press, where the movement velocity associated with 50% of 1 RM was 0.49 m/s^{-1}, whereas the same velocity was equivalent to a load of 82% of 1 RM in the young individuals (Conceiçao et al., 2016).

By monitoring repetition velocity during resistance exercise, exercise professionals can prescribe resistance exercises through the "velocity-based resistance training." This type of training uses the mean velocity of the first repetition, which is intrinsically related to loading intensity, or the maximum percent velocity loss to be allowed in each set.

i. Velocity-based control and high-velocity resistance training

However, while numerous studies have investigated the optimal velocities at which young athletes should train to enhance or maximize a specific component or physical capacity (e.g., an average velocity of 0.75-1.0 m/s compared to 1.0-1.5 m/s in a resistance training program will optimize different aspects of strength-power continuum; Jandacka & Beremlijski, 2011; Jidovtseff et al., 2009; Mann et al., 2015), there are little data on whether there is an optimal velocity at which older adults can produce the maximal peak power outcome or on the optimal velocity at which they should train to enhance specific functional performance tasks, particularly in power strength training interventions. Of special interest is the velocity at which the load is moved in the high-velocity resistance interventions performed by older adults and the velocities and loads at which the maximal power is produced, or the velocity-thresholds at which certain improvements occur. It is well-known that there is considerable variation in self-selected maximal velocity during high-velocity resistance training by older adults, despite instructions to participants to move the weight "as fast as possible" (Bottaro et al., 2007; de Vos et al., 2008; Fielding et al., 2002; Henwood et al., 2008, Henwood & Taaffe, 2005; Katula et al., 2008; Marsh et al., 2009; Pereira et al., 2012; Piirainen et al., 2014; Reid et al., 2008; Reid, Martin, 2014; Sayers, 2007; Sayers & Gibson, 2010, 2012, 2014; Sayers et al., 2012), due to the different characteristics of the participants in terms of the broad range of functional abilities, strength, power, and age, as well as the different genders.

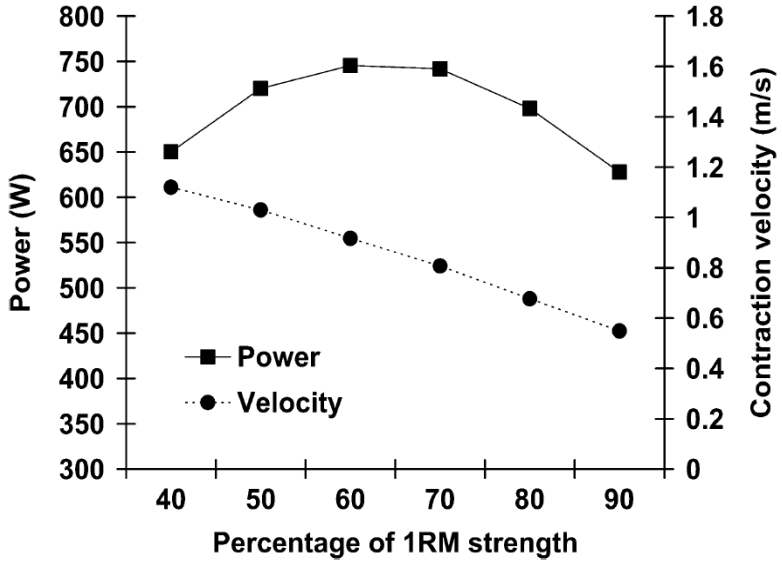
The study by Richardson and colleagues (2017) is the only one to date that has measured the mean velocity movement of eight resistance exercises in a high-velocity training session, with a small group of older adults, using a two-dimensional video analysis. For upper-limb exercises performed by older women, the authors found a mean velocity of 1.2 m/s, 0.7 m/s, 1.2 m/s, and 1 m/s for the bicep curl, chest press, seated row, and tricep

extension, respectively. For the lower limb exercises, a mean velocity of 0.4 m/s, 1 m/s, 1.2 m/s, and 0.8 m/s were reported for the calf raise, leg curl, leg extension, and leg press (Richardson et al., 2017). All the exercises were performed using machines at 40% of 1 RM (three sets, 14 repetitions). Bautista, Chirosa, Chirosa et al. (2014) report that light intensity (< 40% 1 RM) corresponds to a velocity exceeding 1 m/s^{-1}, while moderate intensity (40% to 70% 1 RM) corresponds to a velocity of between 0.6 m/s^{-1} and 0.7 m/s^{-1}, and heavy loads (< 70% 1 RM) to a velocity of less than 0.4 m/s^{-1} in the bench press exercise performed by young males.

To determine the optimal load for peak power in older adults, some studies have compared different loads for multiple exercises performed in pneumatic (Potiaumpai et al., 2016) or plate-loaded (Strand et al., 2019) resistance machines. Potiaumpai et al. (2016) report specific optimal load ranges for muscle power in the chest press (40% to 60% 1 RM, with peak power at 50%), seated row (40% to 60% 1 RM, with peak power at 50%), pull-down (30% to 50% 1 RM, with peak power at 40%), leg curl (50% to 70% 1 RM, with peak power at 60%), leg press (50% to 70% 1 RM, with peak power at 60%), and calf raise (60% 1 RM). Likewise, Strand et al. (2019) report the same peak ranges for the leg press, chess press, seated row, and calf raise, and they also analyzed the peak power of the shoulder press (60% 1 RM), hip adductor (50% 1 RM), hip abductor (50% 1 RM), leg curl (50% 1 RM), bicep curl (60% 1 RM), and tricep extension (60% 1 RM). In general, the peak power outcome for older adults of upper and lower limb exercises seems to be achieved at loads of between 40% and 60% of 1 RM. It is important to note that the different velocities at which power is obtained could be a key factor in the functional responses. This means that, although muscle power output could be similar at low (40% 1 RM) and high (90% 1 RM) loads (Figure 10), the velocities at which these power outputs were developed would differ notably between loads, with the power output produced at low loads and high velocities being better indicators of

physical function in older adults (Sayers & Gibson 2010), as a greater velocity component is needed. However, this does not mean that the muscle power produced at high loads and lower velocities is unrelated to physical function. In fact, some functional tasks (such as climbing the stairs or slowly getting up from a chair) require power with a greater component of force than velocity (force-power tasks), while in others (such as postural rebalances), the velocity component is predominant (velocity-power tasks). To date, the study by Sayers et al. (2016) is the only one to report that an average muscle contraction of 0.88 m/s during high-velocity resistance training is necessary to ensure optimal improvements in functional performance for older adults. However, further investigation is needed to corroborate this threshold in other elderly samples.

Figure 10. *Power and contraction velocity curves in older men and women.*



Note. Solid squares represent peak muscle power and solid circles represent peak velocity obtained across a range of external resistance (40-90% 1RM). Reproduced from "A comparison of high-speed power training and traditional slow-speed resistance training in older men and women" (p. 3370), by Sayers and Gibson, 2010, *The Journal of Strength & Conditioning* Research, 24(12).

C. Methods based on level of effort

The aforementioned approaches require the use of additional devices – such as velocity transducers, mobile phones, cameras, and video-analysis systems – and specific exercise conditions (i.e., the load must predominantly move in vertical displacements). However, these are not suitable for all resistance training exercise and such devices are not always available. As such, researchers have sought easier methods of quantifying and controlling intensity in the strength-training context, where it is not the load but the perceived effort that plays a central role. As one possibility, rather than exposure to the maximal external resistance (1 RM), the intensity might be controlled by achieving the maximal effort for any range of loads, usually submaximal loads (Drinkwater et al., 2007; Folland et al., 2002; Izquierdo et al., 2006; Sanborn et al., 2000). Maximal effort is typically reached when performing a set of repetitions to the point of momentary muscle failure (Van Roie et al., 2013). The training method known as "training to repetition failure" is based on this approach. Unlike RM and maximal effort at any given load, where subjects perform each set until failure, the "repetitions in reserve" (RiR) method considers the feeling or perception of the subject as to how many repetitions they are able to perform before failure, and the subject then stops when they perceive that they have only one or two repetitions "left in reserve" before muscle failure (Helms et al., 2016; Zourdos et al., 2016).

However, the most common approach to controlling training intensity by effort is probably the use of ratings of perceived exertion. For this method, it is necessary first to know what is understood by "perception of effort." Previous studies have defined perception of physical effort or exertion as the ability to detect and interpret organic sensations (effort, strain, discomfort, fatigue) while performing exercises (Noble & Robertson, 1996; Pegeaux, 2016; Robertson et al., 2003). Thus, it is the subjective feeling of effort that an individual perceives during exercise. Initially, RPE was measured to control the intensity of aerobic

activities such as cycling or running (Foster et al., 2001); but in recent years, this method has been shown to be effective for controlling the intensity of resistance exercises in different populations (Lagally et al., 2004; O'Connor et al., 2002; Robertson et al., 2005). The tool used to monitor the perceived response to the exercise is the RPE scale (Hampson et al., 2001). This dates back to the middle of the 20th century, with the studies performed by Weber and Fechner on muscle sensations in relation to weight (Stevens, 1957, 1961), but it was more than 40 years ago that Gunnar Borg created the original RPE scale – which rated exertion from 6 to 20, matching it with heart rate – for monitoring different aerobic exercises (Borg, 1970). This was followed by the development of the Borg category (C) ratio (R) 10 scale, also known as the "Borg CR10," which was the first to provide exertion ratings from 1 to 10 and with the visually aid of the 1-10 RPE scale, known as the "OMNI scale" (Faulkner & Eston, 2008). Some years later, Robertson and colleagues (2003) validated the first RPE-OMNI scale for resistance exercises, presenting the "OMNI-RES scale." The Borg CR10 and the original 15 (6-20) category scales have also been used to monitor the intensity of strength exercises (Buckley & Borg, 2011; Day et al., 2004; Gearhart et al., 2009; Lagally & Roberson, 2006; Row et al., 2012; Tiggemann et al., 2010). They are characterized by the inclusion of an image of the scale of perceived exertion (often from 1 to 10), with pictures of a person engaging in the specific activity (cycling, running, resistance exercise, etc.) at increasing intensities, usually combined with visual and verbal descriptors of the intensities (Robertson, 2004).

The RPE scales assume a strong association between the perceptual (perceived exertion), performance (total load, percentage of 1 RM, velocity, muscle power), and physiological (heart rate, VO_2 max, lactate, ventilatory threshold, respiratory rate, sweating, muscle fatigue, myoelectric activity) responses (Chen et al., 2002; Groslambert et al., 2006; Irving et al., 2006; Robertson et al., 2005; Robertson & Noble 1997) that, according to the

basic principle of the Borg continuous-effort model, occur simultaneously when there are increases in the intensity of a certain physical activity (Borg, 1982). It has been demonstrated that monitoring subjectively perceived exertion with these scales is an effective method of quantifying the intensity of aerobic and resistance exercises (Day et al., 2004; Soriano-Maldonado et al., 2014).

However, varying rates of RPE can be registered during resistance training exercises. RPE scores can be obtained from global, which are associated with total body effort perception, and peripheral exertional signals, which are associated with anatomically regionalized perceptual signals such as specific active muscle groups or areas (e.g., lower limbs; Colado, Garcia-Masso, Triplett et al., 2012; Colado et al., 2014, 2018; Robertson et al., 2003, 2005), It has been demonstrated that localized or peripheral RPE is usually higher than the RPE score for the overall body (Colado, Furtado et al., 2020), with both types of RPE being useful for prescription and monitoring of intensity in resistance training programs (Robertson, 2004). In addition, rather than obtaining the general or located RPE after each resistance exercise, it is possible to use the session RPE (sRPE), whereby the RPE for the entire training session is recorded 30 minutes after completion (Ferreira et al., 2014; Foster et al., 2001). This method thus measures the feeling of global exertion experienced during the entire session. This modification of the classic RPE scale can be used to monitor the global intensity of resistance training over time, as well as to prescribe intensity for an entire session (Day et al., 2004; McGuigan & Foster, 2004). Interestingly, Colon et al. (2015) conclude that sRPE can be used to prescribe and monitor resistance training sessions in older subjects, as this produced similar scores to traditional RPE for exercises sessions that involved concentric, eccentric, and dynamic resistance exercises.

In recent years, RPE scales have been successfully used to regulate resistance-exercise intensity, and other interesting applications of this approach have also been studied.

Previous studies indicate that this method can reliably estimate 1 RM for upper- and lower-body exercises (Buckley & Borg, 2011; Robertson et al., 2003), allowing the replacement of traditional strength tests and, thus, removing the need for maximum effort (Tiggemann et al., 2010). The use of RPE to predict 1 RM has been even validated in older adults at a variety of intensities in multi-joint (leg press) and single-joint (knee extension) exercises (Bove et al., 2016; Desgorces et al., 2015). Nevertheless, although the RPE method has been endorsed by the ACSM as a feasible method for training intensity adjustment in clinical and sports settings, most interventions with older adults prescribe intensity based on maximal tests or maximum repetitions. Other practical uses for the RPE method described in the literature rely on its utility for estimating changes in movement, velocity, or power within a specific exercise set (Naclerio et al., 2011); selecting initial training load (Lagally et al., 2009); monitoring the progression of fatigue during resistance training sessions (Kraft et al., 2014); and determining the RiR based on a valid scale in which RPE value corresponds to the number of RiR (Zourdos et al., 2016).

It is noted that the most significant limitation of the RPE method is that less than maximal RPE scores are sometimes reported, even when the maximal number of repetitions is performed at moderate and high loads (Hackett et al., 2012; Pritchett et al., 2009; Shimano et al., 2006). However, this does not occur often, and previous studies have demonstrated that RPE is similar, regardless of load (60%, 80%, and 90% 1 RM), for upper-limb resistance exercises (arm curl and bench press) when repetitions are taken to muscle failure (Shimano et al., 2006). Thus, when performed to muscular failure, regardless of load, each exercise is of the same intensity. In the case of the lower-limb exercises (squat), higher RPE scores have been found at lower loads (60% 1 RM) than at higher loads (80% and 90% 1 RM; Shimano et al., 2006). In addition, RPE is related not only to load but also to velocity contraction, being a useful tool for controlling intensity during resistance exercise performed at slow, moderate,

and fast velocities (Gearhart et al., 2002; Lagally et al., 2002a; Row et al., 2012). RM, percentage of RM, RiR, and RPE have all been shown to be effective and valid for prescribing and controlling training intensity in resistance-training interventions for older adults. Buskard et al. (2019) found all to be effective methods of improving muscular strength and functional performance in an older population, but they conclude that RPE is optimal, as it is likely to be perceived as the most tolerable and enjoyable, which are important factors in older adults' continued participation in resistance training programs.

Due to their special relevance to the present PhD dissertation, RPE scales are discussed in the following sections in relation to their use in controlling and monitoring intensity with variable resistance training devices, such as elastic bands, and in high-velocity resistance exercises.

i. Elastic resistance and training intensity control through rate of perceived exertion[3]

Health professionals involved in resistance-training interventions can assess the exact external load or total volume mobilized when free weights or resistance machines are used by calculating the total number of sets × repetitions and the load (kg) used in each resistance exercise. However, a common issue when elastic bands are employed as the resistance-training device is the difficulty with obtaining an accurate estimation of the training intensity in terms of load and effort. This is because, without the kilogram measures of the free weights or machines, there is no simple visual indicator of tension (load) or the extent of the elongation of the elastic band (the load is not constant, but variable). An accurate estimation of the training intensity is of critical importance for achieving the goals and avoiding or minimizing deleterious effects such as muscle and joint injuries. In 2013, Martins et al.

[3] Related publication: Colado, J. C., Pedrosa, F. M., Juesas, A., Gargallo, P., Carrasco, J. J., Flandez, J., Chupel, M. U., Teixeira, A. M., & Naclerio, F. (2018). Concurrent validation of the OMNI-Resistance Exercise Scale of perceived exertion with elastic bands in the elderly. *Experimental Gerontology, 113*, 11-16. https://doi.org/10.1016/j.exger.2017.12.009

(2013) conducted a review to analyze the effectiveness of strength programs for older adults, using elastic-resistance devices. The results confirm that elastic resistance training is an effective exercise strategy for increasing muscle strength in older adults. However, the authors also highlight the methodological shortcomings of the analyzed works, including the absence of a quantitative control of intensity in the resistance exercises with elastic bands (Martins et al., 2013).

In an attempt to resolve this problem, some authors have sought to determine the specific loads of the different percentages of elongation of the different-colored (thickness) elastic bands, creating reference tables of the length-tension and load relationship (McMaster et al., 2010; Page & Ellenbecker, 2005; Uchida et al., 2016). These tables provide a representation of the amount of weight added when the bands are stretched to a particular length. This information is based on the measurements of the bands at an initial length at rest (non-stretched), and their relative tension, load, or resistance are measured for every x cm (e.g., for every 10 cm until deformed to 150% of the initial length; McMaster et al., 2010) or for various specific elongations (e.g., at 25%, 50%, 75%, and so on, up to 200% of the resting length; Uchida et al., 2016). Although this seems to be an accurate method of measuring training intensity in elastic-based resistance-training interventions, it is based only on load and does not take into account the variable of effort. In addition, it is important to note that not all elastic bands around the world will have identical length-tension relationships. Even the same elastic band will produce different loads at the same elongation during its life cycle. This means that the actual load may – and most likely *will* – vary between and within each elastic band.

Due to the need for a precise method to control and monitor training intensity in resistance exercises performed with elastic bands, Colado and Triplett (2008) propose a useful and complete method based on three elements: the color of the elastic band (load); the

grip width (load); and the perceived exertion, as measured by the OMNI-RES scale (effort) created by Robertson et al. (2003). This initial proposal was improved upon in 2012, when Colado and colleagues (Colado, Garcia-Masso, Triplett et al., 2012) validated the modified version of the OMNI-RES scale (Robertson et al., 2003) for elastic-band resistance exercises in healthy, young, resistance-trained males. Some years later, the same research group validated a new scale for monitoring the intensity of the perceptual signal of exertion when exercising with this type of elastic device, with this scale including specific verbal descriptors (Colado et al., 2014). This facilitated its applicability to a wider range of populations, notably including those who have difficulty using the classical numerical category scales.

To explain this method in greater detail, training intensity during elastic resistance training is monitored by associating the target number of repetitions (predefined based on a training goal) with the grip width used, and the resulting RPE score is expressed at the end of the set (Colado, Furtado et al., 2020). This means that the subject holds the elastic band, estimating the grip width associated with the previously determined number of repetitions; this is then adjusted to the objective of the training, and the corresponding RPE is expressed at the end of the set. If individuals complete the prescribed repetitions and express a higher RPE than prescribed, they are asked to change the band to a "softer" one or to use a wider grip, according to the requested level of effort. Conversely, a narrower grip or a thicker elastic band is used if participants express a lower RPE than prescribed. It is necessary to remember that the different colors of the elastic bands indicate different band thicknesses; and when changing from one color to another, there is an increase in resistance of approximately 20% to 30% when the band is stretched up to twice its length at rest (Page & Ellenbecker, 2005).

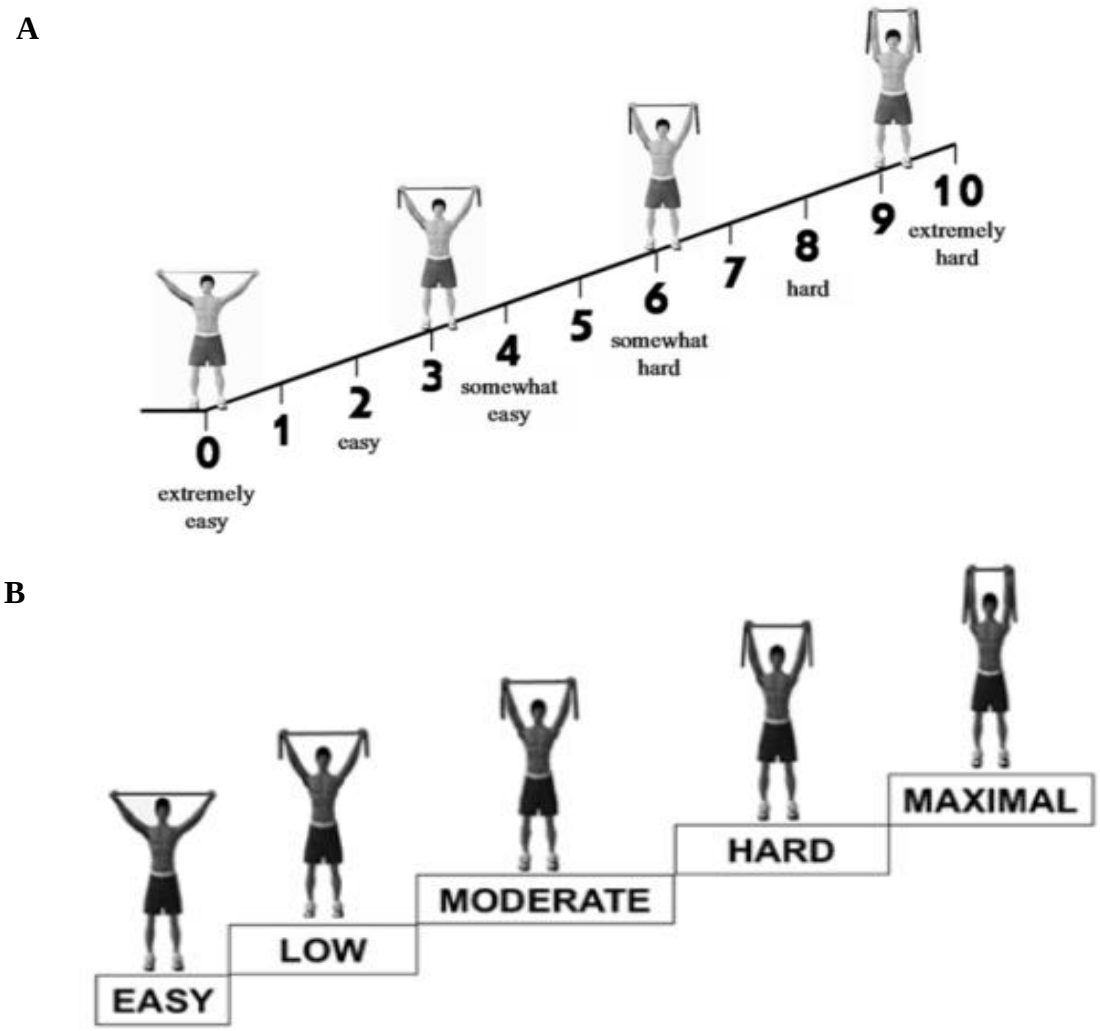
Over the years, this methodology has been widely used for different populations, such as adult women with metabolic syndrome (Flandez et al., 2017), middle-aged and

postmenopausal women (Colado & Triplett, 2008; Colado, García-Masso, Rogers et al., 2012), physically active young adults (Colado et al., 2010), and older adults **(**Chupel et al., 2017; Fritz et al., 2018, 2021; Fukuchi et al., 2016; Gargallo et al., 2018; Gómez-Tomás et al., 2018; Li et al., 2017; Rieping et al., 2019; Smith et al., 2017), but the OMNI-RES for elastic bands was not initially validated for most of these populations. The validation of this type of scale in older adults is especially important, as the perceived exertion can be considered a cognitive function and, as such, it reflects the progressive aging process (Guidetti et al., 2011). Therefore, older individuals differ markedly from young individuals in their willingness and ability to share their experiences (Griep et al., 1998), and cognitive decline could be a determining factor in this, affecting the ability of older adults to link their exercise perceptions with numbers, words, and pictures on an RPE scale (Dunbar & Kalinski, 2004; Groslambert & Mahon, 2006).

For these reasons, Colado et al. (2018) validated the aforementioned method, a pictorial-verbal OMNI-RES scale with elastic bands, for use with female and male older adults (Figure 11), as prescribing and monitoring strength-training intensity using RPE may be particularly beneficial for this population. The authors found a strong positive and linear relationship between RPE and physiological and performance parameters (both heart rate and applied force) in upper-body (shoulder abduction, elbow flexion) and lower-body (hip abduction, hip extension) resistance exercises **(**Colado et al., 2018). In addition, the findings confirm a strong positive and linear relationship between RPE (both general and located) and elastic band grip and physiological or performance parameters (Colado et al., 2018). The "resistance intensity scale for exercise" (RISE; Figure 11), a new perceptual scale with verbal descriptors to control exercise intensity using elastic bands, has been recently validated for use with elderly populations (Colado, Furtado et al., 2020). This new simplified version of the OMNI-RES elastic-band scale enables a more accurate control of intensity in older adults

and can be used for monitoring exercises of any region of the body, regardless of whether they involve global or regional muscle activation. Therefore, the OMNI-RES elastic-band and RISE RPE scales appear to be equally valid metrics for measuring RPE in older adults performing resistance exercises with elastic bands.

Figure 11. *Scales of perceived exertions with elastic bands*.



Note. A. OMNI-RES scale of perceived exertion with elastic bands; B. RISE scale of perceived exertion with elastic bands. Reproduced from "Concurrent and construct validation of a new scale for rating perceived exertion during elastic resistance training in the elderly" (p. 177), by Colado, Furtado et al., 2020, *Journal of Sports Science & Medicine, 19*(1).

This validated methodology was used in both projects of the present PhD dissertation to prescribe, monitor, and control the training intensity in resistance training interventions using elastic bands as the main training device.

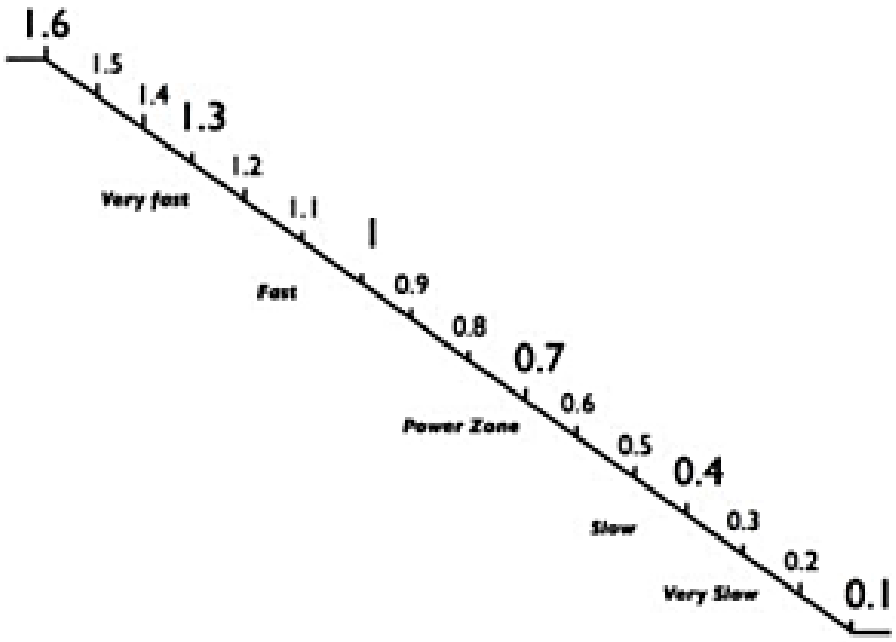
ii. High-velocity training and intensity control through rate of perceived exertion

It is difficult to determine the optimal intensity in high-velocity resistance training interventions performed with elastic bands. To date, only Buskard et al. (2018) has proposed an objective method of determining the optimal tubes (load) in power training performed by young adults with elastic resistance. However, this method is dependent upon establishing the individual's 1 RM and creates a significant technical challenge, making it difficult to apply in large groups (Buskard et al., 2018).

However, one interesting application of the RPE scales involves its use to prescribe intensities when resistance exercises are performed at high velocity. Previous studies have shown that RPE scores are correlated with contraction velocity and muscle power, both in young people **(**Bautista, Chirosa, Chirosa et al., 2014; Bautista, Chirosa, Tamayo et al., 2014; Naclerio et al., 2011; Suzuki et al., 2006) and older individuals (Row et al., 2012; Row Lazzarini et al., 2017). This is due to the association between perceived velocity and real mean velocity of the concentric phase and the muscle power produced. Thus, it is possible to establish the optimal training zone for maximum power output, based on RPEs. For instance, Bautista, Chirosa, Chirosa et al. (2014) found that light intensity (< 40% 1 RM) corresponds to a bar velocity exceeding 1 m/s^{-1} and a verbal perception of velocity of "fast" and "very fast" in the bench press exercise (with young males), while the medium intensity (40% to 70% 1 RM) corresponds to bar velocities of between 0.6 m/s^{-1} and 0.7 m/s^{-1} and verbal instructions in the power zone. Finally, the velocity of the bar for the heavy loads was less than 0.4 m/s^{-1} and verbal descriptions of the velocity were "slow" and "very slow" (Figure 12; Bautista, Chirosa, Chirosa et al., 2014). In another study by the same author, OMNI-RES

scale values of 4-6 corresponded to the maximal power zone, with mean velocities of 0.54 m/s^{-1} to 0.76 m/s^{-1} for the same exercise and population. Therefore, the OMNI-RES scale can be used to control the intensity and velocity of resistance exercise and to predict mean velocity in the bench-press exercise (Bautista, Chirosa, Chirosa et al., 2014).

Figure 12. *Scale of perception of velocity*.



Note. Velocity (m/s represented at the top of the line and perception at the bottom. Reproduced from "Development and validity of a scale of perception of velocity in resistance exercise" (p. 543), by Bautista, Chirosa, Chirosa et al., 2014, *Journal of Sports Science & Medicine*, *13*(3).

Naclerio et al. (2011) established a strong association between RPE, muscle power, and velocity and determined the RPE at which the set should begin with a predetermined load to improve muscular power. The authors indicate that, with a light load of between 30% and 60% of 1 RM, the set should begin with a load that is equated to an RPE of between 1 and 3 (expressed immediately after doing the first repetition) and the set should finish before the subject expresses an RPE value of 4. For heavier loads (60% to 80% 1 RM), RPE should

initially be between 1 and 5, and the set should finish before the subject expresses a value of 6 or 7 (Naclerio et al., 2011). Moreover, the authors determined different ranges of RPE associated with three different strength-training zones (light-load explosive strength, moderate-load explosive strength, and maximal strength), determined by the inferior and superior mean confidence intervals (CIs) of the RPE reported. However, this study was performed with only one multiple-joint upper body exercise (bench press), with only young active males.

However, Row et al. (2012) and Row Lazzarini et al. (2017) have demonstrated that RPE can also be used as an adequate tool for controlling and predicting training intensity for lower (leg press) and upper (chest press) resistance exercises, performed at high velocities by older people. These studies show that loads of between 40% and 60% of 1 RM were equivalent to RPE values of 2-5 (9-12 in a 6-20 RPE scale) for leg press exercises (Row et al., 2012) and 3-6 (10-13 in a 6-20 RPE scale) for chest press exercises (Row Lazzarini et al., 2017). Thus, the intensity of resistance training exercises of the upper and lower limbs performed at high velocity by older adults can be regulated using classic OMNI-RES RPE scales, along with RPE-velocity scales. It is important to note that, in high-velocity resistance training with light loads (40% 1 RM), RPE responses are lower than those reported in resistance training performed with larger loads (80% 1 RM) and low velocity (2-second concentric phase) by older adults (Richardson et al., 2017).

Due to the lack of studies validating the use of RPE in high-velocity strength exercises with elastic bands (despite this being the only method currently available and validated for different populations and several resistance training exercises) it was used in both projects of the present PhD dissertation.

II.IV.III. A view of intensity in resistance training interventions in elderly populations

To produce desirable resistance training adaptations for older adults, world-leading organizations in exercise research have recommended the used of moderate-to-high intensities (60% to 80% 1 RM; Chodzko-Zajko et al., 2009; Fragala et al., 2019; Peterson & Gordon, 2011). In addition, several meta-analyses have provided support for these recommendations when comparing resistance training interventions at different intensities, showing greater gains in muscle strength and muscle mass for higher intensities or loads (Peterson et al., 2010; Steib et al., 2010; Silva et al., 2014). However, these findings of a lower or limited response by the elderly to resistance training at lower intensities may be due to an excess of caution in relation to prescription intensity (in terms of both load and effort), leading to an underestimation of the adaptive capacity of older adults. In fact, several researchers have attempted to challenge this accepted notion that only high intensities can produce substantial adaptations in older adults (Schuenke, Herman & Staron, 2012; Burd et al., 2013; Schoenfeld, 2013a), and they have demonstrated that the problem has been due to a singular focus on load as an indicator of intensity, leaving effort out of the equation. However, when resistance training interventions have been implemented with a low-effort prescription, there have been no significant improvements in any outcome measures (Martins, Safons et al., 2015). In contrast, when light or moderate loads have been applied with a high level of effort, significant improvements are achieved in different health-related outcomes for older adults (Steele et al., 2017). This indicates that light-to-moderate resistance training can provide an excellent stimulus when a set of repetitions is implemented with a high degree of effort. In fact, when resistance training interventions have been matched for mechanical work or effort, improvements are similar for varying intensities (Léger et al., 2006; Alegre et al., 2015).

The message that is often sent to this population is to "just move," but the reality is that optimal and greater stimuli are needed. Movement alone, at low intensities (low load or low effort), may provide only minimal benefits. Interesting articles by Hunter et al. (2017) and Gentil et al. (2017) entitled, "Why intensity is not a bad word," support this conclusion and present an important message about the need for applied higher intensities in resistance training programs for older adults, essentially in terms of effort. Thus, based upon Henneman's size principle of high motor efforts, only three training strategies have been demonstrated effective for activating the mTOR axis, which is related to type II fiber activation in older adults; and these are as follows: resistance training with heavy loads, high-velocity resistance training, and training to muscle failure (Gentil et al., 2017). Thus, high-effort resistance training with heavy or light loads or the application of high muscle-contraction velocities should be considered to reverse and prevent age-related impairments in elderly populations.

It has been suggested that lower exercise intensities may lead to higher adherence rates among older adults, likely due to participants' increased enjoyment of the experience (Ekkekakis et al., 2011; Van Roie et al., 2015). However, as when heavy loads are applied with even low levels of effort, resistance training performed with light loads and high effort presents challenges in terms of adherence and engagement. Fortunately, some studies have demonstrated success in the progressive introduction of higher effort resistance training programs to this population (Fritz et al., 2018; Gargallo et al., 2018; Steele et al., 2017). In addition, despite the undeniable efficacy and safety of resistance training with heavy loads (Csapo & Alegre 2015), the use of low and moderate resistance intensities may make resistance training safer and more accessible for a broader spectrum of the older-adult population. Furthermore, training with smaller loads has been related to a lower RPE, even when the total training load, effort, and volume are matched (Alegre et al., 2015).

In summary, in older adults, positive adaptations through resistance training interventions can be achieved with different intensities (in terms of load), but it appears that, to produce similar adaptations, substantial effort is required when resistance is mobilized, independent of the load applied. When resistance training is prescribed to older adults, the greatest challenge may be in combining efficiency and safety. Using the aforementioned evidence, in the training projects in the present PhD dissertation, training intensity was prescribed in terms of load and effort to obtain the greatest possible adaptations in each of the exercise strategies designed, following the training principle of progression.

II.V. TRAINING MODALITIES

In recent decades, many studies have examined the effects of different exercise modalities in an attempt to identify the training strategy with the greatest possible health-related benefits for older adults (Borde et al., 2015; Byrne et al., 2016; Fragala et al., 2019; Marín-Cascales, Alvaraz, Ramos-Campo & Rubio-Arias, 2018; Marín-Cascales, Alvaraz, Ramos-Campo, Martínez-Rodriguez et al., 2018; Tschopp et al., 2011). In terms of training intensity, it is well accepted that the proper selection of a training modality is key to maximizing the target adaptations in elderly populations. The selected training strategy is a crucial factor for maximizing the performance of a given individual or group, and additional research is needed to better inform relevant professionals of the exercise modality most beneficial for older populations.

Of the different training modalities, three are especially important – not only due to their reported benefits for the elderly population, but also their characteristics, their applicability, and safety factors. These training modalities are multi-component training, power training, and traditional resistance training. Their effectiveness has been analyzed for the present PhD dissertation, and a brief review of each is presented in the following sections.

II.V.I. Multi-component training

Multi-component training – or "multi-modal" (though this term also refers to nutritional and pharmacological interventions; Thompson & Osness, 2004) or "functional" training (though, in this case, it does not have to include certain physical components; Neves et al., 2014) – is defined as a well-rounded exercise program in which capacities such as strength, endurance, balance, coordination, flexibility, and agility are developed in the same session, with the potential to affect a wide range of health-related parameters, such as functional performance and neuromuscular measures in older adults (Bangsbo et al., 2019; Beaudart et al., 2019; Cress et al., 2006; Fragala et al., 2019; Piercy et al., 2018; Zaleski et

al., 2016). Current recommendations suggest that, when a combination of balance, flexibility and coordination exercises is added to traditional strength and aerobic exercises, physical function in older adults can be maintained and increased to a greater extent (Cress et al., 2006).

To be classified as multi-component training, the exercise intervention must include at least a combination of three physical capacities (Bouaziz et al., 2016). The inclusion of just two physical components would comprise "combined" or "concurrent" training. The three most common physical capacities to be combined are strength, endurance, and balance; but the heterogeneity of studies in multi-component interventions is high, and some multi-component training programs include three, four, or five physical components (Bouaziz et al., 2016). In some cases, multi-component programs are designed with a more focused attention on one of these physical components to meet a specific objective (for example, strength in sarcopenic elderly people).

Multi-component training interventions has been applied for a wide range of populations, such as older adults after hospitalization (Echeverria et al., 2020); frail elders (Casas-Herrero et al., 2019; Izquierdo et al., 2019); individuals with fibromyalgia (Araya-Quintanilla et al., 2020); community-dwelling older adults (Binder et al., 2002); healthy older adults (Toraman et al., 2004; Toraman & Sahin, 2004); and older women (Carvalho et al., 2009; Marques et al., 2009). In most of these, as highlighted by the systematic reviews of Bouaziz et al. (2016) and Marín-Cascales, Alvaraz, Ramos-Campo & Rubio-Arias (2018), multi-component training appears to be associated with several health benefits, having a significant impact on cardio-respiratory fitness, metabolic profile, physical function, lean and bone mass, fat mass, cognitive performance, muscle strength, and quality of life of older people with and without frailty. In addition, multi-component programs have other associated

advantages, such as improving long-term adherence by participants and encouraging social interactions between subjects.

In the recent review by Marín-Cascales, Alvaraz, Ramos-Campo & Rubio-Arias (2018), the authors conclude that multi-component training programs are more effective when they are implemented over the period of a year, with benefits appearing after six months. The effectiveness of multi-component training programs has, thus far, been difficult to assess, due to the extensive heterogeneity in the training protocol designs and the intensities, loads, exercises, training devices, and duration applied. As a result, there is no single and standardized multi-component protocol. In fact, few studies have used elastic bands as a training device in this exercise modality for an elderly population.

In summary, this aforementioned body of scientific evidence – along with the recently published WHO framework on healthy aging, which suggests that comprehensive care for older people should be assessed more on the basis of their intrinsic physical and mental capacity (Lopez et al., 2017) than on other clinical manifestations (Beard et al., 2016) – together underline the importance of encouraging older people to participate in well-designed and well-rounded multi-component training programs to manage and improve their strength, endurance, balance, flexibility, coordination, agility. However, further high-quality research analyzing the effects of this type of training are necessary, as most studies to date have been short-term training interventions (< 12 weeks), with small sample sizes. In addition, further investigation is needed regarding the effectiveness of more portable and user-friendly training devices such as the elastic band in multi-component training interventions for older adults.

In the rest of this paper, this training modality will be referred to as "multi-component training," due to the greater specificity of this term than of the multi-modal or functional

training terms. The effects of this training modality on the different parameters analyzed are described in more detail in the following sections.

II.V.II. Power strength training

One exercise intervention that could alleviate age-related impairments in older adults – especially the loss of muscle-power production – is the power training modality. The power training strategy involves completing the concentric phase of a resistance exercise as quickly as possible and the eccentric phase at slower velocities of approximately 2-3 s (Byrne et al., 2016; Evans, 2000; Reid & Fielding, 2012). This type of resistance training emphasizes the need to contract as quickly as possible in the high-velocity movement, using various external resistances (Porter, 2006; Sayers et al., 2016). In the literature, multiple terms are used to refer to this type of training modality. The most common are "power training," "power strength training," "power resistance training," "high-velocity resistance training," "high-speed resistance training," "high-velocity strength training," "high-speed strength training," "explosive resistance training," "high-speed power training," and "high-velocity low-load training." With the exception of the term "high-velocity speed power training," which refers to a specific method that emphasizes high-velocity movements at low external resistances (40% 1 RM; Sayers et al., 2016), these terms can be used interchangeably. In the present PhD dissertation, this training modality will be referred to as "power training," "power strength training," or "high-speed resistance training."

Power training has been recognized as the benchmark in exercise strategies for improving muscle power among older adults, as this parameter is the best predictor of functional performance in this population (Byrne et al., 2016; Cadore & Izquierdo, 2018; da Rosa Orssatto, Cadore et al., 2019). For this reason, muscle power has been proposed as the primary therapeutic target for resistance training interventions aimed at enhancing physical function in later life (Reid & Fielding, 2012; Izquiedo & Cadore, 2014; Sayers 2008). As the

physiological adaptations in response to a training intervention are specific to the resistance training stimulus, following the training specificity principle (Chodzko-Zajko et al., 2009), it has been suggested that high-velocity resistance training should be employed to increase muscle power in older adults (Evans, 2000).

Although muscle strength is an important component of health-related fitness, muscle power appears to be the best neuromuscular indicator of physical function in older adults (Byrne et al., 2016; da Rosa Orssatto, Cadore et al., 2019). Unfortunately, the aging process has a stronger negative effect on muscle power than muscle strength, which may be the result of a reduction in the type II muscle fibers (high threshold) responsible for high-velocity force generation (Aagaard et al., 2010; Cruz-Jentoft et al., 2010; Fielding et al., 2002). In fact, these type II muscle fibers – which generate 4-6 times the power of type I fibers (low threshold) per unit of mass (Trappe et al., 2003) – appear to be more vulnerable than type I fibers to atrophy with aging (Evans & Lexell, 1995). The motor units that originate in the motor cortex of the brain and end in the muscle fiber (Sale, 1987) are recruited based on Henneman's size principle, which stipulates that to recruit high-threshold motor units, lower-threshold motor units must first be recruited (Sale, 1988). Therefore, according to this principle, type I and type II muscle fibers are sequentially recruited. This suggests that high stimulus (in terms of load, effort, or velocity) is needed to achieve maximal motor-unit recruitment. Theoretically, the improvements in muscle power seen in the elderly population due to high-velocity resistance training interventions can be explained as follows: the performance of muscular actions at high velocities involves a greater recruitment of high-threshold motor units than any other training modality (Aagaard et al., 2010).

However, since the first study to investigate the effects of high-velocity resistance training in older adults in 2001 (Earles et al., 2001), several RCTs and meta-analyses have established that power strength training is a successful exercise modality for improving

muscle power and physical function (Steib et al., 2010; Tschopp et al., 2011), muscle strength (Sayers, 2007; Sayers & Gibson, 2010, 2012, 2014), muscle CSA (Claflin et al., 2011), and muscle mass (Bottaro et al., 2007). In addition, power strength training induces less strain on muscles and joints, less fatigue, and lower perceived exertion, making resistance training more tolerable for older adults (Richardson, Duncan, Jimenez, Jones et al., 2018).

Training adaptations achieved by power strength training interventions depend on the prescribed training parameters. Intensity – in terms of load and effort, total volume, exercises selected, type of resistance devices used, and the duration of the training intervention – are all factors to take into account. For instance, recent evidence suggests that both one set and three sets of power training can improve strength and functional performance in older women (Radaelli et al., 2018). High-velocity exercises should be implemented with special attention to reduce the risk of injury and maximize neuromuscular stimuli through correct technique and the avoidance of the deceleration phase (Fragala et al., 2019). Moreover, the ability to generate maximal power in single and multi-joint exercises is dependent on the nature of the movement involved (Cornie et al., 2007; Newton et al., 1996). Thus, the exercises selected may influence the magnitude of the improvements and type of adaptations observed after high-velocity resistance interventions are implemented. Nevertheless, the ability to generate power is not only dependent on the exercises performed, but also on the intensity in terms of load.

While the recommended resistance-training exercise intensity (load) for older adults is 60% to 80% of 1 RM (Ratamess et al., 2009), there is no recommendation for power training in older adults. The evidence suggests that similar neuromuscular and functional adaptations can be achieved by power training across a wide range of intensities (de Vos et al., 2005; Orr et al., 2006; Reid, Martin et al., 2014), from low and through moderate to high. Rather than load, velocity seems to be the key to producing such adaptations. In elderly populations, peak

power has typically been found at or near 70% of 1 RM (Fielding et al., 2002; Sayers & Gibson 2010). However, although power production could be the same at low and high loads, the muscle power developed with lower loads is a better indicator of functional decline in older adults than muscle power produced with higher loads and at lower velocities (Sayers & Gibson 2010). Therefore, even if power output is similar at certain points along a power curve, the different velocities at which power is obtained could be a key factor in functional responses, with certain functional tasks requiring power with a greater velocity component (power at high velocities with low loads), with others requiring power with a greater force component (power at low velocities with heavy loads; Sayers & Gibson, 2010).

Although both low and high loads are effective in producing improvements in muscle power, adaptations occur in different ways. In the case of heavy loads, two main mechanisms have been described. First, due to the positive association between muscle strength and power, increases in maximal strength result in a concurrent improvement in maximal power production (Malisoux et al., 2006; Widrick et al., 2002). Second, according to the size principle for motor-unit recruitment, high-threshold motor units are only recruited during exercises that require near maximal force production (Hannerz, 1974; Henneman et al., 1965, 1974). In the case of light loads, it seems that adaptations are related to the changes in inter-muscular coordination and the rate of neural activation (Cormie et al., 2007; McBridge et al., 2002; Newton et al., 1999; Wisloff et al., 2004).

Although a wide range of intensities have been reported to have positive effects in high-velocity resistance interventions, the literature indicates that there is always a load that elicits maximal power production for the specific movement. This is commonly referred to as the "optimal" load (Dugan et al., 2004; Kawamori & Haff, 2004). Previous research has reported that, in single muscle fibers and single-joint movements, muscle power is maximized at approximately 30% of the maximal force production (Toji et al., 1997; Toji et

al., 2004). However, the load that maximizes muscle power in multi-joint exercises varies depending on the type of movement involved, as previously mentioned. Therefore, the "optimal" load will vary across exercises because power output is influenced by the characteristics of the movement involved. It seems clear that, to optimize muscle power through a high-velocity resistance training modality, regardless of the load used, repetitions should not be performed until concentric failure, which is necessary to avoid muscle fatigue (Gorostiaga et al., 2012). Muscle fatigue may pose safety risks and is not required for neuromuscular adaptations in this kind of training modality (Gorostiaga et al., 2012).

As mentioned above, movement velocity is a key variable in the programming of resistance training interventions, and this is largely influenced by the loading used. In addition, based on the theory of velocity specificity, adaptations following high-velocity resistance training are maximized at or near the velocity of movement used during training (Coyle et al., 1981; Kanehisa & Miyashita, 1983; Moffroid & Whipple, 1970; Narici et al., 1989). However, it has been suggested that training adaptations can be influenced to a greater degree by the intention to move as quickly as possible, regardless of the actual movement velocity produced (Behm & Sale, 1993a). It is believed that the intention to move quickly the load is vitally important during power training, irrespective of the load, movement velocity, or contraction type of the exercises used (Behm & Sale, 1993a; Fielding et al., 2002). However, the literature generally indicates that the actual movement elicits improvements in maximal power (Blazevich et al., 2003; Kaneko et al., 1983; McBridge et al., 2002; Narici et al., 1989). For instance, McBride et al. (2002) report improvements in peak velocity and peak power when squat jumps are performed with the intention of maximal movement velocity at 30% of 1 RM, while this is not the case with high loads (80% 1 RM). Therefore, as both actual and intent movement velocity can independently produce improvements in health-related parameters in older adults, both stimuli are required to elicit the neuromuscular

adaptations that drive performance improvements following high-velocity resistance training. Thus, the development of an effective power training program for older adults must include consideration of the actual and intended velocity of movement involved in the resistance training exercises.

Few studies have used elastic bands as the resistance device in high-velocity resistance training interventions for older adults (Buskard et al., 2018). This may be explained, in part, by the greater complexity of prescribing intensity using elastic bands, compared to free weights and weight machines, where exact loads can be set. However, using the validated OMNI-RES scale for elastic-band resistance training exercises in conjunction with the RPE-velocity scales, intensity could be easily prescribed and controlled, as with the traditional resistance devices.

In summary, a properly designed high-velocity resistance training program for older adults should include an individualized and periodized approach and must involve the use of movement patterns, loads, and velocities that are specific to the demands and characteristics of elderly individuals. The effects of this training modality on the different parameters analyzed are described in more detail in the following sections.

II.V.III. Resistance training

The majority of published data on how exercise affects different health-related parameters in older adults are derived from studies involving resistance training interventions. The resistance training modality, also known as “strength training” and “high-load low-velocity resistance training,” is characterized by exercises in which the subject exerts an effort against an external resistance, usually completing the concentric and eccentric phases at low velocities, with rates of 2-3 s per lifting phase (Chodzko-Zajko et al., 2009;

Papa et al., 2017; Ratamess et al., 2009). It is a safe and effective method, particularly for increasing strength in older adults (Reeves et al., 2004; Vincent et al., 2002).

A growing body of research highlights the favorable neuromuscular adaptations produced by this training modality for both healthy older adults and those with chronic conditions, including increases in muscle strength, muscle power, muscle activation, muscle CSA, RFD, maximum motor-neuron firing frequency, motor control, agonist muscle activation and antagonist muscle coactivation, physical function, and quality of life (Aagaard et al., 2010; Caserotti et al., 2008; Häkkinen et al., 1998a, 1998b, 2000, 2001a). In addition, resistance training mitigates the rate and magnitude of age-related declines associated with balance and BMD and reduces the risk of multiple neuromuscular, metabolic, and cardiovascular chronic diseases, such as type 2 diabetes, heart disease, osteoporosis, and arthritis, while also providing cognitive and psychological benefits (Fragala et al., 2019).

However, as noted by Fragala et al. (2019), despite the widely reported safety of this exercise modality, there are some absolute and relative contraindications to resistance training. Absolute contraindications are primarily cardiac pathologies and they include decompensated heart failure, uncontrolled arrhythmias, severe and symptomatic aortic stenosis, unstable coronary heart disease, acute myocarditis, endocarditis or pericarditis, uncontrolled hypertension, severe pulmonary hypertension, and aortic dissection. High-intensity resistance training (80% to 100% 1 RM) is contraindicated in individuals with active proliferative retinopathy or moderate or worse non-proliferative diabetic retinopathy (Fragala et al., 2019). Relative contraindications include diabetes, low functional capacity, major risk factors for cardiovascular diseases, musculoskeletal limitations, and implanted pacemakers or defibrillators (Ghadieh & Saab, 2015; Whelton et al., 2018).

Although the benefits of resistance training for older adults are well-known, additional research is needed to better understand the effects of this training strategy when performed with elastic bands, at different intensities, and compared with other novel training modalities (such as multi-component or high-velocity resistance training). In the rest of this paper, this training modality will be referred to as "resistance training" or "strength training." In addition, the effects of this training modality on the different parameters analyzed are described in more detail in the following chapters.

II.VI. OXIDATIVE STRESS, FREE RADICALS AND REDOX BIOLOGY

II.VI.I. Free radical, reactive oxygen species, and mitochondrial electron transport chain

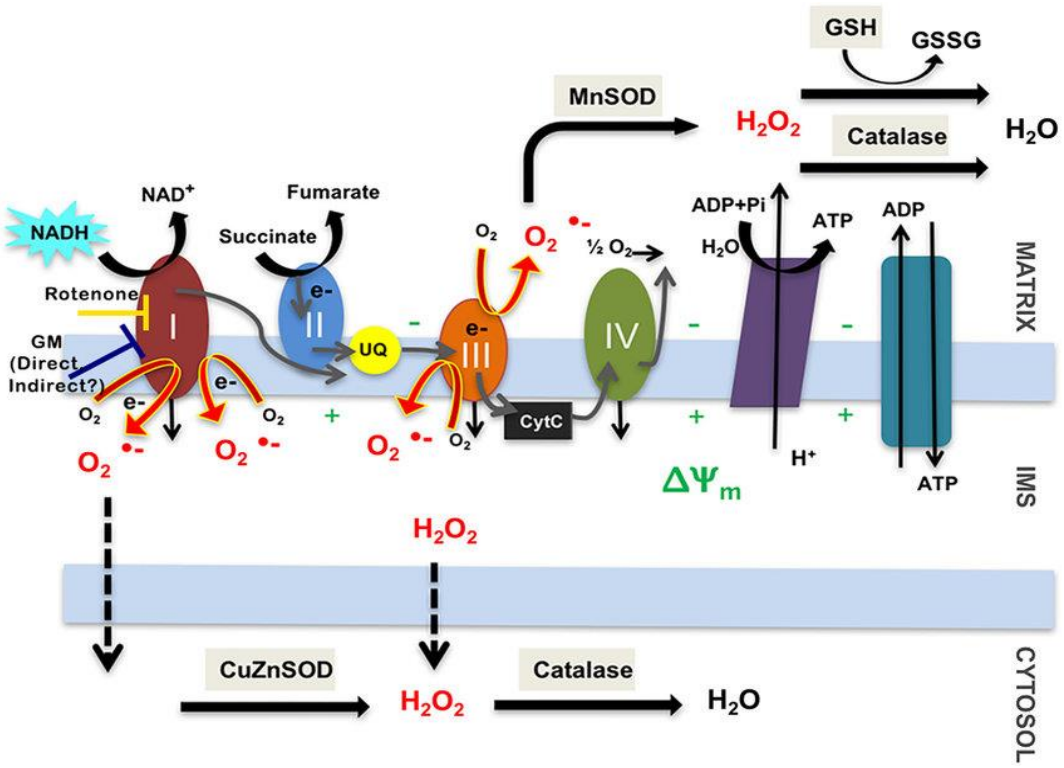
Free radicals, first described by Moses Gomberg in 1900 (Gomberg, 1900), are molecules that contain one or more unpaired electrons in their outer orbital shell (Slater, 1984), making them highly unstable and reactive. Initially, they were not considered to be present in living organisms due to their short lifespan (Lushchak, 2014; Simic & Taylor, 1988). Until Commorer et al. (1954) provided the first proof that they were found in living organisms, it was assumed that free radicals played a deleterious role in biological systems. In recent decades, new evidence has highlighted their important role in the signaling of important biological pathways (Babior et al., 1973, Furchgott & Zawadzki, 1980).

While non-radical molecules typically contain paired electrons in their valence shell, they are nevertheless chemically reactive and can interact with other molecules to form free radicals (Halliwell, 1987). However, most free radicals found in living organisms either are or originate from oxygen or nitrogen compounds, namely reactive oxygen species (ROS) or "reactive nitrogen species" (RNS; Cooper et al., 2002, Fisher-Wellman & Bloomer, 2009).

ROS, the collective term that refers to both free radicals and non-radical oxygen (O_2; Aruoma, 1998; Cheeseman & Slater, 1993), includes oxygen-based radicals such as superoxide (O_2•−), hydroxyl (•OH), and hydroperoxyl (HO_2•; Aruoma, 1998; Di Meo et al., 2016; Dröge, 2002), as well as some derivatives of oxygen that do not contain unpaired electrons, such as hydrogen peroxide (H_2O_2) and lipid peroxides. RNS includes nitrogen dioxide nitric (NO_2•), nitric oxide (NO•), and derivatives of nitric oxide, such as peroxynitrite (Cooper et al., 2002; Di Meo et al., 2016; Halliwell, 1987; Patel et al., 1999). ROS and RNS are collectively referred to as "reactive oxygen and nitrogen species" (RONS).

Although oxygen is necessary for the life of aerobic organisms, it is also detrimental to them because its molecular structure allows it to act as a terminal oxidant in the mitochondrial respiratory chain (Figure 13). In fact, the human body produces RONS as a by-product of numerous biochemical and physiological processes, but primarily as a result of aerobic metabolism (Uttara et al., 2009).

Figure 13. *mtROS and electron transport chain.*



Note. Reproduced from "Aminoglycosides rapidly inhibit NAD (P) H metabolism increasing reactive oxygen species and cochlear cell demise" (p. 10), by Desa et al., 2018, *Journal of Biomedical Optics, 24*(5).

Mitochondria are the major intracellular source of ROS in the majority of eukaryotic cells. They consume nearly 95% of the total oxygen in the process of producing oxidative phosphorylation and cellular adenosine triphosphate (ATP; Brown, 1992), during which the

flow of electrons down the respiratory chain eventually culminates in the reduction of molecular oxygen to water at complex IV (Comporti et al., 2008).

However, it is estimated that, in this process, 2% to 5% of oxygen consumption can be reduced via a univalent pathway even under normal conditions, leading to the formation of reactive intermediates such as superoxide anion (O_2•−), hydrogen peroxide (H_2O2), and hydroxyl radical (•OH), especially during the electron flow through the Q cycle in complex III (ubiquinone-cytochrome c reductase) or in the reverse electron transport at the level of complex I (NADH dehydrogenase; Castro & Freeman, 2001; Holmström & Finkel, 2014; Murphy, 2008; Turrens, 2003). Under normal metabolic conditions, complex III is the main site of ROS production.

RONS play a crucial role in the normal functioning of the human body, as they are involved in basic activities such as the control of cell signaling pathways and regulation of gene expression (Di Meo et al., 2016; Powers, Talbert & Adhihetty, 2011; Uttara et al., 2009; Valko et al., 2007). However, they can also be deleterious, causing oxidative damage in biomolecules when there is an overproduction of free radicals or when the reduction-oxidation (redox) regulation of the physiological processes is affected (Valko et al., 2007).

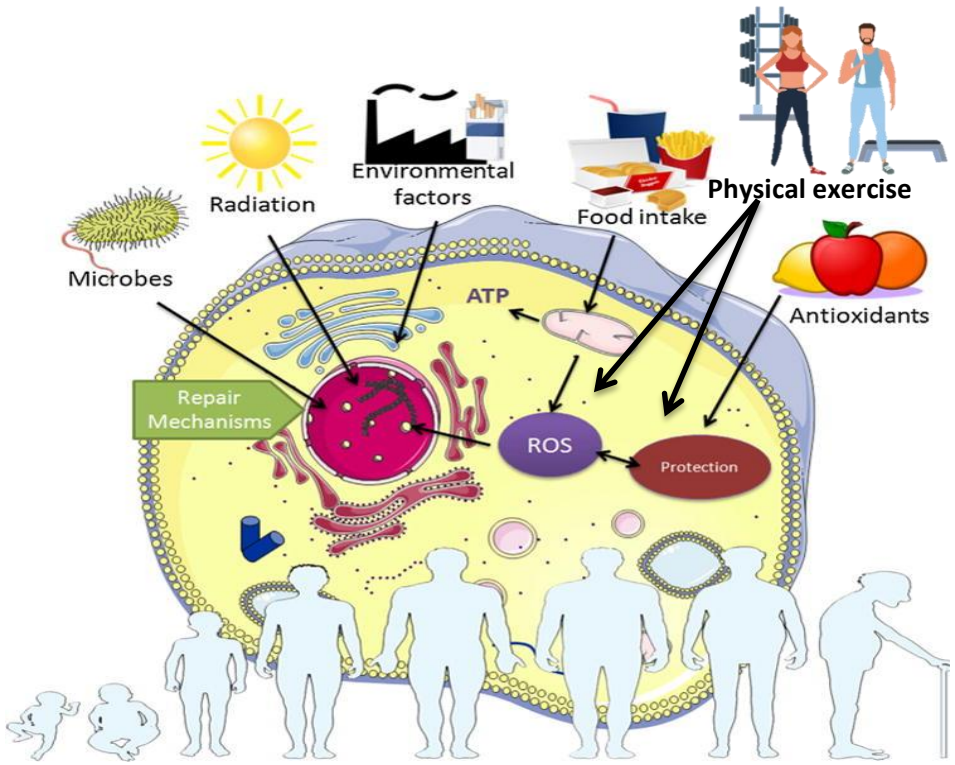
The three main classes of biological macromolecules susceptible to free radical attack or oxidative stress are nucleic acids, lipids, and proteins (Beckman & Ames, 1998; Bokov et al., 2004; Sies, 1983). It is well documented that the alteration of these molecules by RONS contributes to the pathogenesis of conditions such as cancer, hypertension, diabetes mellitus, atherosclerosis, cardiovascular diseases, and neurodegenerative diseases (Valko et al., 2007). For this reason, part of the focus of this PhD dissertation pertains to the effect of physical exercise on certain ROS biomarkers of nucleic acids, lipids, and proteins.

A. Sources of reactive oxygen species

The sources of ROS in cells may be classified as endogenous and exogenous (Finkel & Holbrook, 2000; Freeman & Crapo, 1982; Frei, 1994). Endogenous ROS are generated inside the cell. Although mitochondria are thought to be the main endogenous source of ROS, others have been identified, including the metabolism of lipid oxidation within peroxisomes (Antonenkov, 2010), the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system of leucocytes (Babior, 2004), cytochrome P450 oxidase (Zangar et al., 2004), and the enzymatic synthesis of nitric oxide and xanthine oxidase (McCord, 2000). Along with the mitochondria, the endogenous sites of free-radical formation are the plasma membrane, sarcoplasmic reticulum, and phospholipase (Inoue et al., 2003; Morgan & Liu, 2010).

In addition to the intrinsic ROS generation in the body, humans are constantly exposed to exogenous sources of ROS such as ionizing (X-rays and γ-rays) radiation, ultraviolet light, some metals, environmental pollutants, pesticides, tobacco smoke, some pro-oxidant compounds ingested with the diet, chemotherapeutics, xenobiotics, heat shock, psychological stress, and mechanical and physiological stress induced by exercise (Ames, 1983; Cadenas & Sies, 1998; Ermak & Davies, 2002; Fisher-Wellman & Bloomer; Moller et al., 1996; Valko et al., 2006). Figure 14 illustrates some of the exogenous stress factors that produce the cumulative effect of ROS over a lifetime.

Figure 14. *Exogenous sources and cumulative effect of ROS over life time.*



Note. Reproduced and adapted from "A synopsis on aging—Theories, mechanisms and future prospects" (p. 93), by da Costa et al., 2016, *Ageing Research Teviews, 29.*

II.VI.II. Oxidative stress

A. Concept of oxidative stress

The term "oxidative stress" was first defined in 1985 by Helmut Sies as "disturbance in the pro-oxidant-antioxidant balance in favor of the former" (Sies, 1985). It has been suggested that this term should be redefined as "a disruption of redox signaling and control" (Jones, 2006). More recently, Helmut Sies and Dean Jones have proposed a definition of "an imbalance between oxidants and antioxidants in favor of the oxidants, leading to a disruption of redox signaling and control and/or molecular damage" (Sies, 2007; Sies & Jones, 2007).

Oxidative stress is associated with beneficial or at least nondetrimental effects such as the modulation of gene expression and the regulation cell signaling pathways (Davies, 2000),

and antioxidant defenses can effectively regulate the levels of RONS. However, it has been also associated with the aging process (Harman, 1956) and many disease pathologies (Butterfield et al., 2006; Ceriello & Motz, 2004; Dhalla et al., 2000; Seven et al., 2008) when there is a constant imbalance in the redox state in favor of the oxidants products, leading to a disruption of redox signaling or molecular damage. It has been argued that the increase in oxidative stress could be the result of four different factors: an increase in RONS production, a decline in antioxidant defenses, a combination of both previous conditions at the same time, and an impaired ability to repair or remove damaged molecules (Sohal & Weindruch, 1996).

Lushchak (2014) proposes a theoretical classification of oxidative stress that represents its intensity at four levels: basal, low intensity, intermediate intensity, and high intensity. At the basal level, RONS and antioxidants are in balance, as the oxidative stress is negligible. At low intensity, there is an adaptive response because RONS are able to overwhelm the antioxidants, but the imbalance is not damaging at this level. At intermediate intensity, there is a combined response of damage and adaption to cellular components, whereas high intensity involves cellular apoptosis and necrosis. This theoretical classification bears a similarity to the free radicals hormesis theory proposed by Radak et al. (2005).

When there is a substantial pro-oxidant shift in the balance between RONS and antioxidants, one very harmful effect is oxidative damage to macromolecules – primarily to lipids, proteins, and nucleic acids, as their physiological functions are altered and impaired (Bokov et al., 2005)

B. Oxidative stress products

As mentioned above, the impairment caused by ROS includes damage in the nucleic acids, lipids, and proteins macromolecules (Birben et al., 2012), which results in DNA, lipid,

and protein oxidation (Finaud et al., 2006). The following section provides a detailed explanation of these damages.

i. DNA oxidation

In the 1990s, the first study of DNA damage caused by the accumulation of ROS due to aging was published (Richter et al., 1988). RONS can cause oxidative stress damage to both nuclear DNA (nDNA) and mitochondrial DNA (mtDNA), though the latter is more vulnerable due to several factors: lack of histones (Backer & Weinstein, 1980; Richter et al., 1988), less efficient repair mechanisms (Suter & Richter, 1999; Yu, 1994), and the fact that mitochondria are the main producer of oxygen-derived free radicals (Garcia-Ruiz et al., 1995; Yu, 1994).

Chronic stress produces DNA damage through different mechanisms, such as the degradation of base, single-, and double-stranded DNA breaks and purine, pyrimidine, or sugar-bound modifications, mutations, deletions, or translocations, with defective DNA transcription and translation leading to the synthesis of less protein or defective protein (Barzilai & Yamamoto, 2004; Cooke et al., 2003; Kong & Lin, 2010; Sies et al., 1985). This DNA damage has been implicated in several neurodegenerative diseases (Murata et al., 2008) and various cancers, such as colorectal (Oliva et al., 1997), hematologic (Ivars et al., 2017), gynecologic (Sanchez et al., 2006), metabolic (Cerdá et al., 2014), and digestive (Borrego et al., 2013).

Of the four DNA bases, guanine has been indicated as the most prone and most abundant site of DNA mutagenic lesions (Loft & Poulsen, 1996; Wilson et al., 2003), due to its low oxidation potential (Kawanishi et al., 2001). Although DNA oxidation produces more than 20 by-products (Fraga et al., 1990), the 8-oxo-dG product produced by guanine oxidation is the marker most commonly used to assess DNA oxidative modifications (Ames

et al., 1993; Bokov et al., 2004; Cooke et al., 2006; Finaud et al., 2006; Richter et al., 1988; Valavandis et al., 2009).

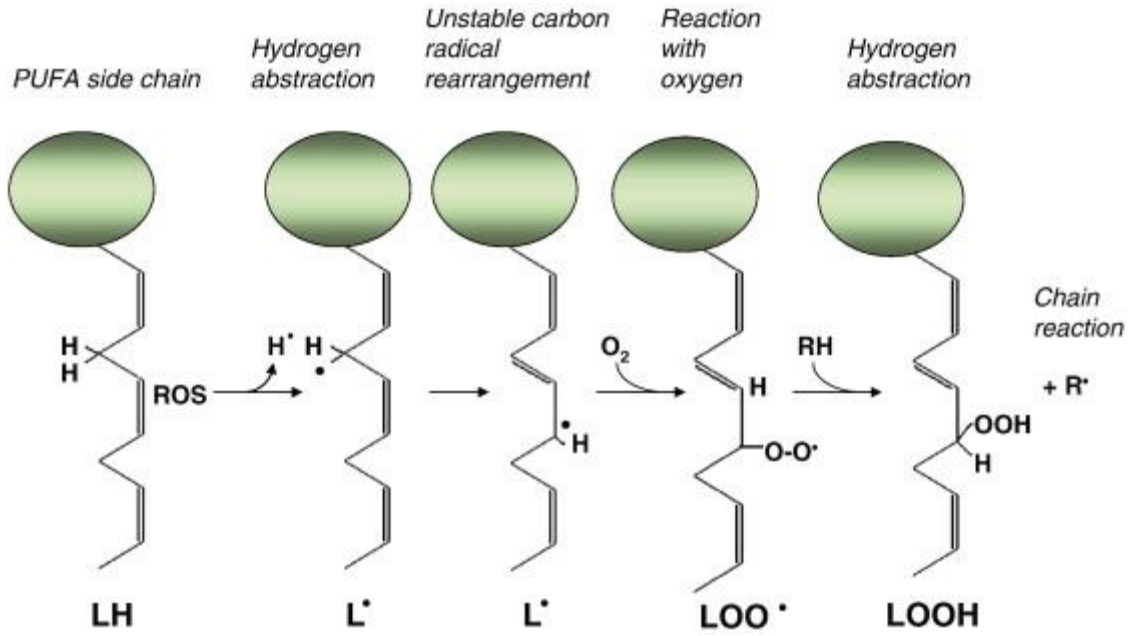
The 8-oxo-dG is excreted via the blood and urine (Finaud et al., 2006). An important characteristic is that it does not experience degradation once in circulation (Cathcart et al., 1984; Cooke et al., 2008; Shigenaga et al., 1989) and, as such, it is considered a stable marker for the examination of DNA damage. Indeed, it is also considered to be a biomarker of "whole body" DNA damage (Guetens et al., 2002).

ii. Lipid peroxidation

Cells contain in their membranes a vast quantity of lipids, especially polyunsaturated fatty acids (PUFAs; Coskun & Simons, 2011). The lipids are the biomolecules most susceptible to oxidative degradation (Halliwell & Chirico, 1993; Niki, 2009) in a process referred to as "lipid peroxidation" (Burton & Traber, 1990; Cheeseman & Slater, 1993; Rikans & Hornbrook, 1997; Vasilaki & McMillan, 2012), with PUFAs the most prone to this process (Gardner, 1989).

In the lipid peroxidation process, PUFAs are particularly susceptible to becoming attached to hydroxyl radical, the most prominent ROS involved in the process of lipid peroxidation (Ayala et al., 2014), while other oxidants facilitate the abstraction of the hydrogen atom due to their double bonds (Cheeseman & Slater, 1993; Gaschler & Stockwell, 2017; Halliwell & Chirico, 1993) that contain methylene carbon groups in their biochemical structure (Vasilaki & McMillan, 2012), which produce lipid peroxyl radicals upon attack (Kanti Das et al., 2014). These radicals contribute to the spreading of the lipid peroxidation chain reaction by pulling out hydrogen from proximal fatty acid side chains (Figure 15; Barnham et al., 2004, Davies, 2000; Halliwell, 1994; Halliwell & Chirico, 1993).

Figure 15. *Lipid peroxidation process on PUFA side chain.*



Note. Reproduced from "Oxidative risk for atherothrombotic cardiovascular disease" (p. 1686), by Leopold and Loscalzo, 2009, *Free Radical Biology and Medicine, 47*(12).

As a result, the lipid peroxidation damage modulates lipid metabolism (Fuhrman et al., 1995) and can lead to the rearrangement of the membrane lipid bilayer, hence inactivating membrane-bound receptors and enzymes by forming protein cross-linkages (Esterbauer et al., 1984), ultimately altering fluidity, permeability, and functioning of cell membranes (Gaschler & Stockwell, 2017; Giugliano et al., 1996; Nikolaidis et al., 2011). In addition to damaging cells by destroying membranes, lipid peroxidation can trigger a chain reaction that causes further damage to proteins and DNA through the reactive intermediate products (Hulbert et al., 2007; Niki et al., 2005). Accordingly, excess lipid peroxidation is associated with numerous diseases (Barrera, 2012; Pillon et al., 2011; Pillon et al., 2012; Sayre et al., 1997).

As lipids break down due to oxidation, multiple lipid peroxidation primary products and by-products are formed. These include conjugated dienes, lipid hydroperoxides, and aldehydes of short (MDA, 4-hydroxynonenal [4-HNE]) and long chains (F2-isoprostanes;

Buettner, 1993; Cheeseman & Slater, 1993; El-Aal, 2012; Frankel, 1984; Freeman & Crapo, 1982; Halliwell, 1994; Niki, 2009).

From all of these products, MDA and 8-iso-P are two of the most representative and useful biomarkers for the measurement of age-related lipid peroxidation, as they increase their levels with age (Bokov et al., 2004; Roberts & Reckelhoff, 2001) and are involved in aging-related disorders (Barrera et al., 2018; Frei, 1994). Furthermore, 8-iso-P is regarded as one the most reliable measures of lipid peroxidation (Dalle-Donne et al., 2006). These lipid peroxidation products can be valuable for the measurement of oxidative stress in different biological tissues (Dalle-Donne et al., 2006).

iii. Protein oxidation

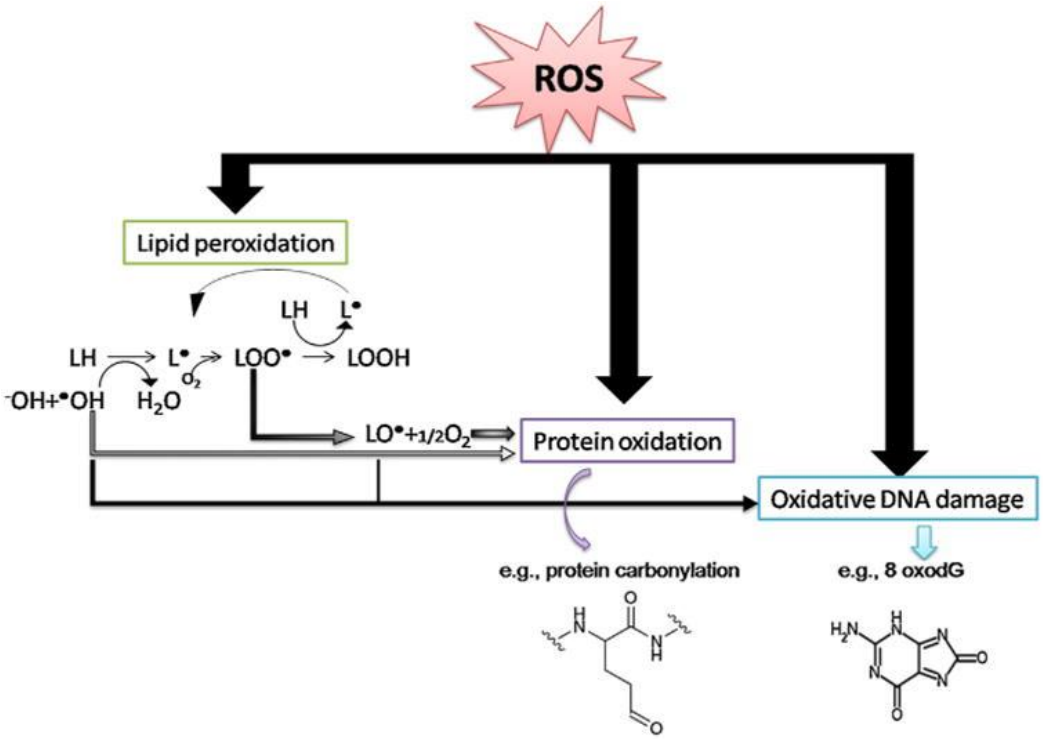
The abundance of proteins in biological systems and their essential role in biological processes makes them the major targets for RONS (Dalle-Donne et al., 2006; Levine & Stadtman, 2001). Indeed, proteins scavenge the majority (50% to 75%) of produced RONS (Dalle-Donne et al., 2006; Davies et al., 1999). Sustained oxidation of proteins by reactive radicals can result in modifications of the protein side chains, fragmentation of peptide bonds (Chakravarti & Chakravarti, 2007), protein inactivation (Dhalla et al., 2000), production of protein-protein cross linkage (Stadtman, 2006), and structural unfolding and conformational changes (Davies, 2005). The major issue is that protein damage is frequently irreparable and irreversible and very often leads to a loss of structural function in the affected proteins (Dean et al., 1993; Levine & Stadtman, 2001).

Modification of proteins by RONS leads to the formation of different protein adducts such as dityrosine, as well as protein-protein cross linking and protein carbonyl groups. Protein carbonyl products are the result of the carbonylation process by which amino acids such as lysine, threonine, proline, and arginine are irreversibly oxidized to carbonyl derivates

(Stadtman, 1992). These protein carbonyl products are among the most stable of all the adducts formed by interaction between RONS and biomolecules (Dalle-Donne et al., 2003), as the reference biomarker for protein oxidation.

The carbonylation process has been shown to increase after 60 years of age (Oliver et al., 1987), and it has been proposed that this mechanism is one of the most relevant in the development of various diseases during the aging process (Goswami et al., 2006; Stadtman et al., 1992). However, it is not the only mechanism. Another reason for the higher levels of oxidized proteins during aging is that degradation capacity is lessened with age (Dean et al., 1993; Stadtman, 2006) **a**nd the oxidized proteins that need to be degraded continue to accumulate in the organism (Berlett, 1997). As a result of oxidative stress, almost one-third of the proteins of old animals are dysfunctional (Poon et al., 2004). In Figure 16, we see the oxidative damage to the three primary macromolecules and ROS products.

Figure 16. *DNA, lipid and protein oxidative damage by ROS species.*



Note. Reproduced and adapted from "A synopsis on aging—Theories, mechanisms and future prospects" (p. 93), by da Costa et al., 2016, *Ageing Research Reviews, 29.*

II.VI.III. Antioxidant system

A. Role and classification of cellular antioxidant systems

Counterbalancing the reactivity of RONS, human beings have developed an elaborate system of antioxidant defense as a protective mechanism (Birben et al., 2012; Sardesai, 1995).

There are multiple definitions of the term "antioxidant," but the best known is that of Halliwell and Gutteridge, namely, "any substance that, when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate" (Halliwell, 1990; Halliwell & Gutteridge, 1990,1995; Sies, 1993).

The antioxidant system includes different types of antioxidants. These can be classified based on various criteria. From the biochemical point of view, the antioxidant network includes enzymatic and non-enzymatic antioxidants (Valko et al., 2007). Enzymatic antioxidants include SOD, GPx, and CAT, while non-enzymatic antioxidants include uric acid, lipoic acid, melatonin, bilirubin, ascorbate, pyruvate, taurine, flavonoids, carotenoids, coenzyme Q10, vitamins C and E, and – perhaps the most well-studied and best-known – glutathione (Castro & Freeman, 2001; Halliwell & Gutteridge, 1990; Masella et al., 2005; Sardesai, 1995; Sies & Stahl, 1995)

In terms of the source or location, antioxidants can be classified as either endogenous or exogenous. Endogenous antioxidants are synthesized in vivo by the organism, and these include SOD, GPx, CAT, and glutathione; while exogenous antioxidants are not produced by the human body and instead come from the environment, primarily the diet. Examples of exogenous antioxidants include vitamins C, E, B1, B2, B6, as well as folic acid, carotenoids, and polyphenols (Comhair & Erzurum, 2002).

Finally, the cellular physiology criteria indicate three groups of antioxidants: primary, secondary, and tertiary. The first of these limits the formation new products of free radicals, converting existing free radicals into less damaging molecules. This group comprises SOD, CAT, GPx, and metal binding proteins (Halliwell & Gutteridge, 1990; Matés et al., 1999). The second group is comprised of non-enzymatic defenses such as glutathione, albumin, bilirubin, uric acid, vitamins C and E, natural flavonoids, carotenoids, and melatonin (Halliwell & Gutteridge, 1990; McCall & Frei, 1999). They play an important role in preventing chain reactions where there is an excess of free radicals and enzyme systems are oversaturated. Tertiary antioxidants also play an important role in repairing biomolecules damaged by free radicals. This group includes methionine sulfoxide reductase, phospholipase $A_{2,}$ and DNA repair enzymes, among others (Demple & Halbrook, 1983; Dizdaroglu, 1993; Sevanian & Kim, 1985).

It is important to highlight that all antioxidants work in conjunction synergistically and in combination with each other to protect biomolecules against damage caused by RONS, thus maintaining the redox balance. Antioxidants have different mechanisms for decreasing oxidative damage (e.g., reducing oxidized substrates [Nordberg & Arner, 2001], stimulating the transcription of other antioxidant systems [Burke-Gaffney et al., 2005], intercepting attacks by RONS [Halliwell & Gutteridge, 1995]), but their effect depends on the type of ROS produced, the location and manner in which they are generated, and the purpose of the damage measured (Halliwell & Gutteridge, 1995).

In the following section, enzymatic and non-enzymatic antioxidants are further explained in terms of their implications for this PhD dissertation.

B. Endogenous enzymatic antioxidants

The primary endogenous enzymatic antioxidant sources include SOD, CAT, and GPx (Gomes et al., 2012; Sardesai, 1995). The enzymatic antioxidant system demonstrates their antioxidant activity either by inhibiting activities of the RONS (catalyzing the one-electron reduction of RONS; Jezek & Hlavata, 2005; Meister & Anderson, 1983; Yu, 1994) or by eliminating these reactive species (Sies, 1997).

i. Superoxide dismutase

SOD, discovered by McCord and Fridovich (1969a), represents a family of metalloenzymes that act as a catalyst for the dismutation of the superoxide radical (O_2•−) to form dioxygen (O_2) and the less-reactive hydrogen peroxide (H_2O_2; Figure 17; Finaud et al., 2006; Palomero & Jackson, 2010). Therefore, SOD typically appears near sites of active O_2•− (Treweeke et al., 2012), as it is the major defense against O_2•− and the first line of defense against oxidative stress.

Figure 17. *Conversion of superoxide ions to molecular oxygen and peroxide by SOD.*

$$2O_2\bullet^- + 2H^+ \rightarrow O_2 + H_2O_2$$

Several forms of this antioxidant have been described, depending on the metallic prosthetic group bound to the enzyme and their location (Fridovich, 1975; Marklund et al., 1982; Sardesai, 1995). The three isoforms of SOD – indicating the metal ion in the active site – are as follows: copper-zinc SOD (Cu/ZnSOD or SOD1), manganese SOD (MnSOD or SOD2), and iron SOD (FeSOD; Fridovich, 1975). Cu/ZnSOD is primarily located in the cellular cytosol and in a small portion of the intermembrane mitochondrial space (Weisiger & Fridovich, 1973). MnSOD is predominant in the mitochondria matrix (Weisiger & Fridovich, 1973), while FeSOD is located in the cytosol, glycosomes, and mitochondria. Importantly,

the activity of this kind of antioxidants depends on the nutritional availability of the so-named antioxidant minerals: manganese, selenium, zinc, and copper (Sardesai, 1995).

An additional and more recently characterized isoform of SOD is the extracellular SOD isoenzyme (ecSOD or SOD3; Marklund et al., 1982), which is present in the extracellular fluids and interstitial spaces of many cell types and tissues (Culotta et al., 2006; Zelko et al., 2002). SOD3 accounts for the majority of the SOD activity in plasma, synovial fluid, and lymph (Mates, 1999; Mates, Pérez-Gómez & De Castro, 1999).

ii. Catalase

H_2O_2 produced from SOD, is toxic and needs to be removed. CAT, an iron containing enzyme found primarily in peroxisomes acts to reduce H_2O_2 to water (H_2O) and oxygen (O_2) (Bai & Cederbaum, 2001; Finaud et al., 2006) (Figure 18). This antioxidant contains a heme in its active site responsible for its catalytic activity (Michiels et al., 1994).

Figure 18. *Conversion of two hydrogen peroxide molecules into water and oxygen by action of CAT.*

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

Although both CAT and GPx have a similar primary function of decomposing H_2O_2 to H_2O, CAT is more efficient at a lower H_2O_2 concentration (Antunes et al., 2002; Jenkins & Goldfarb, 1993). CAT can be found in cell structures that use oxygen to detoxify toxic substances, as well as in mitochondria, cytosol, and other intracellular organelles (Antunes et al., 2002; Bai & Cederbaum, 2001).

iii. Glutathione peroxidase

The GPx enzyme is a selenoprotein with four identical subunits (tetrameric structure), each containing one atom of selenium as a selenocysteine involved in the catalytic activity (Michiels et al., 1994). It is primarily located in the mitochondria and in cytosol (Antunes et al., 2002; McCord, 2000). As CAT, GPx catalyzes the reduction of hydrogen peroxide to water (Antunes et al., 2002; McCord, 2000), as well as the reduction of lipid hydroperoxides to their corresponding alcohols (Imai & Nakagawa, 2003). GPx and CAT have the same action on H_2O_2, but GPX is thought to be more efficient in higher ROS concentration (Antunes et al., 2002; Jenkins & Goldfarb, 1993).

However, in the GPx reaction to the neutralization of H_2O_2, GSH is used as a cofactor and converted into its oxidized form: GSSG (Figure 19; Flohe & Brand, 1969). Adequate function of GPx requires the regeneration of GSH from its oxidative product, GSSG (Ji, 1995). This process is dependent upon sufficient NADPH availability (Bloomer, 2008; Figure 20), and it is very important for protecting mammalian cells against oxidative damage. In fact, this reaction ensures that cells are kept in a reduced environment, which is essential for the function for many enzymes, cofactors, and molecules, as the GPx metabolism is an essential anti-oxidative defense mechanisms (Rikans & Hornbrook, 1997).

Figure 19. *Conversion to hydrogen peroxide and reduced glutathione molecules into water and oxidized glutathione by action of GPx.*

$$2\ GSH + H_2O_2 \rightarrow GSSG + 2H_2O$$

Figure 20. *Reaction of regeneration of reduced glutathione from its oxidative form by action of GPx.*

$$GSSG + NADPH + H_+ \rightarrow 2\ GSH + NADP_+$$

C. Endogenous non-enzymatic antioxidants

Non-enzymatic antioxidants, also called "secondary antioxidants," are indispensable when enzyme defenses are ineffective or completely lacking certain type of RONS (Sardesai, 1995), such as singlet oxygen and •OH. As mentioned previously, there are different kinds of non-enzymatic antioxidants, but due to their relevant role in the antioxidant system and the implications for this PhD dissertation, we will focus on glutathione.

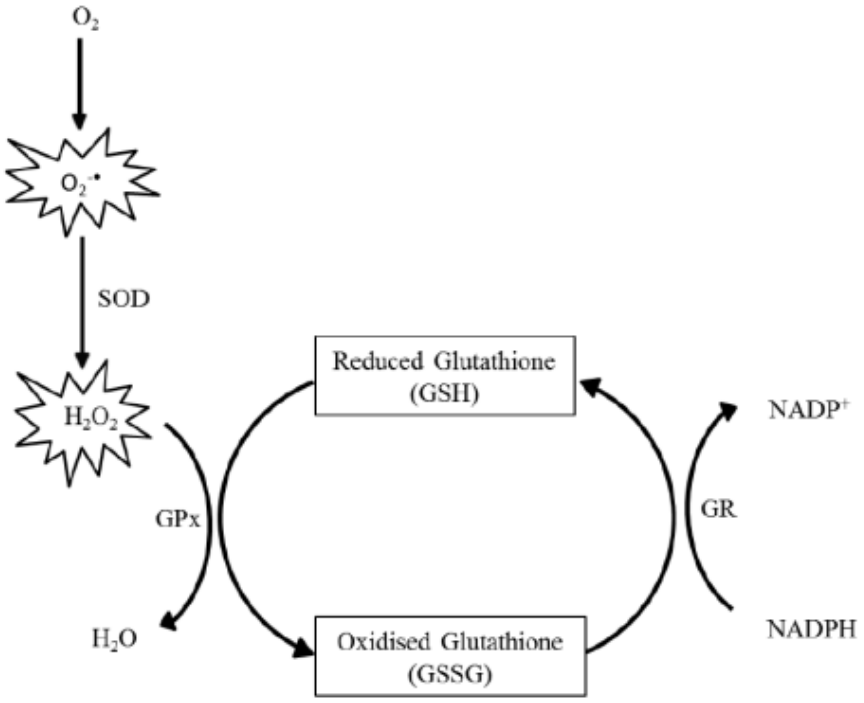
Glutathione was discovered in 1921 by Sir Frederic Gowland Hopkins. Today, it is well-known as one of the most important non-enzymatic antioxidants and the most abundant non-protein thiol synthesized intracellularly by the mammalian cells (Meister & Anderson, 1983). In other words, it is the most abundant antioxidant in the body (Kim & Vaziri, 2010). It is present in almost all mammalian tissues and produced in all organs – the highest rate of production being in the liver (Radak, 2000). The cytosol is the largest reservoir of glutathione in the eukaryotic cells (90%), followed by the mitochondria and the endoplasmic reticulum (Franco et al., 2007).

The molecular structure is a ubiquitous tripeptide: γ-glutamyl cysteinyl glycine. This structure – formed by glutamic acid, cysteine, and glycine – makes glutathione essential for a multitude of cellular functions, such as protein synthesis redox signaling (Ochoa, 1983), cell biogenesis (Terradez et al., 1993), DNA synthesis (Suthanthiran et al., 1990), absorption of amino acids in several tissues (Viña et al., 1989), calcium homeostasis (Bellomo et al., 1982), immunity modulation (Sies, 1999), and of course protection against oxidative stress (Sies, 1986).

There are two forms of glutathione, depending on its oxidation or reducing state: GSH and GSSG (Hwan et al., 1992). In relation to the antioxidant function of glutathione, GSH provides a first line of defense against ROS, as it reduces the endogenously produced H_2O_2 using the selenium-dependent enzyme GPx (Pastore et al., 2003; Powers & Jackson, 2008).

As a result, GSH is oxidized to GSSG, which in turn is reduced back to GSH by GSSG reductase, at the expense of an electron from NADPH, forming a redox cycle (Halliwell & Gutteridge, 2015; Lu, 1999; Meister & Anderson, 1983; Radak, 2000). To maintain a constant intracellular GSH concentration, GSH is synthetized by its constituent amino acids in the cytosol of virtually all cells (DeLeve & Kaplowitz, 1991). Therefore, the redox cycle of the glutathione comprises two reactions (Masella & Mazza, 2009): one reduces H_2O_2 where the presence of the GPx is necessary as a cofactor, and the other prevents the repletion of GSH and reduces the GSSG, where NADPH is needed as a reducing agent cofactor (see Figure 21).

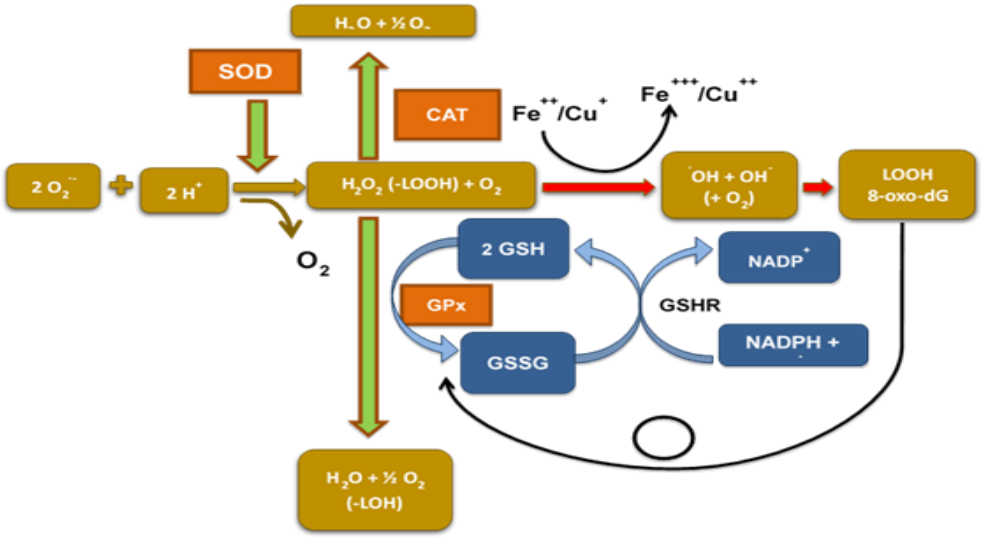
Figure 21. *Glutathione redox cycle.*



However, GSH plays a multifunctional role in protecting tissues from oxidative damage, not just reducing H_2O_2 but also for instance, tocopherol radicals either by directly or indirectly reducing semidehydroascorbate radicals (preventing lipid peroxidation) and acting as a scavenger of singlet oxygen and •OH (Ji, 1995). In addition, due to its nucleophilic

properties GSH can act as a direct free radical scavenger interacting with O_2^{-}• and or •OH directly to form stable adducts (Muñiz et al., 1995; Sáez et al., 1982, 1993). A loss of thiol proteins can occur during a period of oxidative stress; therefore, one biomarker of oxidative stress status that provides better knowledge of the redox state relative to the glutathione is the GSSG/GSH or GSH/GSSG ratio (Svensson et al., 2002, Tauler et al., 2006). The increase of GSSG or the reduction of the GSH concentration results in the alteration of the GSSG/GSH ratio in favor of oxidative stress damage, as this imbalance ratio is one of the most important markers of oxidative stress (Sies, 1986). To maintain the optimal ratio, cells are capable of exporting GSSG (Meister & Anderson, 1983). The imbalance in favor of the oxidative environment during repeated periods has been cited as one of the primary factors in the etiology of neurodegenerative diseases such as Alzheimer's and Parkinson's. This is observed in aging and more acutely among older people who engage in less physical activity or who are more frail (Steinbeck et al., 1993; Tauler et al., 2006). In Figure 22, we see a summary of the antioxidant mechanisms mentioned in the previous sections.

Figure 22. *The antioxidant strategy*.



Note. Reproduced from *Antioxidant Enzymes*, by Sáez and Están-Capell, 2014, Encyclopedia of Cancer.

II.VI.IV. Role of oxidative stress on aging and diseases

A. Oxidative stress and aging

As we saw above in the free radicals theory of aging, in all aerobic organisms, RONS plays an important role in aging and in age-related diseases (Kostka et al., 2000; Venkataraman et al., 2013), due to the accumulation of oxidative stress damage in DNA, lipid, and protein macromolecules, which induces age-associated biological functional losses (Bailey et al., 2010; Beckman & Ames, 1998; Kędziora-Kornatowska et al., 2009). There is both direct and indirect evidence that senescent organisms are more susceptible to oxidative stress. In terms of ROS products, there is growing evidence that an accumulation of nDNA and mtDNA damage can contribute to impairments in the maintenance and function of organs during aging and chronic disease (Nalapareddy et al., 2008). In fact, a variety of studies have provided evidence for an increase in DNA damage in aging human tissues (Sedelnikova et al., 2008, Singh et al., 2003; Schmid et al., 2006).

In addition, an age-dependent increase in human urine and serum levels of DNA biomarkers such as 8-oxo-dG (Tamae et al., 2009) is reported in apparently disease-free individuals of 15-91 years of age (Rattan et al., 1995). Numerous studies have reported the accumulation of 8-oxo-dG – and hence other lesions – with age, both in vitro and in vivo nDNA and mtDNA (Hamilton, Van Remmen et al., 2001; Sohal et al., 1994).

Oxidative stress associated with aging has been reported in most tissue types (Martin et al., 2004, Terman et al., 2004, Zerba et al., 1990). The most affected tissues are the most oxygen-dependent, with the brain and skeletal muscles being the primary sites of oxidative damage (Fugere et al., 2006; Gianni et al., 2004; Radak et al., 2002; Terman & Brunk, 2004). For instance, in the skeletal muscle, the process of aging and the loss of muscle mass are both associated with higher levels of DNA damage and deteriorated antioxidant defense (Fulle et al., 2004; Gianni et al., 2004). Recent data from young and older subjects show that 8-oxo-

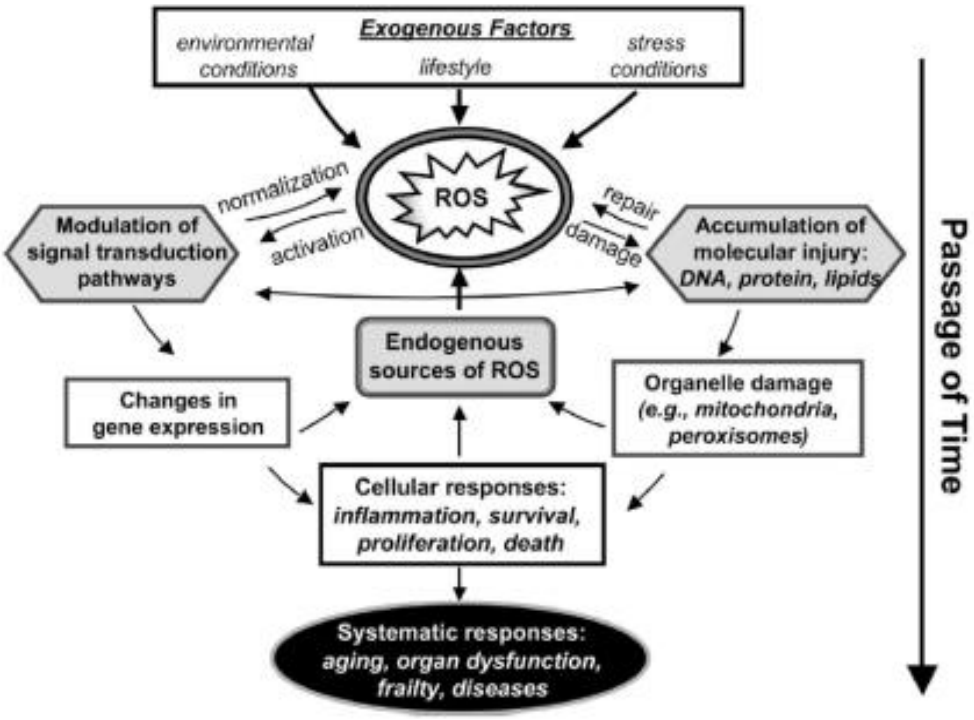
dG, protein carbonyls, MnSOD, and CAT activity are significantly higher in muscles of the elderly than in those of young people (Gianni et al., 2004).

It has also been demonstrated that the protein carbonyl content and lipid peroxidation products increase with age in several mammalian tissues as a consequence of oxidative stress (Sohal, 2002), thus playing an important role in many age-related diseases. Regarding the antioxidant system, it appears that the age-dependent increase in oxidant production overwhelms the endogenous antioxidant defense system, resulting in a reduced ability of the endogenous antioxidant defenses to convert oxidants into more inert species (Cui et al., 2012; Ji, 1993; Pansarasa et al., 1999) and therefore allowing the persistence of damage and a subsequent increase in replication errors. Despite the wealth of information about the behavior of ROS products during aging, discuss remains about how the levels of antioxidant enzymes change during aging. Some authors report a general elevation in the activity basal levels of the antioxidant enzymes within older people as a result of increased oxidative stress (Ji, 1993; Pansarasa et al., 1999). However, it is also suggested that age appears to have no effect of the activity levels of the major antioxidant enzymes such as CAT, GPx, MnSOD, and Cu/Zn SOD (Hamilton, Van Remmen et al., 2001). Similarly, no differences were noted in the levels of SOD, GPx, and CAT for the age groups analyzed (i.e., 35-39 years, 50-54 years, and 65-69 years; Barnett & King, 1995). Others found a decline in antioxidant glutathione levels, as GSH metabolism is linked to diseases associated with aging (Lang et al., 1992, Maher, 2005, Puertas et al., 2012).

These discrepancies could be associated with the different human tissues and enzymes analyzed. For instance, one of the most identifiable age-associated changes in the endogenous antioxidant defenses is an increase in MnSOD activity in the skeletal muscle as a result of the increased oxidant production from within the mitochondria of the aged muscle (Gianni et al., 2004; Hollander et al., 2000; Ji, 1993; Lambertucci et al., 2007; Leeuwenburgh et al., 1994;

Pansarasa et al., 1999). However, with GPx and CAT, not all have reported age-dependent changes (Gianni et al., 2004; Hollander et al., 2000, 2009; Ji et al., 1990; Lambertucci et al., 2007; Leeuwenburgh et al., 1994; Pansarasa et al., 1999). In fact, this response may differ slightly, depending on the muscle being investigated (Hollander et al., 2000; Leeuwenburgh et al., 1994). Finally, Pansarasa and colleagues (1999) found that people aged 66-75 years have significantly lower total SOD activity but greater MnSOD activity than younger people, suggesting a decrease in CuZnSOD activity (Figure 23). In addition, a recent work by our group has demonstrated the reduction of antioxidant levels and the increase of oxidative stress products with progressively changes depending on age in a cohor of patients with ages ranging from 25 to 99 years (Amaya, 2020).

Figure 23. *Mechanisms by which ROS could contribute to the process of aging.*



Note. Reproduced from "An integrated view of oxidative stress in aging: basic mechanisms, functional effects, and pathological considerations." (p. R29), by Kregel and Zhang, 2007, *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 292*(1).

B. Oxidative stress and disease

Chronic oxidative stress may play primary or secondary roles in the development of more than 100 acute and chronic human pathological processes (Dalle-Donne et al., 2006; Fisher-Wellman & Bloomer, 2009; Kalogeris et al., 2014; Valko et al., 2007). These include accelerated aging, cancer, types 1 and 2 diabetes, cardiovascular diseases, rheumatoid arthritis, osteoporosis, neurodegenerative diseases, acute and chronic kidney disease, macular degeneration, biliary diseases, decreased skeletal muscle force production, and chronic obstructive pulmonary disease (Barnham et al., 2004; Battershill et al., 2008; Beckman & Ames, 1998; Chandrasekaran et al., 2017; Franzke, Neubauer & Wagner, 2015; Kehrer, 1993; Liguori et al., 2018; Müllner et al., 2013; Packer, 1997; Powers & Jackson, 2008; Reid, 2001; Valko et al., 2007; Wiseman H & Halliwell, 1996).

i. Oxidative stress and cardiovascular diseases

In terms of cardiovascular diseases, the evidence currently suggests significant associations between oxidative stress and atherosclerosis (Gradinaru et al., 2015), higher arterial stiffness (Brinkley et al., 2009), vascular endothelial dysfunction, and hypertension (Siti et al., 2015), especially where there are increased levels of DNA damage (Battershill et al., 2008; Müllner et al., 2013). Indeed, it is well documented that a reduction in the concentrations of GPx and SOD in the heart tissue will provoke a decrease in the heart's oxidative stress tolerance with age, contributing to the development of cardiovascular alterations (Abete et al., 1995).

ii. Oxidative stress and metabolic diseases

Metabolic diseases such as diabetes mellitus (types 1 and 2) are associated with increased levels of oxidative stress biomarkers (i.e., 8-oxo-dG, MDA) in elderly populations (Bashan et al., 2009; Battershill et al., 2008; Brownlee, 2001 Müllner et al., 2013). Regarding the implications of the antioxidant system for these pathologies, some results suggest that,

while there is increased oxidative stress in the elderly with type 2 diabetes, in subjects with impaired glucose tolerance, the oxidative stress can be partly balanced by the increased antioxidant defense system, especially where there are increasing increments of GPx and CAT (Atli et al., 2014).

iii. Oxidative stress and bone diseases

Glowing whole-body evidence has linked bone biology and redox balance regulation, indicating that RONS may play a major role in bone diseases such as osteoporosis (Bai et al., 2005; Dreher et al., 1998; Samelson & Hannan, 2006; Yang et al., 2001) and osteoarthritis (Ziskoven et al., 2010).

In osteoporosis, the imbalance in favor of RONS leads to inhibition osteoblast generation by osteoprogenitors cells (Bai et al., 2005; Samelson & Hannan, 2006) and increased osteoclastic activity (Altindag et al., 2007); while in osteoarthritis, ROS are involved in cartilage homeostasis and degradation (Ziskoven et al., 2010). It has been suggested that the level of RONS in patients with rheumatoid arthritis (an autoimmune disease characterized by chronic inflammation leading to joint destruction) is higher than that found in healthy subjects (Vasanthi et al., 2009). In addition, it has been demonstrated that osteoblasts produce antioxidants such as GPx to protect against ROS (Dreher et al., 1998; Fuller et al., 2000).

iv. Oxidative stress and chronic kidney/pulmonary diseases

Chronic kidney disease accelerates normal aging by placing patients in a chronic inflammation state, which enhances the formation of ROS (Putri & Thaha, 2014; Walker et al., 2014). Meanwhile, the severity of the airflow limitation in elderly patients with pulmonary diseases such as chronic obstructive pulmonary disease (COPD) has been associated with increased levels of oxidative stress biomarkers such as 8OHdG and 8-iso-P

(Choudhury et al., 2017). In particular, some authors have shown that protein carbonylation plays an important role in the etiology of this condition, as it modifies the function of the key enzymes and structural proteins involved in muscle contractile performance, leading to consequent skeletal muscle dysfunction (Barreiro, 2016).

v. Oxidative stress and cancer

Many studies have demonstrated a direct relationship between chronic oxidative stress and carcinogenesis, due to the mutagenic or carcinogenic potential of RONS in the DNA (Battershill et al., 2008; Khansari et al., 2009; Marnett, 2000; Müllner et al., 2013). These accumulations of RONS-induced DNA damage with age can be confirmed by the progressive and statistically significant increase in levels of 8OHdG, possibly, the "gold standard" biomarker of the carcinogenesis induced by inflammation or oxidation in elderly people (Khansari et al., 2009; Olinski et al., 2007).

vi. Oxidative stress and cognitive diseases

Oxidative stress is thought to play an important role in the pathogenesis of neurodegenerative diseases such as Parkinson's, Huntington's, mild cognitive impairment, and multiple sclerosis and amyotrophic lateral sclerosis (Butterfield et al., 2002; Mariani et al., 2005). Indeed, there is a large amount of compelling data demonstrating that oxidative stress plays a pivotal role in the pathophysiology of dementia (Chen & Liu, 2017) – more specifically, the most common form of dementia, Alzheimer's disease (Bennett et al., 2008; Bonda et al., 2010; Nunomura et al., 2001; Sultana and Butterfield, 2010). Several studies have evaluated the relationship between the levels of oxidative stress biomarkers and cognitive function (with the MMSE) and found that increased oxidative stress biomarkers (e.g., MDA) are correlated with low cognitive performance in the elderly population (Baierle et al., 2015). Furthermore, the levels of GPx and GSH antioxidants enzymes are highly relevant, as some authors have shown that cognitive impairment is slower in patients with

high GPx activity, while high levels of GSH seem to accelerate cognitive decline in the elderly (Revel et al., 2015).

vii. Oxidative stress and neuromuscular diseases

Finally, oxidative stress has been associated with skeletal muscle alterations and strength deficits (Fugere et al., 2006; Gianni et al., 2004; Radak et al., 2002; Terman & Brunk, 2004), which are related to physical disability, loss of independence, and frailty (Abete et al., 2003).

As mentioned above, skeletal muscle tissue generates a large amount of RONS, as it consumes large quantities of oxygen. Therefore, this accumulation of RONS is thought to be a common determinant in the loss of muscle quantity and quality, due to several mechanisms (Gomes et al., 2017). In aged animals, the ability to buffer increased oxidant production is lower than that of the muscle of young animals (Fulle et al., 2004), which could be a substantial hindrance to muscular adaptation to loading (Bejma & Ji, 1999; Brickson et al., 2001; Ji et al., 1998; Ji & Peterson, 2004).

Oxidative stress is associated with the loss of muscle, referred to as "sarcopenia." However, the mechanisms at work here remain unknown. Evidence suggests that RONS contribute to sarcopenia by decreasing muscle-protein synthesis and increasing proteolysis, leading to a reduction in the quantity of muscle mass (Powers, Talbert & Adhihetty, 2011). Nevertheless, not all the fibers are equally affected. In fact, type II fibers undergo faster age-induced decline, partially attributable to greater apoptosis and oxidative injury, as this type of fiber has less mitochondrial content and is more susceptible to atrophy than the type I fibers, which have more mitochondrial content (Lexell et al., 1988; Phillips & Leeuwenburgh, 2005).

In terms of quality, several mechanisms that act on neuromuscular function are involved in the reduction of muscle strength, termed "dynapenia" (Baumann et al., 2016), which occurs as an effect of RONS (Clanton et al., 1999). Some of the mechanisms collected in the literature are as follows: 1) changes in the morphology of the neuromuscular junction causing a reduction in the innervation and fibers (Baumann et al., 2016); 2) alteration of contraction-induced calcium release (Anzueto et al., 1994; Diaz et al., 1993; Eu et al., 2000; Posterino et al., 1996); 3) up-regulation of catabolic gene expression (DeMartino & Ordway, 1998; Li et al., 2003; Mantovani et al., 2004; Wouters et al., 2002); 4) modification in actin and myosin structures, significantly reducing the cross-bridge cycling within the myofibrillar apparatus (Baumann et al., 2016); 5) activation of apoptotic pathways (Kagan et al., 2006; Lysiak et al., 2007; Siu & Always, 2005); 6) reduction of acetylcholine release at the synaptic cleft, which could lead to failure in the generation of an potential action by the sarcolemma (Baumann et al., 2016); and 7) myofilament dysfunction (Andrade et al., 1995; Kondo, Kodama et al., 1993; Kondo, Miura et al., 1993).

Finally, several recent systematic reviews and cohort studies have found an association between higher levels of systemic oxidative stress biomarkers (such as MDA, 8-iso-P, protein carbonyls, and lower antioxidants parameters) and frailty or even pre-frailty (Liu et al., 2016; Saum et al., 2015; Soysal et al., 2017) in geriatric populations (Ingles et al., 2014; Liu et al., 2016). Thus, oxidative stress is closely related to aging and seems to be potential driver of frailty pathogenesis.

This situation – and the fact that the measurement of basal systemic oxidative stress has been proposed as a marker for predicting the onset of disease and for evaluating the effect of interventions designed to treat oxidative stress (for instance, by physical exercise; Margaritelis et al., 2016) – is partially why the current PhD dissertation research was

conducted. For more information about age-related diseases and oxidative stress biomarkers, see the reviews of Cooke et al. (2003), Frijhoff et al. (2015), and Syslová et al. (2014).

II.VI.V. Methods of detecting and measuring oxidative stress and antioxidant enzyme biomarkers

The WHO defines a biomarker as "any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease" (WHO, 2001). The NIH defines this term as "[a] characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" (Biomarkers Definitions Working Group, 2001).

As we can see, one characteristic of the biomarkers is that they can be measured. In humans, oxidative stress biomarkers have been measured in different tissues and fluids (e.g., blood and urine; McCord & Fridovich 1969b; Oh-ishi et al., 1997; Tauler et al., 1999). Commonly used markers of oxidative stress include the oxidation products mentioned above – from DNA (8-oxo-dG), lipid (MDA, 8-iso-P), and protein (protein carbonyls) macromolecules – and the level of certain antioxidants, such as GSH, SOD, GPx, and CAT (Lushchak, 2014). Due to the complexity of the responses of these biomarkers, especially those of the antioxidants, an ideal assessment of the disturbance in the redox balance would include the measurement of several oxidatively modified macromolecules, along with an assessment of the antioxidant system (Lushchak, 2014).

However, free radicals are very reactive and short-lived and their detection can be difficult (He et al., 2014). Direct detection of free radicals is only possible with electron paramagnetic resonance spectroscopy (Ashton et al., 1998; Bailey et al., 2007; Davies et al., 1982). The use of this direct method can be complicated, but indirect methods allow the

quantification of free radicals through the examination of the "footprints" that their reactions leave behind (Bailey et al., 2003). These indirect approaches include a range of tests and techniques, such as enzyme-linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), chromatographic, mass spectrometry, and colorimetric (Poljsak et al., 2013).

In blood, biomarkers can be measured in plasma, serum, and peripheral blood mononuclear cells (PBMCs), with the most common being PBMCs or plasma, which have been shown to correlate well with similar measurements in tissues (Veskoukis et al., 2009). Thus, markers of oxidative stress in peripheral blood or plasma can provide an indication of whole-body oxidative stress (Veskoukis et al., 2009). PBMCs are composed of monocytes (≈ 10%) and lymphocytes (≈ 90%) and are a "site" for oxidative modification (Sureda et al., 2005; Tauler et al., 2006). Changes in PBMC adduct provide a more specific indicator of oxidative stress, compared to whole blood or plasma.

Due to the wide variety of analytical methods and techniques available for evaluating biomarkers of oxidative stress, the "National Institute of Environmental Health Biomarkers of Oxidative Stress" study investigated which of these methods provide valid read-outs, concluding that the mass spectrometry-based measurement of 8-iso-P is the "gold standard" biomarker of free-radical damage (Kadiiska et al., 2005). The variety of available analytical methods provides many possibilities for determining the biomarkers. One recent review (Frijhoff et al., 2015) provides a deep analysis of the current status of oxidative stress biomarkers as clinically useful tools, as well the most valid methods of analysis.

ELISA is one of the most frequently used methods. This option allows the determination of lower concentrations than those methods combining chromatographic methods and mass spectrometry. It exists in a range of modifications, which are all based on a highly specific interaction of antigens and antibodies. However, the disadvantage of

biochemical methods is the possibility of cross-reactions, which may cause false-positive or false-negative results (Senturker et al., 1997).

A. DNA oxidation biomarkers

Research has often used 8-oxo-dG as a critical biomarker of oxidative stress of DNA damage (Valavandis et al., 2009). The quantity of this product in the blood, urine, and tissues is used as a marker of DNA damage in vivo (Cooke et al., 2006; Fraga et al., 1990; Mastaloudis et al., 2004b).

The scientific and biomedical interest in the study of this mutagenic basis has led to the establishment of an international consortium for the study and validation of the suitable methods of quantification of 8-oxo-dG and the identification of its normal levels in different human biological fluids (Barregard et al., 2013; Evans et al., 2010).

As the levels of 8-oxo-dG reflect the oxidative stress changes in the overall body (Olinski et al., 2006), several techniques have been implemented to determine this biomarker. These include the use of chromatographic techniques such as high-performance liquid chromatography, coupled with electrospray ionization mass spectrometry (HPLC-ESI-MS; Allgayer et al., 2008); gas chromatography-mass spectrometry; high performance liquid chromatography with electrochemical detection (EC); HPLC tandem mass spectrometry (Valavanidis et al., 2009); and immunosorbent assay techniques, such as the ELISA (Harms-Ringdahl et al., 2012; Orhan et al., 2004).

The advantages of ELISA are that it is easy to use and inexpensive, in comparison with chromatography methods (Kau et al., 2006). In addition, it can be used in different media, such as plasma (Tope & Panemangalore, 2007), serum (Breton et al., 2003), cell culture (Kantha et al., 1996), and urine (Orhan et al., 2004). However, chromatography methods have been shown to more accurately estimate DNA damage, compared to ELISA,

which has been shown to overestimate DNA damage (Cooke et al., 2008). The current "gold standard" is ultra-high-performance liquid chromatography with tandem mass spectrometry for quantification (Rasmussen et al., 2016).

In terms of fluid, blood could be a problematic matrix for measuring DNA damage, as any method will necessarily be invasive (~5 mL is typically needed), and, for instance, the PBMCs must be isolated before analysis or storage, which is a time-consuming process and artefactual damage can occur if the whole blood is frozen without a cryopreservative (Egea et al., 2017).

However, urine 8-oxo-dG has been proposed as a useful biomarker for the assessment of aging (Shi et al., 2012). The urinary matrix provides a non-invasive method (Lam et al., 2012), as the chromatography coupled with the mass spectrometric approaches the "gold standard" for assessment of urinary 8-oxo-dG (Weimann et al., 2001; Weimann et al., 2002; Weimann et al., 2012), although ELISA commercial assays have improved its accuracy (Rossner et al., 2013; Rossner et al., 2016). Nevertheless, some authors have questioned the clinical significance of this method (Barregard et al., 2013).

B. Lipid oxidation biomarkers

Frequently used measures of lipid peroxidation include the assessment of end-products such as conjugated dienes, oxidized low density lipoproteins, lipid hydroperoxides, and isoprostanes. The assessment of 8-iso-P, the most common isoprostane, is the most reliable measure of lipid peroxidation (Dalle-Donne et al., 2006), albeit the most difficult to determine (Janicka et al., 2010).

In fact, as a result of their sensitivity to changes in response to oxidative stress and their chemical stability, they are often considered the best product with which to evaluate lipid peroxidation and the most reliable markers for monitoring oxidative stress in vivo

(Kadiiska et al., 2005), due to their implication in the pathogenesis of several diseases (Liguori et al., 2018).

Despite strong evidence for their utility as biomarkers of oxidative stress, the most reliable methods for their quantitation (such as LC-MS/MS, or gas chromatography-mass spectrometry) require expensive and specialized instrumentation (Awad et al., 1993; Milne et al., 2007). To overcome this problem, some commercial immunoassays have been developed as alternatives to mass spectrometry (Il'yasova et al., 2004; Proudfoot et al., 1999) and successfully validated (Senturker et al., 1997).

One of the most useful methods for assessing 8-iso-P involves the urine fluid. 8-iso-P is a biologically active compound, whose level in the urine is an independent predictor of death in older adults. The advantages of determination by this product are as follows: a) it can be measured accurately, b) it is quite stable; c) it does not exhibit diurnal variations; d) it can be detected in almost all biological tissues; and e) its levels are modulated by the antioxidant state of the body, but not by the lipid composition of the diet (Halliwell & Gutteridge, 2015).

Among other biomarkers of lipid peroxidation, the aldehyde MDA has been a widely used oxidation-derived product (Esterbauer et al., 1991) since Spiteller and others reviewed its involvement in several chronic diseases (Negre-Salvayre et al., 2010; Spiteller, 1998; Zarkovic; 2003).

Different methods are available for the detection of MDA. However, most are questionable and have various pitfalls (Spickett et al., 2010), as they use thiobarbituric acid reactive substances, which is used as a colorimetric or fluorescent assay to determine the reaction of thiobarbituric acid in the presence of MDA (Moselhy et al., 2013). The issue is that thiobarbituric acid reactive substances react with all the aldehydes in the sample. Therefore, this reaction is nonspecific to MDA and measures many parameters in addition to

lipid peroxidation (Esterbauer et al., 1999; Janero, 1990), providing usually overestimated values (Liu et al., 1997; Khoubnasabjafari et al., 2015).

The use of other methods to measure MDA more precisely has also been investigated (Knight et al., 1988). For instance, the HPLC method has been found to be more accurate for lipid peroxidation (Moselhy et al., 2013). However, this method also has potential issues, such as increasing time and cost demands (Kil et al., 2014). Quantification of lipid peroxidation products can also be achieved by other methods, including spectrofluorescence, spectrophotometry (Urso & Clarkson, 2003; Vasankari et al., 1997), antibody technology, and mass spectrometry (Breusing et al., 2010).

C. Protein oxidation biomarkers

Protein carbonyls are the most general and extensive marker of protein oxidation both *in vivo* and *in vitro* (Dalle-Donne et al., 2003, 2006; Levine et al., 1994) due to their ability to derivatize with 2,4-dinitrophenylhydrazine to form a 2,4-dinitrophenyl group and their immunogenic properties (Oliver et al., 1987; Reznick & Packer, 1994; Wehr & Levine, 2013). They must be derivatized before its detection and quantification (Wehr & Levine, 2013).

Protein carbonyls are among the most successful markers of oxidative stress and are associated with multiple diseases (Frijhoff et al., 2015). These can be detected spectrophotometrically (Carty et al., 2000), or by antibody technology (e.g., ELISA; Buss et al., 1997), immunohisto- and cytochemistry, HPLC, or Western blot (Keller et al., 1993; Levine et al., 1994). Concerning clinical settings, ELISA and HPLC are the only methods that seem applicable due to requiring significantly less sample volume than other methods and involving high internal/external standards (Buss et al., 1997; Mendis et al., 1994; Tauler

et al., 2003). However, these methods have been criticized as being nonspecific and unreliable in human studies (Inal et al., 2001).

D. Antioxidant enzyme biomarkers

Common measures of antioxidant capacity include the assessment of thiol groups such total glutathione, GSH, GSSG, GSSG/GSH ratio, or GSH/GSSG ratio and RONS-specific antioxidant enzymes such as SOD, GPx, or CAT. These antioxidant enzymes are measured by a variety of techniques, including enzymatic methods, HPLC with fluorometric, UV, LC-MS/MS, or electrochemical detectors (Frijhoff et al., 2015) and are usually conducted on blood samples (whole, plasma, or serum; Bartosz, 2010). Despite substantial interest in the measurement of antioxidant enzymes in blood, there is currently no "gold standard" protocol for sample preparation and analysis in biological samples (Giustarini et al., 2013), especially relating to whether it is better to evaluate plasma, serum, or whole blood.

In the case of thiols, many studies have measured GSH, GSSG, and the ratio in plasma (Bartosz, 2010) due to several meta-analyses confirming a decrease in plasma GSH and an increase in plasma GSSG in patients with chronic conditions related to oxidative stress (Frustaci et al., 2012; Murri et al., 2013; Ng et al., 2008; Sabuncu et al., 2001). Other studies have measured GSH and GSSG in whole blood (erythrocyte) as the concentrations are higher than in plasma. However, higher concentrations might not necessarily be a good indicator of oxidative stress across tissues (Frijhoff et al., 2015). In erythrocytes (within cells), GSH is present in millimolar concentrations, resulting in higher GSH/GSSG ratios (>30; Hwang et al., 1992), while the GSH/GSSG ratio in serum is substantially lower than in plasma and whole blood (Alvarez & Radi, 2003).

One of the main concerns during sample manipulation of the thiols is that GSH can be easily auto-oxidized to GSSG, which may lead to overestimation of the results of GSH, GSSG, or the ratio (Asensi et al., 1994). To prevent this issue, various agents such as 2-vinyl pyridine and N-ethylmaleimide are used to block thiol groups (Asensi et al., 1994).

II.VI.VI. Exercise-related effects on oxidative stress and antioxidant defenses

Since the first report that documented exercise-induced oxidative stress in humans (Dillart et al., 1978), wherein the authors reported an increase of lipid peroxidation after 60 min of endurance exercise at 60% of VO_2max, and the following study by Davies et al. (1982), which provided the first evidence that skeletal muscle tissue produces RONS after exhausting running in rats, the research topic of exercise-induced oxidative stress has grown and advanced markedly in the last three decades, with more than 300 investigations published (Bloomer, 2008; Fisher-Wellman & Bloomer, 2009; Gomes et al., 2012; Powers, Nelson & Hudson, 2011). In recent years, there has been major progress in research about the redox biology adaptive response to exercise, making this PhD dissertation highly relevant to the area of sport science.

However, due to the vast amount of literature on this topic, it is necessary to condense the material presented in this section. For this reason, the approach is to provide a summary of major findings rather than a detailed review of individual reports, focusing more on chronic effects or adaptations of exercise on aging populations. Readers seeking more details should consult the following reviews and reference papers: Bloomer (2008), Bloomer and Goldfarb (2004), Bouzid et al. (2015), Close et al. (2005), Gomes et al. (2012), Gomez-Cabrera, Domenech, & Viña (2008), Ismaeel et al. (2019), Ji (2001, 2002, 2008), Leeuwenburgh and Heinecke (2001), Mcardle and Jackson (2000), Mcardle et al. (2002), Nikolaidis et al. (2008), Powers, Nelson and Hudson (2011), Radak et al. (2008), Simioni et al. (2018), and Thirupathi et al. (2002).

The effects of exercise-induced oxidative stress are subject to debate. Commonly, the main focus of research has concentrated on the harmful effects (Packer, 1997; Vollaard et al., 2005). However, more recent research has indicated that RONS produced during exercise are key to certain adaptive processes (Fisher-Wellman & Bloomer, 2009; Ji, 2008; McArdle et al., 2001) being several of the health adaptations derived from the exercise mediated through redox-sensitive signaling (Kesaniemi et al., 2001; Radak et al., 2005, 2008). Thus, there currently is equal interest in further investigating the positive role of the redox adaptations in such exercise as the negative effects (Gomez-Cabrera et al., 2005).

Several studies have investigated oxidative stress responses following exercise (Bloomer et al., 2005; Diaz et al., 2011; Friedenreich et al., 2016; Gougoura et al., 2007; Morales-Alamo & Calbet, 2014; Niess et al., 1996; Park & Kwak, 2016; Seifi-Skishahr et al., 2016; Vezzoli et al., 2014). However, in all analyzed populations (young, adult, older adults, athletes, and clinical), results vary notably across studies due to the exercise protocol (intensity [low, moderate, high], mode [aerobic/anaerobic training, resistance, power, multi-component, eccentric, isometric, dynamic, jump training], volume, frequency, and duration; Alessio et al., 2000; Bloomer, 2008; Bloomer & Fisher-Wellman, 2008; Elosua et al., 2003; Finaud & Filaire, 2006; Fisher-Wellman & Bloomer, 2009; Jenkins, 2000), redox products (different oxidative stress and antioxidant biomarkers analyzed; Forman et al., 2015), sample matrix (different fluids and tissues; Bloomer, 2008), biochemical analysis methods (HPLC, ELISA, etc.; Forman et al., 2015), nutritional status and training level of the subjects (Bloomer & Fisher-Wellman, 2008; Elosua et al., 2003; Finaud & Filaire, 2006; Fisher-Wellman & Bloomer, 2009), and sampling time points (minutes, hours, days; Bloomer, 2008; Draeger et al., 2014). This, to some extent, could possibly impede our knowledge for a more definitive answer to the fundamental questions about exercise-induced oxidative stress, but at

the same time, exercise can be found in many forms and is characterized by this wide range of variability.

Despite such variations, it is now widely accepted that while intense or prolonged acute bouts of aerobic or anaerobic exercise can transiently promote oxidative damage to DNA, lipids, and proteins in a variety of tissues and body fluid (Alessio et al., 1988; Davies et al., 1982; Elosua et al., 2003; Fisher-Wellman & Bloomer, 2009; Gomez-Cabrera, Domenech & Viña, 2006; McBride et al., 1998; Nikolaidis et al., 2007; Powers & Jackson, 2008; Radak et al., 1999; Steinbacher & Eckl, 2015), a continuous exercise stimulus is necessary to produce healthy amount of RONS capable of exerting positive stress, which has been termed eustress (Niki, 2018), especially in aging populations (Laforest et al., 1998). Notably, each RONS and antioxidant enzyme has a specific reactivity and specificity to the exercise (Niki, 2018).

As mentioned in previous sections, oxidative stress and mitochondrial dysfunctions are relevant factors in the complex aging process. However, healthy amounts of ROS can have positive effects on aging, and physical exercise is one of the most important contributors to this process; due to the muscle, RONS generation during contractions increases the expression of genes involved in both mitochondrial biogenesis and antioxidant defense (Bouzi et al., 2015; Cartee et al., 2016; Yoo et al., 2018). Conversely, exercise may aggravate oxidative damage if its performance is not adequate in terms of intensity, duration, or type.

Finally, although there is a general consensus that one of the main sources of RONS is the skeletal muscle through contractions during physical exercise (Cartee et al., 2016; Yoo et al., 2018), there is not enough evidence to know which protocol in terms of intensity or type of exercise would be better to produce adaptive responses, especially in older adults, where the muscle adaptation and regeneration are even more necessary due to sarcopenia

(Thirupathi et al., 2020). Thus, the balance between deleterious and beneficial effects of exercise on oxidative stress in the elderly remains unclear (Fatouros et al., 2004; Laforest et al., 1998; Polidori et al., 2000) since a limited number of studies has investigated the relationship between different exercise modalities or intensities and oxidative stress markers in this population.

A. The exercise paradox theory

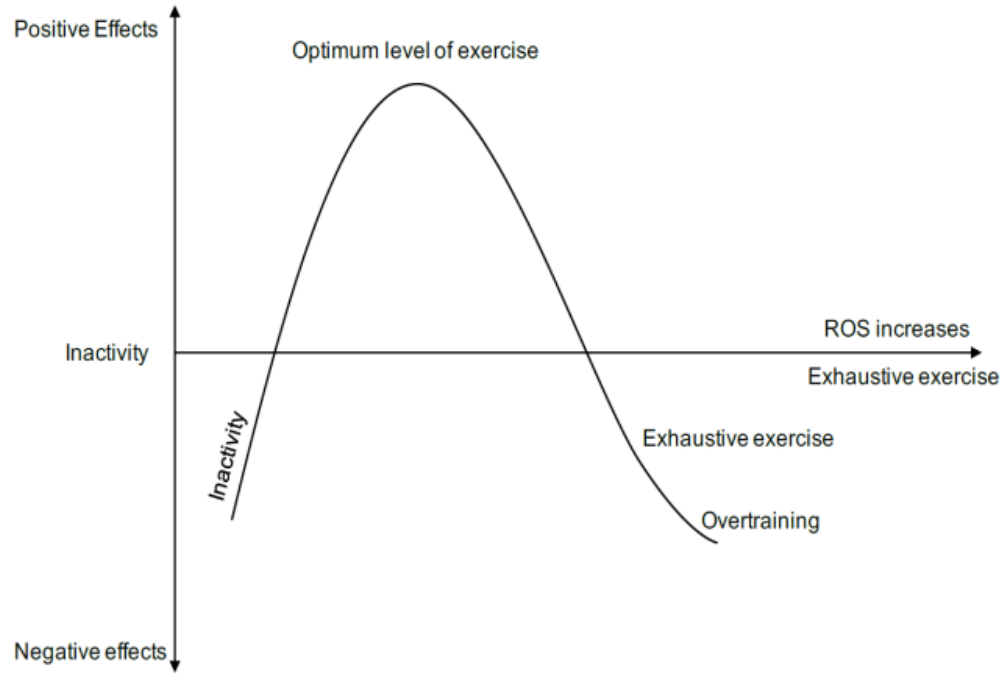
Growing evidence has suggested that maintaining chronic low basal levels of oxidative stress can help to prevent disease and extend lifespan though the adaptations that low levels of RONS induce in multiple signaling pathways, for instance, inducing the expression of antioxidant enzymes (Gomez-Cabrera, Domenech & Viña, 2008). The basis for this phenomenon may be justified by the concept of hormesis (Calabrese & Baldwin, 2003). The hormesis theory suggests that biological systems respond to toxins, chemicals, and radiation with a bell-shaped curve, existing a dose-response phenomenon characterized by a low dose or stimulation (positive effect) and a high dose or inhibition (negative effect). Therefore, there is an optimal dose to produce beneficial effects (Calabrese & Baldwin, 2001; Calabrese & Baldwin, 2002; Cook & Calabrese, 2006).

Radak and colleagues have extended the hormesis theory to the RONS-generating effects of exercise (Radak et al., 2005), terming it the exercise paradox theory (Ji, 2006a). According to this theory, the production of free radicals from exercise also follows a bell-shaped curve behavior (Figure 24), wherein there is an optimum dosage characterized by low ROS exposure during exercise, which can provide beneficial and adaptive responses while training. However, if the dosage is higher or lower than the optimal threshold (which is currently an undefined level), the production of RONS may exceed the hormesis, overwhelm the antioxidant system, and thus may result in oxidative damage of cellular biomolecules

(Fisher-Wellman & Bloomer, 2009; Ji et al., 2006b; Packer, 1997; Radak et al., 1999, 2005, 2008).

In the phenomenon proposed by Radak, there are three points where levels of RONS lead to harmful effects: during inactivity, during strenuous exercise (high intensity or duration, acute exercise), and during overtraining. Specifically, oxidative stress increases in both an intensity- and a duration-dependent manner.

Figure 24. *Model of exercise-induced ROS and hormesis based on the paradox theory.*

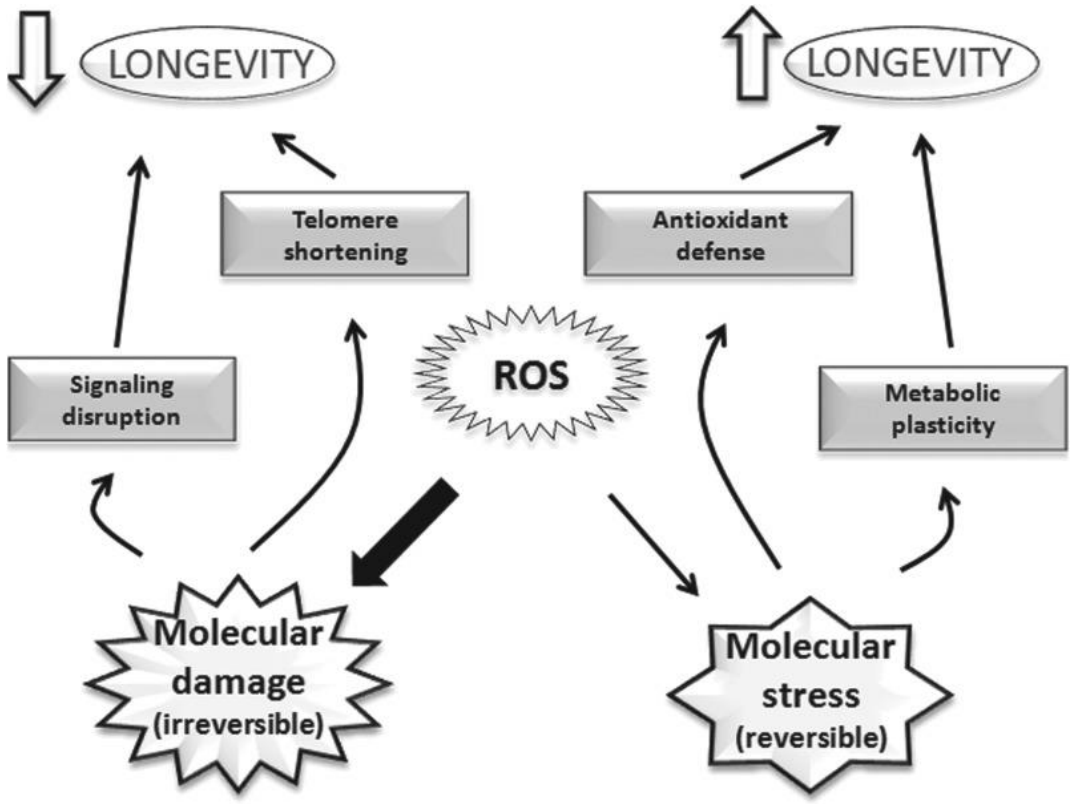


Note. Reproduced and adapted from "Exercise and oxidative stress: potential effects of antioxidant dietary strategies in sports." (p. 917), by Pingitore et al., 2015, *Nutrition, 31*(7-8).

Thus, physical exercise is a double-edged sword (Figure 25). Practiced at moderate intensity and duration, it should be considered as an antioxidant due to increasing the expression of antioxidant enzymes through the low levels of RONS produced. However, when exercise is practiced strenuously, it causes oxidative stress cell damage due to the high levels of RONS overwhelming the antioxidant defense; therefore, it should be considered as

an oxidant (Gomez-Cabrera, Domenech & Viña, 2008). This paradox is widely supported by evidence. For instance, muscle biopsies have shown increased CAT expression and reduced oxidative stress in trained older adults compared with their untrained counterparts (Bowen et al., 2015; Cobley et al., 2014). Indeed, animals and humans involved in regular training have shown less oxidative damage after a single strenuous exercise than the untrained subjects (Avogaro et al., 1986;Nishiyama et al., 1998; Simioni et al., 2018). This could be explained because after each individual exercise bout, a signal for the stimulation leading to the long-term modulation must occur. Thus, an adaptive response of the endogenous antioxidants could result from the cumulative effects of repeated exercise bouts (Hollander et al., 2001; Salminen & Vihko, 1983).

Figure 25. *The double edge sword of free radicals.*



Note. Reproduced from "The free radical theory of aging revisited: the cell signaling disruption theory of aging." (p. 917), by Viña et al., 2013, *Antioxidants & Redox Signaling, 19*(8).

In addition, the damaging effects of exercise-induced oxidative stress during intense, prolonged, or acute bouts of physical activity have been proven in human and rats (Fisher-Wellman & Bloomer, 2009; Gomez-Cabrera et al., 2009; Gomez-Cabrera, Martínez et al., 2006; Powers & Jackson, 2008; Powers et al., 2007). For instance, Ca^{2+} release from the sarcoplasmic reticulum and force production increases when the concentrations of hydrogen peroxide at skeletal muscles are low, whereas a sharp decrease in force output results in high concentrations after an acute exercise bout (Andrade et al., 2001).

Conversely, it has been widely accepted that chronic exercise promotes adaptations in muscle contractile function (Andrade et al., 2001; Barbieri & Sestili, 2012; Gomez-Cabrera et al., 2005; Hamilton et al., 2003; Issmael et al., 2019; Merry & Ristow, 2016; Mollica et al., 2012; Paulsen et al., 2014; Reid et al., 1993; Ristow et al., 2009) and in antioxidant activity (Ji, 1999; Niki, 2018) through the low levels of ROS induced. For instance, Radak et al. (1999) have shown the beneficial responses from regular exercise by a reduction in 8-oxo-dG (Radak et a., 1999). In addition, it has been suggested that a certain degree of exercise-induced muscle damage is needed to achieve muscle hypertrophy through chronic exercise (Evans & Cannon, 1991; Powers et al., 2010; Scheele et al., 2009).

Based on such evidence, it is clear that exercise of sufficient intensity and duration increases the formation of RONS, creating a redox imbalance in favor of oxidants. However, the dose (i.e., intensity, frequency, duration, and modality) of exercise to achieve optimal adaptations remains unclear. One of the reasons for presenting this PhD dissertation is because more evidence is needed that focuses on the relationship among exercise intensity, type of exercise, and oxidative stress responses in the elderly population.

B. Mechanism for exercise-induced oxidative stress and the beneficial effects of reactive oxygen and nitrogen species

Despite evidence showing that RONS production increases during exercise, the mechanisms by which this occurs have not been totally clarified (Cooper et al., 2002; Di Meo et al., 2016; Powers et al., 2016). Mitochondria are often cited as the predominant source of RONS due to the common assumption that because exercise causes an increase in mitochondrial oxygen consumption, these organelles increase RONS production through the increment of the superoxide (Cooper et al., 2002; Di Meo & Venditti, 2001; Powers & Jackson, 2008; Vollaard et al., 2005). However, recent data have suggested that the rate of oxygen used by mitochondria resulting in superoxide production is 0.15%, considerably less than the earlier estimates of 2–5% (St-Pierre et al., 2002). Furthermore, growing evidence has indicated that mitochondria produce more RONS in basal respiration (State 4) compared to active respiration (State 3 [maximal ADP-stimulated respiration]; Adhihetty et al., 2005; Herrero & Barja, 1997; Kavazis et al., 2009; Kozlov et al., 2005; Powers, Nelson & Hudson, 2011; Vollaard et al., 2005). Thus, the magnitude of ROS production by mitochondria via exercise is likely to be much smaller than originally thought.

Other main mechanisms of RONS formation through exercise are believed to include the activation of endothelial xanthine oxidase, NADPH oxidase complex, ischemia reperfusion, phospholipase A2-dependent processes, neutrophils and inflammatory response, increased release and autoxidation of catecholamines, and phagocytic respiratory burst (Gomes et al., 2012; Groussard et al., 2003; McBride et al., 1998; Sahlin et al., 1992; Powers, Nelson & Hudson, 2011; Radak et al., 2013). Although several mechanisms have been identified, there is still a lack of understanding of how each of them contributes to the total amount of RONS produced. In addition, different mechanisms may act synergistically

(Vollaard et al., 2005), and different types and intensities of exercise probably elicit different pathways of free radical production (Suemoto, 2016).

It is necessary to know the responses that different mechanisms of RONS production have to various exercise stimuli so that it will be possible to increase the potential role that RONS play in many key functions such as cell signaling (particularly the mitogen-activated protein kinase and nuclear factor kappa B pathways; Haddad, 2002; Powers & Jackson, 2008), production of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 alpha; Henderson et al., 1989; Kang & Li, 2012; Liu & Chang, 2018), cellular immunity (Fialkow et al., 2007), apoptosis (Lee & Wei, 2007), redox regulation of gene transcription (Liu et al., 2005), cell proliferation (Egan & Zierath, 2013; Kramer & Goodyear, 1985; Radak et al., 2013), adaptive gene expression and protein synthesis (Gomez-Cabrera et al., 2008), upregulation of antioxidant defense (Gomez-Cabrera, Domenech & Viña, 2008; Morrison et al., 2015), skeletal muscle inflammatory response and repair capabilities (Michailidis et al., 2013; Olesen et al., 2014), insulin sensitivity (Ristow et al., 2009), mitochondrial biogenesis (Ristow et al., 2009), and endurance capacity (Gomez-Cabrera, Domenech, Romagnoli et al., 2008).

C. Resistance training, variable resistance, and redox status[4]

The majority of published data on the effects of exercise and associated changes on oxidative stress and antioxidant enzymes are derived from studies involving endurance training (Bouzid et al., 2014; Fatouros et al., 2004; Sackeck et al., 2003; Takahashi et al., 2012), young people (Nordin, Done, & Traustadottir, 2014), or those analyzing only acute effects (Cakır-Atabek et al., 2015). Although resistance training is a safe and effective

[4] Related publication: Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing*, *20*(2), 205-217. https://doi.org/10.1177/1099800417753877

method for increasing muscle strength, physical function, and muscle mass in older adults (Liu & Latham, 2009; Peterson et al., 2010), and this effect is supported by Category A evidence (Chodzko-Zajko et al., 2009), few studies have described redox state changes that are provoked by chronic strength training in healthy older adults (Alikhani et al., 2019; Bobeuf et al., 2011; Gargallo et al., 2018; Liao et al., 2016; Padilha et al., 2015; Parise et al., 2005; Parise et al., 2005b; Ribeiro et al., 2017; Vincent et al., 2002, 2006) or those institutionalized (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018) or with pathological conditions such as sarcopenia, rheumatoid arthritis, or hypertension (Dantas et al., 2016; Rall et al., 2000; Shahar et al., 2003; Vezzoli et al., 2019), and the results of these studies have been contradictory. Moreover, most of them were performed on older women.

Several studies have analyzed the effects of resistance training on redox activity in combination with aerobic training in the same session (concurrent training; Bachi et al., 2019; Mota et al., 2019; Soares et al., 2015) or compare the effects of strength training with other therapies such as supplementation (Amaral et al., 2020; Bobeuf et al., 2011; Carru et al., 2018; Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018; Giolo et al., 2018; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Cavalcante et al., 2019; Shahar et al., 2013), cognitive training (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018), or aerobic training (Raungthai et al., 2019) in aging populations.

In addition, redox response to resistance training in older adults has mainly been studied in the context of training with machines, while the response to resistance exercise with various equipment such as elastic bands has been less defined (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018; Gargallo et

al., 2018; Liao et al., 2016; Shahar et al., 2013), with the added issue that most studies were conducted on institutionalized or clinical populations but not on healthy older women, except the study by Gargallo et al. (2018).

It is necessary to note that the effects of oxidative stress are especially marked in older women because they are exposed to particular risk due to loss of the antioxidant effects of estrogen during menopause (Moreau & Hildreth, 2014). Indeed, oxidative stress also has been associated with the loss of muscle mass and strength with aging (Cesari et al. 2012; Howard et al. 2007). One of the most relevant consequences is that older women are particularly susceptible to the damaging effects of sarcopenia and dynapenia associated with chronic oxidative stress (Cesari et al., 2012; Howard et al., 2007) due to this population possessing lower levels of muscular strength and muscle mass compared to men (Brady et al., 2014; Goodpaster et al., 2006; Hughes et al., 2001).

i. Effects on oxidative stress biomarkers

To date, only several studies have investigated resistance training effects on oxidative stress biomarkers in older adults, with contrasting findings (Bouzid et al., 2015; Cuyul-Vasquez et al., 2020). Regarding DNA damage, studies have reported decreases (Gargallo et al., 2018; Mota et al., 2019; Parise et al., 2005), increases (Gargallo et al., 2018), or no change (Rall et al., 2000) in levels of DNA oxidation after resistance training programs.

Certain investigations have observed improvements in DNA oxidative stress in older individuals after resistance training protocols were applied for 12 or more weeks. For instance, Parise and colleagues have shown that in individuals with a mean age of 71 years, 14 weeks of circuit resistance training three times a week at 50–80% of their 1 RM significantly reduced their urinary levels of 8-oxo-dG (Parise et al., 2005). In addition, Soares et al. (2015) have concluded that 16 weeks of resistance training three times a week at 75% of

1 RM significantly decreased DNA damage (Soares et al., 2015). Vezzoli et al. (2019) have also reported a decrease in 8-oxo-dG after 12 weeks of resistance training three times a week at 60% of 1 RM. However, other studies (e.g., Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018) have found higher levels of DNA damage after six months of strength training in the institutionalized elderly. On the other hand, Rall et al. (2000) did not observe any significant change in the urinary 8-oxo-dG of older adults with rheumatoid arthritis after 12 weeks of resistance training two times a week at 50–80% of 1 RM (Rall et al., 2000).

Similar to studies on DNA damage, contrary results were reported regarding lipid peroxidation. On one side, most studies showed improvements in oxidative stress with the reduction of lipid peroxidation markers following resistance or concurrent training programs in older women (Alikhani et al., 2019; Amaral et al., 2020; Bachi et al., 2019; Carru et al., 2018; Dantas et al., 2016; Mota et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Raungthai et al., 2019; Vezzoli et al., 2019; Vicent et al., 2002, 2006). On the contrary, others showed no changes (Bobeuf et al., 2011; Franzke et al., 2018; Giolo et al., 2018; Liao et al., 2016; Ribero et al., 2017; Shahar et al., 2013). For example, a study by Bobeuf et al. (2011) did not detect any differences in plasma MDA and urinary 8-iso-P levels after resistance training in older adults (Bobeuf et al., 2011).

Among studies that have reported positive changes on lipid peroxidation, it is necessary to highlight the one by Carru et al. (2018), which showed statistical reductions in plasma MDA only in females, not in males, after 18 weeks of resistance training two days a week at 70% of 1 RM, suggesting that strength training might have beneficial effects on lipid peroxidation, particularly in older women. In addition, research by Alikhani et al. (2019) and Shakar et al. (2013) has shown significant effects of lipid peroxidation decreasing the levels of serum MDA after 12 weeks of resistance training, while Vincent et al. (2006) have found

oxidative stress reduction in individuals ranging from 60 to 72 years old following 24 weeks of resistance training (Alikhani et al., 2019; Shakar et al., 2013; Vincent et al., 2006).

In addition to DNA and lipid oxidation, several investigations have measured protein oxidation following resistance training in older adults, specifically analyzing protein carbonyls as biomarkers. For example, Vezzoli et al. (2019) have reported a decrease in protein carbonyl levels following 12 weeks of resistance training three days a week at 60% of 1 RM (Vezzoli et al., 2019). However, most studies reported no changes in protein oxidation after applying strength training programs (Ceci et al., 2014; Padihla et al 2015; Parise et al., 2005b; Shahar et al., 2013).

Of the studies that analyzed the effects of resistance training using variable resistance such as elastic bands, detrimental effects of DNA damage were found in the institutionalized elderly after six months (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018), while Gargallo et al. (2018) have found positive effects on the decrease of 8-oxo-dG after 16 weeks of resistance training at moderate intensity but deleterious effects at high intensity. Indeed, no changes were found on lipid peroxidation biomarkers after 12 weeks (Shakar et al., 2016) and six months (Liao et al., 2016; Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer & Wagner, 2015, Franzke et al., 2018) of resistance training in older adults. The same results were reported by Shahar et al. (2013) regarding protein oxidation, which showed no change in protein carbonyls after 12 weeks of strength training in the sarcopenic elderly.

The differences in these studies' results may be related to the variability in the training protocols applied as well as the numerous oxidative biomarkers and compartments (blood, muscle, plasma, serum, saliva) analyzed. Nonetheless, these differences make it

difficult to draw a conclusion about the effect of resistance training on oxidative stress damage markers.

ii. Effects on antioxidant enzymes

In the process of aging, a phenomenon called anabolic resistance occurs, resulting in a decrease in muscle plasticity and adaptability in response to training, particularly to resistance training (Meng & Yu, 2010); the main factors are chronic inflammation and oxidative stress. Similar to the skeletal muscle, the body's antioxidant system slows down as a result of aging (Cui et al., 2012).

There is an abundance of literature reporting that chronic exercise training can up-regulate endogenous antioxidant defense systems (Gomez-Cabrera, Domenech, Viña, 2008; Ismaeel et al., 2019; Jenkins, 1998; Meydani & Evans, 1993; Ji, 1995; Sen, 1995; Reid, 2001). For instance, Li and colleagues (Ji et al., 2008) have reported several interesting conclusions about the responses of the antioxidant system in skeletal muscle to exercise, particularly to endurance training: (1) SOD activity has consistently been shown to increase with exercise training in an intensity-dependent manner, (2) MnSOD is primarily responsible for the increase in SOD activity, (3) CuZnSOD activity is only slightly affected, (4) GPx activity also increases after endurance training, and (5) the effect on CAT activity has been inconsistent and controversial. More recently, the question has been whether these same beneficial effects occur in response to resistance training.

Few studies have examined the effects of resistance training programs on antioxidant activity in older adults. SOD, GPx, and CAT are the most commonly analyzed enzymes, but the thiol state and total antioxidant capacity have been widely studied as well. In general, research has shown that resistance training results in the increase of all or some of the antioxidant enzymes (Alikhani et al., 2019; Amaral et al., 2020; Bachi et al., 2019; Dantas et

al., 2016; Franzke, Halper, Hofmann et al., 2015; Mora et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturiniet al., 2019; Padilha et al., 2015; Parise et al., 2015b; Raungthai et al., 2019; Ribeiro et al., 2017; Soares et al., 2015; Vezzoli et al., 2019) or produces no changes (Bobeuf et al., 2011; Carru et al., 2018; Franzke, Halper, Hoffann et al., 2015, 2018; Gargallo et al., 2018; Giodo et al., 2018; Liao et al., 2016; Mora et al., 2019; Parise et al., 2005; Ribero et al., 2017; Shahar et al., 2013; Valls et al., 2014). In contrast, several authors have found a decrease in some or the total antioxidant capacity after resistance training (Amaral et al., 2020; Gargallo et al., 2018; Vincent et al., 2002; Shahar et al., 2013). Notably, Padilha and colleagues have shown that after 12 weeks of detraining, the positive adaptation achieved in the total antioxidant capacity after 12 weeks of resistance training still remained in a cohort of obese older women (ages 68.7 ± 4.8 years; Padilha et al., 2015).

Regarding SOD, most of the studies have identified a positive adaptive response with their increase following the resistance training program (Amaral et al., 2020; Franzke, Halper, Hoffmann et al., 2015; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Cavalcante et al., 2019; Parise et al., 2005b). Other researchers have found no changes (Frantzke et al., 2018; Giolo et al., 2018; Parise et al., 2005), and only one study (Shahar et al., 2013) has reported that SOD levels decrease after resistance training. In the case of GPx, strength training seems to have less impact compared to SOD. Only Raungthai et al. (2019) have found an increase in this antioxidant enzyme in older men and women with hypertension after 12 weeks of resistance training. In the rest of the studies, no changes were found (Liao et al., 2016; Franzke, Halper, Hofmann et al., 2015, 2018). Likewise, similar results as with SOD were shown for CAT; thee articles reported an increase of this enzyme (Franzke, Halper, Hofmann et al., 2015; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Cavalcante et al., 2019;

Parise et al., 2005b), three observed no changes (Franzke et al., 2018, Mora et al., 2019; Parise et al., 2005), and only one reported a decrease (Amaral et al., 2020).

Finally, regarding thiols, Gargallo and colleagues have determined a decrease in GSH activity in the high-intensity group, while no changes were found in the moderate-intensity group after 16 weeks of progressive resistance training by older women (Gargallo et al., 2018). In the same study, GSSG and the ratio GSSG/GSH remained unchanged. Vincent et al. (2002) have found that after 24 weeks of resistance training at low vs high intensity in older men and women, GSH levels increase in both groups but more so in the low-intensity group (Vincent et al., 2002). On the other hand, Peters et al. (2006) have reported that after six weeks of isometric exercise training, the whole blood GSH/oxidized GSH ratio increased (61%) in hypertensive adults (Peters et al., 2006).

Based on the available evidence, specific conclusions about the redox state following resistance training are difficult to compose at the present time, even more so if we take into account the wide variety of research designs used. However, in general, although results are somewhat mixed, it appears that resistance training can benefit the redox state by reducing oxidative stress and improving the antioxidant system in older adults. Still, additional studies are needed in this area before accurate answers to these questions can be provided.

It is also important to emphasize that endogenous antioxidant adaptations are dependent on the magnitude of RONS produced acutely by each exercise session (Radak et al., 2001) as training intensity is a key factor in achieving adaptations in the antioxidant system, as detailed in the next section.

C. Exercise intensity and redox status[5]

Physical training has been recommended to the elderly as a means of improving their redox status (Rowinski et al., 2013; Traustadottir et al., 2012). However, it should be noted that adaptations in oxidative stress biomarkers and endogenous antioxidants in older adults as a result of resistance training may be dependent on exercise intensity (Azizbeigi, et al., 2015; Cakir-Atabek et al., 2010, 2015; Carteri et al., 2015; Goto et al., 2003; Parker et al., 2014; Wang & Huang, 2005), as previously demonstrated with muscle mass, muscle strength, and physical function (Borde, Hortobagyi, & Granacher, 2015; Liu & Latham, 2009; Peterson et al., 2010). Therefore, determining the appropriate exercise intensity for older people is fundamental in evaluating the beneficial or adverse effects of exercise-related ROS production.

i. Effects on oxidative stress biomarkers

Despite all the information on exercise modulating the redox state, there is little knowledge on the best intensity to prevent or treat age-induced oxidative stress (Gomes et al., 2017). The studies that have been performed in different populations have generally shown an increase in oxidative stress following a high-intensity or supramaximal exercise such as the Wingate cycle test, intermittent running, or resistance training (Frank et al., 2000; Goldfarb et al., 2005; Groussard et al., 2003; Radak et al., 1998). More recent evidence has supported these findings in that exercise intensity plays a major role in post-exercise magnitude of RONS formation and thus the magnitude of oxidative stress response (Goto, Nishioka et al., 2007; Lamprecht et al., 2008; Lovlin et al., 1987; Quindry et al., 2003; Wang & Huang, 2005), at least in aerobic training, where data from literature suggest that

[5] Related publication: Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing*, *20*(2), 205-217. https://doi.org/10.1177/1099800417753877

improving oxidative/antioxidant balance can be achieved with intensities between the two ventilator thresholds (50–80% of VO2 max; Bouzid et al., 2015; Goto, Naito et al., 2007; Leaf et al., 1997; Lovlin et al., 1987).

However, regarding resistance training and older adults, the effect of exercise intensities is not yet clear. Heterogeneity in the intensity applied in different older adult training protocols may be one of the causes of variations in oxidative stress and antioxidants levels obtained in these studies. Is not clear whether differences in the intensities of exercise can generate changes in such markers, but Dixon et al. (2006) and Cakır-Atabek et al. (2015) have hypothesized that there is an exercise intensity threshold beyond which oxidative stress increases.

One of the main issues is that, to date, only two studies have directly compared the effects of resistance training protocols at different exercise intensities on oxidative damage in older adults. Vincent and colleagues have examined the effects on older men and women of long-term (24-week) resistance training with an intensity of 50% (1 set x 13 repetitions) and 80% of 1 RM (1 set x 8 repetitions) three days a week using 12 exercise machines (Vincent et al., 2002). After the training program, they observed a significant reduction in MDA in both groups, by 14% in low intensity and by 18% in high intensity.

In addition, Gargallo and colleagues have compared older women's16-week progressive resistance training programs performed twice a week with elastic bands at two exercise intensities: moderate (70% of 1 RM with a perceived exertion of 6–7 to 8–9 in the OMNI-RES scale for older adults) and high (85% of 1 RM with a perceived exertion of 6–7 to 8–9; (Gargallo et al., 2018). Both groups conducted the same six exercises, performing three or four sets of 15 repetitions in the case of the moderate-intensity group and three or four sets of six repetitions in the case of the high-intensity group. The results showed that

high-intensity resistance training induced significant chromosomal damage in terms of an increase in urine 8-oxo-dG, while moderate intensity produced significantly lower DNA damage.

These results indicate that a moderate level of oxidative stress is essential for adaptive responses to exercise, but very prolonged or exhausting exercise or exercise to which the person is unaccustomed can impair the balance between ROS production and the antioxidant defense system (Radak et al., 2013); this is in accordance with others works (Goon et al., 2008; Schiffl et al., 1997) and Radak and colleagues' postulations (Radak et al., 2013). According to Radak et al. (2005), the differential oxidative stress training adaptation between moderate and high intensity comes from the fact that older tissues need a lower level of ROS to retard the aging process and prevent diseases associated with redox imbalance.

ii. Effects on antioxidant enzymes

Endogenous antioxidants play a vital role in protecting eukaryote cells from exercise-induced oxidative stress. It is important to highlight that biological antioxidant adaptations are dependent on the magnitude of RONS produced acutely by each exercise session (Radak et al., 2001) as training intensity is a key factor in achieving adaptations in the antioxidant system. There is an abundance of literature that correlates the impact of exercise-induced oxidative damage and antioxidant status (Banerjee et al., 2003; Clarkson, 1995; Clarkson & Thompson, 2000; Turrens et al., 1982). For instance, it is well known that an acute bout of exercise increases the activity of antioxidant enzymes such as SOD, CAT, and GPx both in blood (erythrocytes, lymphocytes) and tissues (skeletal muscle, heart, liver; Cases et al., 2005; Clarkson, 1995; Inal et al., 2001; Ji, 1993; Leeuwenburgh et al., 1999; Tauler et a., 2004). However the magnitude and threshold of the increase are different between enzymes and tissues (Banerjee et al., 2003). Indeed, it is unknown if the increase of antioxidant enzyme activity is proportional to the exercise intensity applied (Criswell et al., 1993).

In the review by Bouzi and colleagues, authors have recommended that resistance training protocols for older adults should contain sufficient volume for each muscle group (3–5 sets, 10 repetitions) with intensities between 50 and 80% of 1 RM to improve the antioxidants' defenses (Bouzi et al., 2015). However, this recommendation was made on the basis of seven articles, of which only one compares different intensities. In fact, few studies have examined the relationship between (a limited number of) exercise intensities in resistance training protocols and antioxidant enzymes both in young (Cakir Atabek et al., 2010, 2015; Azibeigi et al., 2015; Carteri et al., 2015) and older people (Vicent et al 2002; Gargallo et al., 2018).

The results of our study presented in 2018 (Gargallo et al., 2018) provide some insight into this area. We found that redox activity is dose dependent in older women after 16 weeks of progressive resistance training. The significant decrease in GSH activity (10.91%) together with the increase in GSSG (7.91%) produced by high-intensity resistance training (85% of 1 RM with a perceived exertion of 6–7 to 8–9 in the OMNI-RES scale for older adults) could be interpreted as evidence of insufficient antioxidant defenses to cope with the enhanced free-radical production resulting from the intervention. In contrast, the reduction in GSSG (7.15%) along with the absence of changes in GSH resulting from moderate-intensity resistance training (70% of 1 RM with a perceived exertion of 6–7 to 8–9 in the OMNI-RES scale for older adults) shows that moderate levels would be the optimal training intensity for older women because it produces the necessary stimulus for effective adaptive changes in the enzymatic antioxidant system while reducing levels of DNA damage.

Our results regarding GSH contrast with those of previous studies, which have suggested that GSH increases after a resistance training exercise program (24 weeks, three days a week) in subjects aged between 60 and 83 years at high (80% 1 RM) and low (50% 1 RM) intensities (Vincent, et al 2002). It could be possible that the training intensities

(between 50% and 80% of 1 RM) and volumes (only 1 set per exercise) reported by Vincent et al. (2002) were not really a high stimulus, both intensities being between the thresholds where the antioxidant defenses can remove the excess of RONS produced.

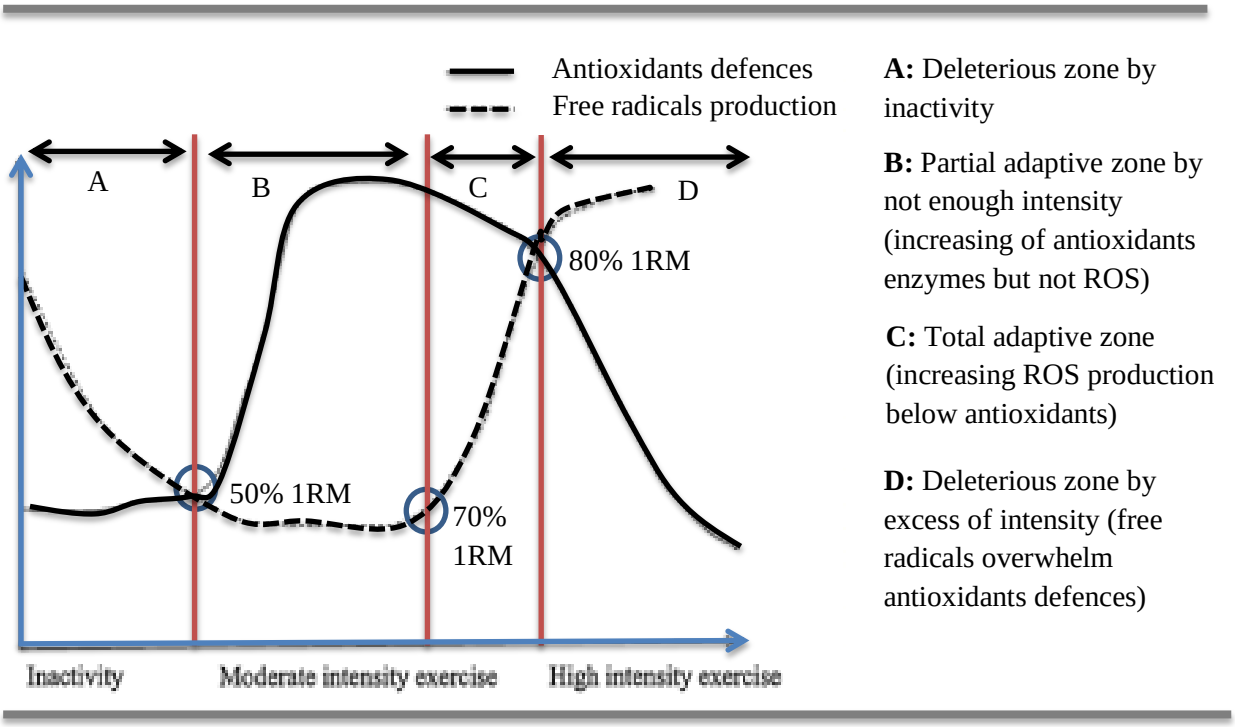
Similar results were also shown in young untrained men after six weeks of progressive resistance training, where the improvement of GSH (24.74% in the moderate-intensity group and 27.55% in the high-intensity group) were independent of the training intensity applied (moderate intensity: 3 sets of 12 repetitions at an intensity corresponding to 70% of 1 RM; high intensity: 3 sets of 6 repetitions at an intensity corresponding to 85% of 1 RM; Cakir-Atabek et al., 2010). Azizbeigi et al. (2015) have found that after eight weeks of progressive resistance training in young men, similar behavior in other antioxidant enzymes due to SOD and GPx activity increased in both moderate- (65–70% 1 RM) and high-intensity (85-90% 1RM) groups .

A possible explanation for these responses might be that as aging progresses, humans gradually become less adaptable to increases in ROS when undergoing high-intensity training, thus increasing their susceptibility to oxidative stress (Ji, 2001; Radak, et al 2013). This observation was clearly manifested in the study by Gargallo et al. (2018),where resistance training at a moderate intensity generated a beneficial adaptive response to oxidative stress, while high intensity produced an imbalance in favor of ROS production and a decrease in antioxidant enzymes.

In fact, if the exercise intensity during training resistance is too low and thus insufficient, the majority of free radicals produced during the sessions will be eliminated by the antioxidant defenses, and consequently there will be no change in the antioxidant system (Lovlin et al., 1987). However, if it is too high, the body's antioxidant system may not be able to effectively remove the excess RONS produced (Kerksick & Willoughby, 2005).

Figure 26 illustrates the theorist relationship between intensity and oxidative stress in older adult.

Figure 26. *Hormesis curve of the effects of training intensity on redox balance in elderly population*.



Note. Reproduced and adapted from "Radical oxygen species, exercise and aging: an update." (p. 1252), by Bouzid et al., 2015, *Sports Medicine, 45*(9).

D. Exercise modality and redox status

Among the different modes of exercise training, most studies on older individuals have examined the isolated effect of strength and endurance training programs or the combination of both. However, recent guidelines recommend multi-component training and power strength training programs to improve different health-related fitness parameters in the elderly population (Bangsbo et al., 2019; Beaudart et al., 2019; Fragala et al., 2019; Piercy et al., 2018; Zaleski et al., 2016).

Multi-component training appears to be associated with several health benefits, having a significant impact on cardio-respiratory fitness, metabolic profile, physical function, lean and bone mass, cognitive performance, and quality of life (Bouaziz et al., 2016; Marín-Cascales et al., 2017). On the other hand, high-speed resistance training is the hallmark strategy to improve muscle power in older adults as this parameter is the most discriminant predictor of functional performance in that population (Byrne et al., 2016; Cadore & Izquierdo, 2018; da Rosa Orssatto, Cadore et al., 2019).

However, although it is well known that the oxidative stress response to exercise, as happened with the intensity, is mode dependent (Bloomer et al., 2005), few studies have analyzed the effects of these two key training modalities on redox balance in older adults (Alcazar et al., 2019; Carvalho et al., 2010; Ceci et al., 2014; Dimauro et al., 2016; Gonçalves et al., 2019; Trapé et al., 2017; Valls et al., 2014; Venorjavi et al., 2013).

i. Effects on oxidative stress biomarkers

As mentioned, the oxidative stress response to distinct forms of exercise is likely variable. However, there is a paucity of data in relation to direct comparisons of exercise modes, in particular with multi-component and power strength training methods. Only several studies have investigated the relationship between multi-component and power strength training on oxidative stress markers in the elderly (Alcazar et al., 2019; Carvalho et al., 2010; Ceci et al., 2014; Dimauro et al., 2016; Gonçalves et al., 2019; Trapé et al., 2017; Valls et al., 2014; Venorjavi et al., 2013), and the results have been inconsistent and controversial.

Focusing on multi-component training, only the study by Trapé et al. (2017) has analyzed the effect of this modality on oxidative stress biomarkers. The authors have found that after 12 weeks of multi-component training with elastic bands and free weights in circuit,

two days a week, MDA levels decreased significantly in older women, producing an adaptive response to oxidative stress related to exercise.

Regarding muscular power-training interventions, Dimauro and colleagues (2016) showed that 12 weeks of low-frequency (two days a week), moderate-intensity (40–70% of 1 RM), explosive-type resistance training could be proposed as an effective exercise intervention for improving lipid peroxidation through a significant decrease in myeloperoxidase. Indeed, Valls et al. (2014), using the same training protocol, have also found a significant improvement in lipid peroxidation by a decrease in the 4-HNE biomarker. On the contrary, Ceci and colleagues, applying the same training program, have discovered no changes in MDA and protein carbonyls after 12 weeks of high-speed resistance training and after an acute session (Ceci et al., 2014). These three studies were conducted on elderly subjects.

The works of Venorjarvi et al. (2013) and Alcazar et al. (2019) were performed on clinical populations. The former observed that 12 weeks of power training combined with aerobic training three days a week, between 50% and 85% of 1 RM, results in no change in MDA in middle-aged men with impaired glucose regulation. Alcazar and colleagues have found a significant decrease in protein carbonylation after 12 weeks of applied power training plus high-intensity interval training (HIIT) three days a week, at 50%–85% of 1 RM, in elderly people with COPD.

ii. Effects on antioxidant enzymes

As with oxidative stress biomarkers, the body of evidence that supports the use of multi-component or power strength training modalities for improving antioxidant defenses is weak due to only few studies having analyzed this link (Carvalho et al., 2010; Ceci et al.,

2014; Dimuro et al., 2016; Gonçalves et al., 2019; Trape et al., 2017; Valls et al., 2014; Venorjarvi et al., 2013).

In the case of the multi-component studies, Carvarhlo et al. (2010) have shown that a moderate-intensity multi-component exercise program, performed three days per week, results in significant and beneficial effects on plasma antioxidant capacity through an increase in the total antioxidant status, GSH, and GPx biomarkers in older women. Gonçalves et al. (2019) have found similar results after 12 weeks of multi-component training, two 90-minute sessions per week and an exercise intensity between 13 and 15 on the Borg scale, with an improvement in redox status in older women. However, Trapé et al. (2017) have indicated that a multi-component-induced response to antioxidant defense varies between antioxidant enzymes. They observed a significant improvement in the total antioxidant capacity parameter, but at the same time no changes were found in the GSH activity after 12 weeks of multi-component training in older women.

Regarding power strength training interventions, most studies found no changes in the antioxidant parameters after applying the training program (Ceci et al., 2014; Valls et al., 2014; Venorjarvi et al., 2013). For instance, Valls et al. (2014) and Ceci et al. (2014) have demonstrated that in the absence of clinical disease, 12 weeks of high-speed resistance training could be well tolerated by adults 70–75 years old, but this program did not induce any change in GSH, GSSG, GSH/GSSG ratio, and total antioxidant capacity. Similarly, Venorjarvi et al. (2013) have also observed no changes in the antioxidant enzyme levels after 12 weeks of power training in combination with aerobic training in men with impaired glucose regulation. Only Dimauro et al. (2016) have found negative effects on antioxidant defense after 12 weeks of high-speed resistance training in healthy older adults, with a significant decrease in MnSOD.

As seen in the evidence above, contradictory findings exist in the literature regarding the effects of multi-component and power strength training on oxidative stress measurements. Differences among studies in methodological procedures, training protocols, sample populations, and selected biomarkers make it difficult to draw a conclusion about the effect of multi-component and power strength training on oxidative stress damage and antioxidant biomarkers. In addition, there is a lack of research that directly compares the effects of different exercise training modalities on the redox status in the elderly population. Thus, more research is required to provide further evidence of exercise-induced oxidative stress during different types of exercise interventions. However, this dissertation helps to advance and develop the understanding of this area of study by comparing, in the same project, the application of different intensities and training modalities on the redox state in older women.

II.VII. BODY COMPOSITION

II.VII.I. Bone tissue

A. Bone physiology

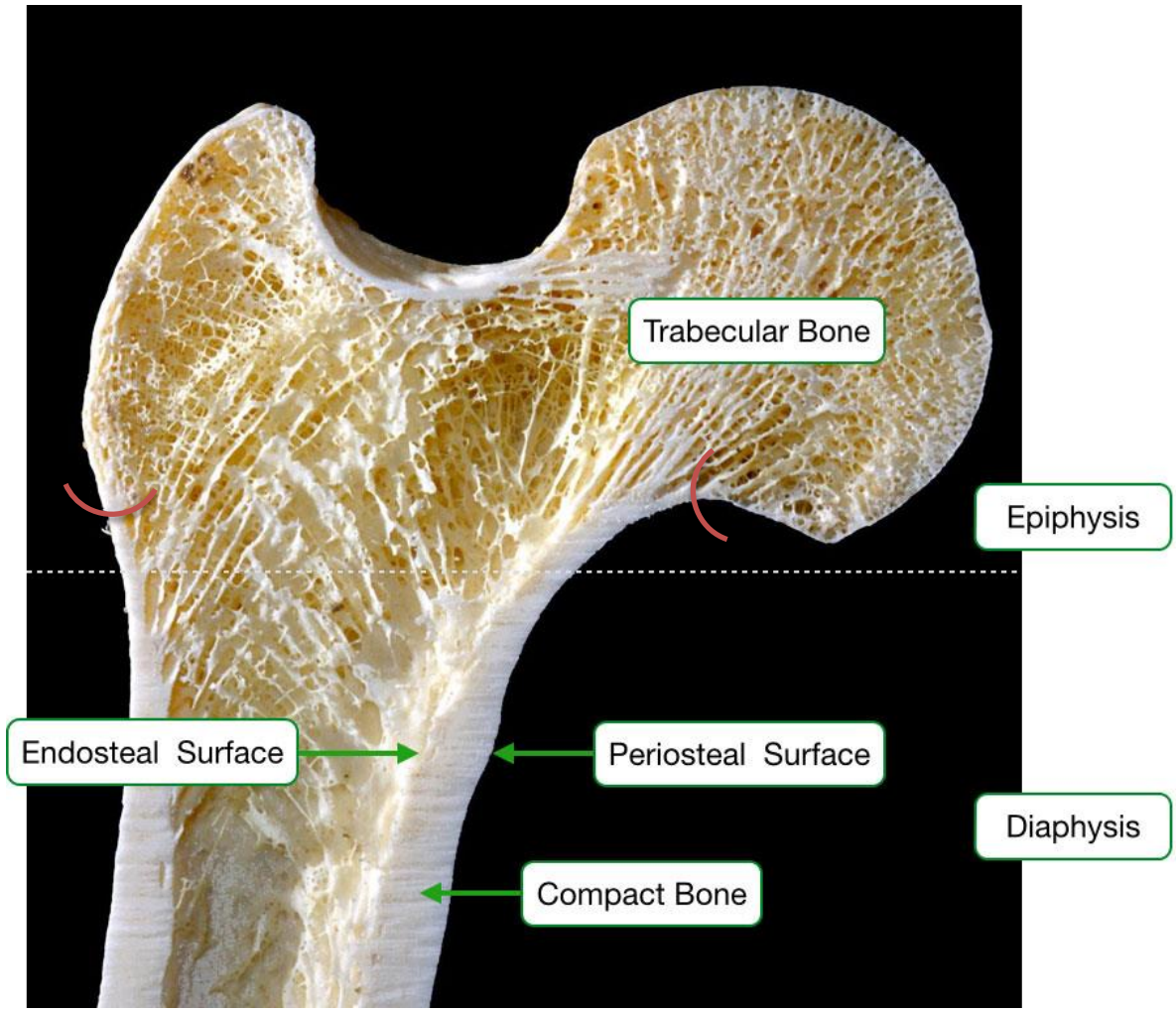
This section details the characteristics of bone tissue and the main findings of the effects of exercise on this tissue in the elderly population

i. Bone characteristics

The adult human skeleton comprises 206 individual bones, each of which consists of various tissues: osseous (also called bone) tissue, cartilage, epithelium, connective tissue, adipose tissue, and nervous tissue (Tortora & Derrickson, 1990). Eighteen percent of the entire weight of the human body comes from bone tissue alone (Tortora & Derrickson, 1990). The framework of bone, along with the ligaments, cartilages, and tendons, compose the human skeletal system (Tortora & Derrickson, 1990).

Bone tissue has a unique hierarchical structure in nature. At the macroscopic level (>1mm), bone is composed of two different types of osseous tissues: cortical and trabecular bone (also known as the compact/dense type and spongy/cancellous type, respectively; Brandi, 2009; Marieb et al., 2014; Yang et al., 2018; Tortora & Derrickson, 1990). Approximately 80% of an adult human skeleton is composed of cortical bone tissue, while the remaining 20% is trabecular bone (Brandi, 2009; Chappard et al., 2008; Ott, 2018; Tortora & Derrickson, 1990). However, the relative proportions of both types of bones vary considerably among different skeletal sites (Brandi, 2009; Tortora & Derrickson, 1990). For instance, cortical bone makes up the outer layer of all bones, surrounds the trabecular bone, and is more pronounced within the diaphysis of long bones (only a thin layer at bone metaphyses and epiphyse); due to its dense structure, it is well suited for the protective, supportive, and mechanical functions of the skeleton (Morgan et al., 2013; Tortora & Derrickson, 1990; Figure 27).

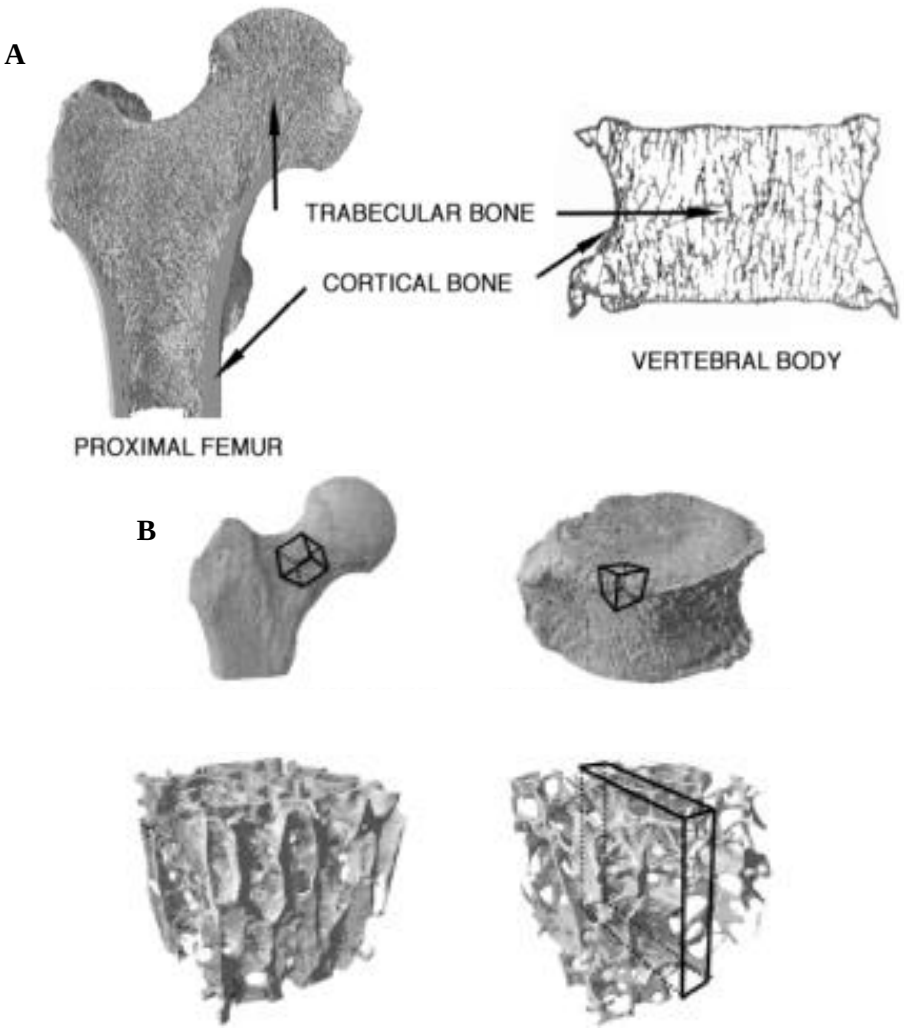
Figure 27. *Cortical and trabecular distribution in the different parts of a long bone.*



Note. Reproduced from http://www.cqvit.org/histo/bone/home.php

Trabecular bone, conversely, forms the inner part of axial bones such as the vertebrae or pelvis and is most pronounced within the metaphyses and epiphyses of long bones, though completely absent in the diaphysis (Brandi, 2009; Morgan et al., 2013; Tortora & Derrickson, 1990). It is found in large quantities in the femoral neck, calcaneus, and vertebral bodies (Osterhoff et al. 2016; Syahrom et al. 2017; Figure 28).

Figure 28. *Cortical and trabecular bone in long and short bones.*



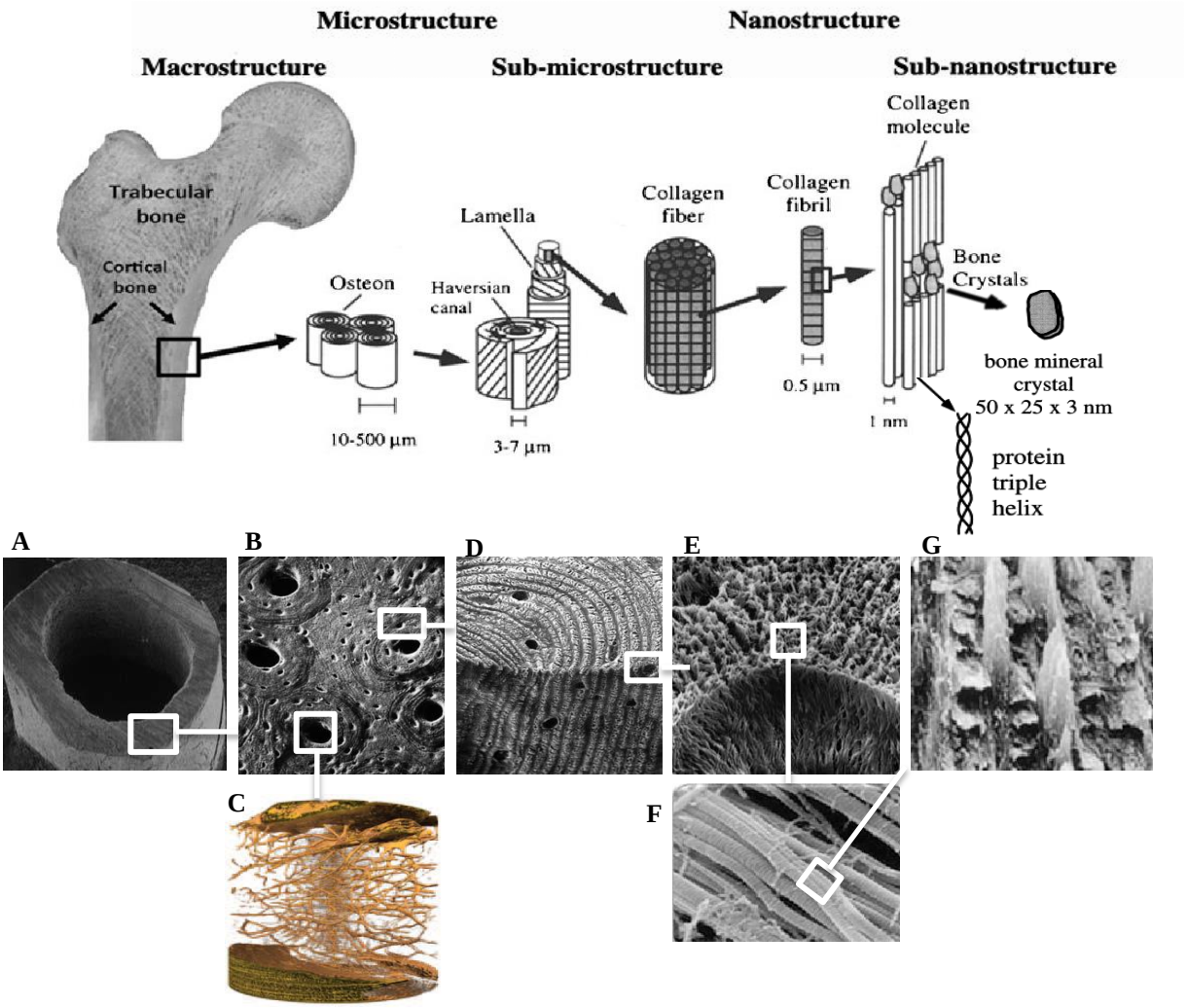
Note. A. Cross-sections of a human proximal femur (hip) and a human vertebra illustrating the large variation in trabecular bone volume and microarchitecture across anatomic sites; B. Images of cubes of trabecular bone from human femoral neck and human vertebrae. Reproduced and adapted from "Effects of osteoporosis therapies on bone biomechanics" (p 13, 25), by Easley, 2010, *Doctoral dissertation*, UC Berkeley.

Despite cortical bone being compact relative to the trabecular compartment, it is important to recognize that the former is also permeated by porosity. In fact, cortical bone tissue comprises approximately 70% mineralized matrix and 30% void volume, while trabecular bone constitutes 10–30% mineralized bone matrix and 70–90% void volume (Aaron et al., 1989; Ramchand & Seeman, 2018). Indeed, these two apparently distinct compartments are intimately linked in terms of porosity because, during the development of the bone tissue, cortical bone can arise from the corticalization of trabeculae in the metaphysis, while in later life, bone loss is associated with trabecularization of cortical bone, particularly at the endosteal surface (Bala et al., 2015).

Continuing with the hierarchical structure of bone, the microstructure of cortical bone (~500 microns) mainly consists of repeated structural units known as Haversian systems or osteons. Osteons comprise 10–15 lamellae arranged in concentric cylinders (known as the concentric lamellae, while the spaces between the cylinders are known as lacunae, where osteocytes are located) about a central Haversian canal, which is lined with osteogenic endosteum that contains nerves, blood vessel capillaries, and bone cells. Osteons are separated by highly mineralized structures called branching Volkmann's canals (also known as the perforating canals or cement lines), which are arranged perpendicularly to the central canal and provide a vascular/nerve supply from the periosteum to the cortical bone tissue (Brandi, 2009; Marieb et al., 2014; Tortora & Derrickson, 1990; Vaughan et al., 2013). In contrast, trabecular microstructure does not consist of central Haversian canals but of packets of 10 primary lamellae along with lacunae and canaliculi, known as trabeculae, which, organized in an irregular pattern, form a highly porous network of plate-like and rod-like structures, which are surrounded by marrow space (Burr & Allen, 2019; Marieb et al., 2014; Tortora & Derrickson, 1990).

At the next level (~10 microns), the sub-microstructure consists of lamellae, which are smaller cylinders of unidirectional fibrils within the osteons in cortical bone and within the trabeculae in trabecular bone tissue (cortical and trabecular lamellae). Following that, the nanostructure (submicron level) consists of the fibrils of the lamellae of cortical and trabecular bone, which are primarily mineralized collagen fibril bundles with diameters around 100 nm and are approximately 100 μm long (Burr & Allen, 2019; Zimmermann & Ritchie, 2015). Finally, at the sub-nanostructure level, the mineralized collaged fibrils are composed of nine calcium-based bone mineral crystals (primarily hydroxyapatite), which are interspersed among type-I collagen molecules; collagen is one of the essential components of this highly hierarchical structure because it composes up to 90% of the organic matrix in a bone (Garnero, 2015; Zimmermann & Ritchie, 2015; Figure 29).

Figure 29. *Hierarchical structural organization of cortical bone.*



Note. A. Cortical bone cross-section; B. Osteons surrounded by interstitial bone and many osteocytic lacunae distributed around the central Haversian canal; C. Haversian and Volkmann canals system in cortical bone; D. High-density and low-density concentric lamellae of an osteon. E. Osteocytic lacuna at a higher resolution showing collagen fibers; F. Collagen fibrils; G. Bone mineral crystals, collagen molecules and non-collagenous proteins. Extracted and adapted from "Mechanical properties and the hierarchical structure of bone" (p. 93), by Rho et al., 1998, *Medical Engineering & Physics, 20*(2) and from "Bone quality--the material and structural basis of bone strength and fragility" (p. 2251), by Seeman and Delmas, 2006, *New England Journal of Medicine, 354*(21).

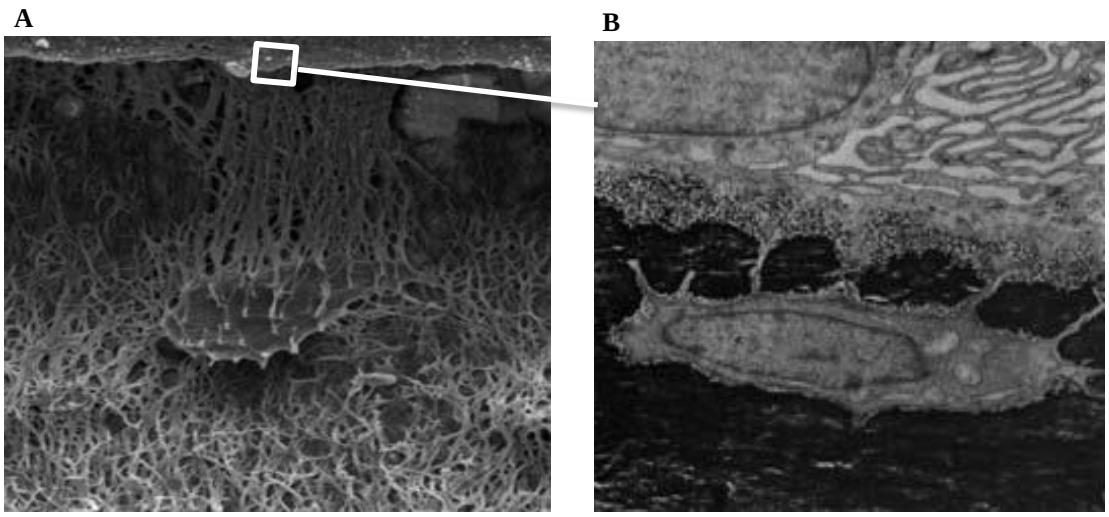
As a self-renewing tissue, bone is highly active and contains multiple cell types. Specifically, at the cellular level, five types of bone cells have been identified: mesenchymal stem/osteogenic cell, osteoblast, osteocyte, chondrocyte, and osteoclast. The first four are in charge of producing or maintaining the bone matrix (bone formation), while the remaining one resorbs/degenerates the osseous tissue (bone resorption; Kenkre & Bassett, 2018; Marieb et al., 2014; Tortora & Derrickson, 2012a).

Particularly, osteoblasts are derived from the mesenchymal cell line and are the bone cells responsible for producing collagen and proteoglycans through the Golgi apparatus. Osteoblasts may be classified as either active or inactive (osteocytes) and can change shape dependent on activity status. The active osteoblasts are single-nucleated cells that form small organelles called vesicles, which accumulate phosphate (PO_{43}-) ions and calcium (Ca_{2+}) to create crystals of hydroxyapatite and form the mineralized bone matrix in the process called ossification, or osteogenesis. These cells also produce type- I collagen in response to parathyroid hormones and osteocalcin when stimulated by 1.25 hydroxyvitamin D (25OHD; Kenkre & Bassett, 2018; Marieb et al., 2014; Tortora & Derrickson, 2012a).

Osteocytes are the most abundant cell type within bone. These cells are essentially mature and relative inactive osteoblasts that are imbedded within the bone matrix. Although these bone cells are relatively inactive and are not directly involved in degrading or forming bone, they play an important role by providing a structure for the creation of new bone. Furthermore, there is an intercellular communication between osteocytes and osteoblasts through the canaliculi (spaces in the bone matric that are occupied by osteocytes) that may be important for relaying stress/strain signals throughout bone tissue, key in the bone modeling and remodeling process (Boskey & Robey, 2013; Kenkre & Bassett, 2018; Marieb et al., 2014; Tortora & Derrickson, 2012a).

Osteoclasts are multinucleated bone-resorbing cells, formed by the fusion of several macrophages and monocytes derived from hematopoietic stem cells in the marrow (Bar-Shavit, 2007). Osteoclastic activity is primarily influenced systemically by parathyroid hormones, calcitonin, and 25OHD (Boabaid et al., 2004). These cells are only capable of resorbing bone tissue when they are in direct contact with it; a series of events is necessary to retract the lining cells that surround osteoclasts in their inactive state, which prevent direct contact with the underlying bone matrix. More information about bone cell types is provided in the article by Kenkre and Basset (2018; Figure 30).

Figure 30. *Osteocytes and osteoblast.*



Note. A. osteocytes connect with lining cells and with one another through a network of canaliculi; B. detail of an osteoblast lining cell connected to an osteocyte. Reproduced and adapted from "Bone quality--the material and structural basis of bone strength and fragility" (p. 2251), by Seeman and Delmas, 2006, *New England Journal of Medicine, 354*(21).

Finally, human bones can be classified anatomically into five subcategories: long (e.g., femur), short (e.g., lateral cuneiform), flat (e.g., sternum), irregular (e.g., vertebra), and sesamoid (e.g., patella; Marieb et al., 2014; Tortora & Derrickson, 2012b). Long and irregular bones experience the majority of the bodily weight-bearing and movement for daily tasks via the vertebral column and lower limbs. Irregular bones can absorb more energy by deforming than long bones can due to having a higher percentage of trabecular bone tissue, achieving lightness and structural flexibility over stiffness (Turner, 2002). However, long bones have the ability to tolerate higher peak loads before cracking by the predominant cortical tissue.

ii. Bone composition

Bone tissue consists of an abundant extracellular matrix surrounding the bone-dwelling cells (Tortora & Derrickson, 2012a). Such a matrix is a composite material comprising inorganic and organic constituents. In mature adult bone, the inorganic material accounts for approximately 65–70% and is composed of ceramic crystalline mineral formed from calcium and phosphate deposited as calcium-phosphate salts, which undergo mineralization to hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$; Tortora & Derrickson, 2012a].

The remaining 30–35% of the bone matrix mass is composed of organic material (20–35%) and water (5–15%). Organic material is primarily type-I collagen (~90%), with small amounts of minor collagens and noncollageneous proteins, including binding proteins and glycoproteins such as osteocalcin (OC), osteonectin, osteopontin, and bone-sialoprotein; growth factors; phospholipids; and glycosaminoglycans (Baron, 1999; Brandi, 2009; Frost, 1997; Tortora & Derrickson, 2012a). The triple-helix-shaped type-I collagen molecules arrange in parallel with gaps between each molecule. These spaces within the bone commonly serve as storage sites for bone marrow or as channels for bone cell networks, blood vessels, and nerves (Dallas et al., 2013; Marieb et al., 2014; Tortora & Derrickson, 2012a). While the bone's flexibility is determined by the organic materials (although

proteoglycans provide strength under compression), the inorganic mineral components provide strength and rigidity of bone, allowing for muscle attachment for mechanical work, bodily support, and protection of vital organs (Baron, 1999; Lian et al., 1999).

iii. Bone function

It is commonly believed that bones serve several functions determined mainly by their sizes and shapes. Throughout life, bones mainly serve, but are not limited to, the following primary functions (Banfi et al., 2010; Baron, 1999; Clarke, 2008; DiGirolamo et al., 2015; Harada & Rodan, 2003; Karsenty & Ferron, 2012; Lian et al., 1999; Lombardi et al., 2015; Marieb et al., 2014; Mera et al., 2017; Mosialou et al., 2017; Oldknow et al., 2015; Rodan, 1998a; Tortora & Derrickson, 2012a, 2012b): provide mechanical support for the body, provide attachments of soft tissues (muscle tendons and ligaments), provide support and protection from mechanical injury for vital tissues and internal organs (the central nervous, cardiovascular, and pulmonary systems), play an important role in mineral homeostasis by storage and release of vital minerals (especially calcium and phosphorus) for the normal functioning of other organs, is a cavity for bone-forming cells, play an important role in haematopoiesis, and store energy and metabolism.

Nonetheless, arguably the most important function of bone tissue related to movement is to withstand and transmit forces without breaking. Bone must be strong to tolerate loading and light at the same time to facilitate the motion as well as rigid to resist bending and to serve as a lever and flexible to store energy by deforming without breaking **(**Currey, 1969; Diab et al., 2005; Schaffler & Burr, 1988). These paradoxical properties depend on the bone's matrix volume, its organic and inorganic composition, and how this material is organized geometrically (shape and size) and microarchitecturally (Bouxsein & Karasik, 2006; Viguet-Carrin et al., 2005) in space with varying volumes of extracellular fluid-filled void (porosity; Seeman & Delmas, 2006). As summarized by Seeman and Delmas, optimal bone tissue

characteristics are defined by optimal levels of flexibility, lightness, and stiffness (2006). These properties are maintained by the bone's adaptation to mechanical loading during daily life.

iv. Bone modeling and remodeling

Throughout a lifespan, the dynamic tissue of bone undergoes continuous construction and reconstruction via two processes: bone modeling and bone remodeling (Seeman & Delmas, 2006).

The modeling process, which begins early in skeletal development, produces changes in shapes and sizes of bone (macroarchitectural changes) when new bone is created without previous bone resorption due to mechanical forces exerted on the skeleton. Therefore, this process is responsible for longitudinal and radial growth during childhood and adolescence (Burr et al., 1989; Krahl et al., 1994). The purposes of this process are to maximize the functions of bones and, specifically, to establish the skeleton's peak bone strength (O'Connor et al., 2010; Olsen et al. 2000). In this process, to incur major changes in bone architecture, bone resorption and formation are uncoupled, occurring independently at distinct skeletal sites. New bone is formed at one anatomical site, and old bone is removed from another. Modeling occurs during growth, and the majority of this process is completed by skeletal maturity. However, modeling can still happen even in adulthood, although less frequently than remodeling (Kobayashi et al., 2003**)**, in response to mechanical loadings, exercise, diseases (hypoparathyroidism, chronic kidney disease, renal bone disease), or treatment with anabolic agents such as teriparatide (Burr et al., 1989; Krahl et al., 1994; Lindsay et al., 2006; Ubara et al., 2003, 2005).

In contrast, bone remodeling, first defined by Frost, is a tightly regulated process that replaces old and damaged bone with new (Frost, 1964). This process occurs continuously

throughout a lifetime to repair skeletal damage, maintain bone strength, prevent accumulation of brittle hyper-mineralized bone, and preserve mineral homeostasis by liberating stores of phosphorus and calcium (Bentolila et al., 1998; Iñiguez-Aria & Clarke, 2015; Kenkre & Bassett, 2018; Mori & Burr, 1993). As opposed to modeling, formation and resorption are tightly coupled both temporally and spatially so that overall structure and volume remain unchanged. Basically, bone remodeling is a sequential action of osteoclastic and osteoblastic bone cells that is regulated by a network of embedded osteocyte bone cells that may sense strain or any other mechanical stimuli (Taylor et al., 2007). This process is highly regulated, lifelong, and essential for maintaining mineral homeostasis and preserving bone integrity; thus, it has a central role in adult bone physiology, especially when its malfunction leads to diseases such as osteoporosis (Allen & Burr 2014; Pivonka et al. 2008).

Around 10% of the total skeleton is replaced each year by the remodeling process (Manolagas, 2007). However, not all bone surfaces in the mature skeleton undergo active remodeling during the bone remodeling process (Brandi, 2009). Small regions or packets of old bone are resorbed by osteoclasts and replaced with packets of newly synthesized proteinaceous matrix by osteoblasts, which subsequently mineralize to form new bone (Parfitt, 1996).

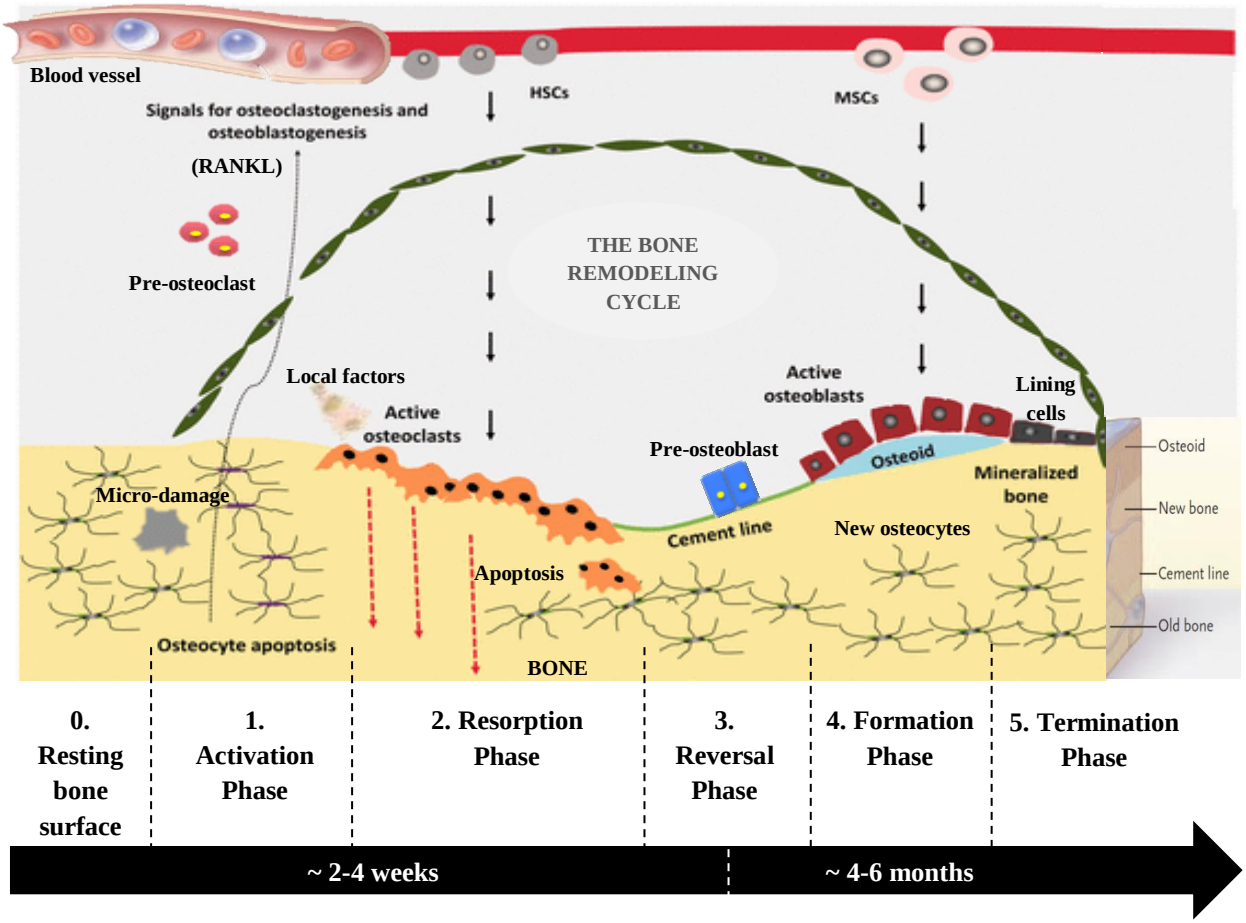
This close coordination between resorption and formation is possible because of the organization of osteoclasts and osteoblasts in local bone remodeling teams, called basic multicellular units (Frost, 1964), which are coordinated and directed by osteocytes, playing the role of coach (Frost, 1990).

Anatomically, the remodeling cycle occurs in these basic multicellular units and comprises five coordinated steps: activation, resorption, reversal, formation, and termination (Kenkre & Bassett, 2018). These steps occur simultaneously but asynchronously in distinct

locations within the skeleton on the three components (endocortical, intracortical, and trabecular) of the endosteal bone envelope and, to a lesser extent, on the periosteal envelope (Orwoll, 2003).

The entire cycle requires three to four and six to eight months (120–200 days) to complete the remodeling in cortical and trabecular bone, respectively (Agerbaek et al., 1991; Brandi, 2009; Mundy, 1999; Figure 31).

Figure 31. *The bone remodeling process.*



Note. Schematic diagram of the bone remodeling cycle with their five phases. HSCs: Haemopoietic stem cells, MSCs: Mesenchymal stem cells. Reproduced and adapted from "Bone quality--the material and structural basis of bone strength and fragility" (p. 2253), by Seeman and Delmas, 2006, *New England Journal of Medicine*, *354*(21).

This process involves some key signaling and hormone pathways that control the osteoclastic and osteblastic activity. Despite many of them still being unknown, several of the main factors suggested by the evidence are: (1) endocrine regulators such as parathyroid hormone, vitamin D (with the active metabolite 25OHD), calcitonin, growth hormone, glucocorticoids, sex hormones, androgens, and thyroid hormone; (2) paracrine regulators such as cytokines, insulin-like growth factor, and prostaglandins, and (3) others such as the receptor activator of nuclear factor-κB (RANK), RANK ligand (RANKL), osteoprotegerin, and canonical Wnt signaling (Kenkre & Bassett, 2018; Mundy, 1999).

In the first phase, activation (approximately eight days), mononuclear monocyte–macrophage osteoclast precursors are recruited from the circulation and activated (Roodman, 1997). The bone surface is exposed as the lining cells separate off the bone surface, lifting off the endosteal membrane and forming a raised canopy over the site to resorb the bone (Hauge et al., 2001). Furthermore, multinucleated preosteoclasts on the surface of the exposed bone are created from the fusion of multiple mononuclear cells. The initiation of this phase is possible due to local or systemic signals. The osteocyte apoptosis induced by bone matrix micro-damage in old bone produces an initial signal in the osteocytes that use their network of dendritic processes to signal to other cells and release factors that increase local angiogenesis to recruit osteoclast and osteoblast precursors (Atkins & Findlay, 2012; Burr, 2002; Goldring, 2015; Mori & Burr, 1993; Parfitt, 2002a; 2002b). Remodeling is also possible in response to systemic changes in hormones such as parathyroid hormone.

The resorption, or second phase (approximately two to four weeks), starts when the differentiated and activated osteoclasts adhere to the bone surface and start to resorb the old bone by secreting hydrogen ions via H+-ATPase proton pumps and chloride channels to dissolve the collagen-mineral bone matrix in the Howship's lacunae (trabecular bone) or resorption cavities/tunnels (cortical bone; Silver et al., 1988; Tolar et al., 2004). This phase

finishes with the programmed apoptosis of osteoclast cells, thus ensuring that excess resorption does not occur (Eriksen, 1986; Reddy, 2004; Tolar et al., 2004).

During the reversal phase (approximately four to five weeks; Delaisse et al., 2003), bone resorption switches to formation, although exact signals that couple bone resorption to subsequent formation are not yet fully understood ___. At the completion of bone resorption in the resorption cavities, pre-osteoblasts remove the unmineralized collagen matrix, and then a non-collagenous mineralized matrix "cement-line" is deposited to enhance osteoblastic adherence (Zhou et al., 1994).

Following this is the formation phase (approximately three to six months; Eriksen et al., 1984), which can be divided in two subphases: nonmineralized new bone matrix (110–160 days) and mineralized bone matrix (10–35 days). In the first part, osteoblasts synthesize and secrete a new type-I collagen-rich matrix, called osteoid. In the bone mineralization part, hydroxyapatite crystals are deposited among collagen fibrils by osteoblasts via the release of small, membrane-bound matrix vesicles that concentrate calcium and phosphate. While this process is still not well understood, it is known to depend on the local concentration of calcium and phosphate within extracellular matrix vesicles, the systemic regulation of the same two minerals, and the local inhibitors of mineralization such as pyrophosphate (Anderson, 2003, 2005; Cui et al., 2016).

Finally, once mineralization is complete, the termination or quiescence phase starts. At the completion of bone formation, about 50–70% of osteoblasts undergo apoptosis, while remaining osteoblasts become bone-lining cells, or those surrounded by and buried within the matrix become osteocytes (Burger et al., 2003). Bone-lining cells retain the ability to differentiate into osteoblasts upon exposure to mechanical forces or changes in the parathyroid hormone (Dobnig & Turner, 1995), and the osteocytes via secretion of

antagonists to osteogenesis play a key role in signaling the end of remodeling (Bonewald, 2011); they will also be the pathway of communication through which stresses and strains (mechanotransduction property) are detected.

The net result of each bone remodeling cycle is a new osteon. The process is essentially the same in both cortical and trabecular bone (Parfitt,1994) and occurs on the bone surfaces, mainly at the endosteal surface. However, remodeling of trabecular bone occurs more often (7% per year) than cortical (2–3% per year) and happens at a much faster rate (approximately 25% faster per year) than cortical bone (Martin et al. 1998; Scheuer & Black 2000). Therefore, as the newly formed bone is less mineralized than mature bone tissue, trabecular bone tends to have a lower mean mineral density than cortical bone. In addition, the bone remodeling rate of cortical bone is adequate to maintain biomechanical strength of bone; however, the higher rate of trabecular bone turnover exceeds the requirements for maintenance of mechanical strength, which indicates that it plays a more significant role in mineral metabolism (Iñiguez-Ariza & Clarke, 2015).

Furthermore, it is necessary to consider that there can be large intra- and interspecimen spatial variation in mineral density within bone tissue due to remodeling being initiated at different times and at different sites in small packets (geographically and chronologically separated; Mundi, 1999) and because mineralization of the new tissue occurs over several months. Thus, it could be possible to have surfaces in the same bone with a lower mineral density than others despite the bone remodeling process being carried out in both because neighboring remodeling areas or packets are in different stages of the remodeling cycle.

It is also important to note that while a decrease in mechanical stress leads to a decrease in osteoblast activity (Cooper et al., 1999), reduced stress due to paralysis,

immobility, or inactivity (sedentary lifestyle) does not affect osteoclast activity (Minaire et al., 1974). Thus, if bone resorption remains normal but bone formation decreases, this leads to a decrease in bone density (one week's immobility may result in bone loss at a rate as great as 2%; Hamdy et al., 1995; LeBlanc et al., 1987).

This situation is very common in old age, when adults tend to move less and the aging process, especially in women with hormonal changes due to menopause, aggravates the problem. That is why properly prescribed physical exercise is a key preventive strategy to maintain bone mass, especially in older women, as it maintains the mechanical stress necessary to create bone.

As shown, bone remodeling is critical for the maintenance of bone balance and calcium and phosphate homeostasis. However, the resorption and formation rates change throughout a lifetime, increasing osteoclast activity and decreasing osteoblast activity at the end of the adult stage, especially after menopause; thus, it is necessary to implement strategies such as exercise to maintain bone health.

B. Mechanical behavior of bone

The relationship between mechanical loading stimuli and weight-bearing stress to the biological response in bone has been the subject of increasing scientific research and theoretical considerations since the earliest suggestions of how bone tissue achieves architectural suitability for its load-bearing role (Wolf, 1982). Bone can adapt its structure and composition to prevailing loads (Frost, 1964), and mechanical loading is a fundamental factor for bone mass accretion (Currey, 2002).

Even though the precise stimuli to which osteoblasts, osteoclasts, and osteocytes respond remains unconfirmed, it is hypothesized that bone cells have sensors within the cell membrane where mechanical strain, pressure/fluid shifts, or electrical charges are converted

into a biomechanical signal to start the bone modeling/remodeling cycle (Smith & Clark, 2005). The theoretical framework about how biochemical and mechanical stimuli interact to create bone adaptations is discussed in the following sections.

i. Wolff's law

Although in 1638, Galilei (Galilei, 1638) noted a relationship between both bone size and shape and body weight, mechanical forces were not identified as being responsible for shaping the architecture of the bone tissue until the studies by Meyer (1867), Culmann (1866), and Roux (1905) in the 19th century. These authors identified arched trabecular patterns, which appeared to be aligned along principal stress directions produced by loading, indicating that bone formation and resorption are biological, stress-controlled processes (Carter, 1984; Huiskes, 2000; Skedros & Brand, 2011).

However, it was in 1892 that the German scientist Julius Wolff, influenced by the previous scientists, stated that "every change in the form and function of bone or of their function alone is followed by certain definite changes in their internal architecture and equally definite alteration in their external conformation, in accordance with mathematical laws" (Wolff, 1893). He was the first one who, through his well-known law of bone transformation, proposed the idea that the skeleton possesses the property of functional adaptation, where bone structure, architecture, and mass are adaptable to the demands of the mechanical loading stresses upon the skeleton (Turner, 1998). This bone strain arising from mechanical loading stimulates the remodeling process, which results in the redistribution and realignment of trabeculae to better withstand the applied load.

More specifically, Wolff formulated a mathematical explanation for the structure of trabecular bone in the femoral neck, demonstrating how the architecture of trabecular bone reflected engineering principles, which later works would expand to the cortical tissue.

However, Wolff's law does not describe the influence that different types of mechanical loads have on bone, which has been examined further by Frost's mechanostat theory.

ii. Mechanotransduction and Frost's mechanostat theory

The process by which the mechanical stress signal through bone induces biophysical signals to a bone cell, and ultimately a cellular network, and produces the initiation of bone remodeling is called mechanotransduction (Donahue, 1998). Four steps are involved in mechanotransduction: mechanocoupling, biochemical coupling, transmission of biochemical signal, and the effector response. The majority of researchers hypothesize that osteocytes and bone-lining cells are responsible for mechanotransduction through strain-induced interstitial fluid flow change (Burger & Klein-Nulend, 1999; Turner, 1998) and strain amplification by proteins adhering to the cytoskeleton (Han et al., 2004; Turner, 1998).

The quantification of normal human bone strain is an important point in understanding the response of bone to mechanical stimuli (Ehrlich & Lanyon, 2002). Hert and colleagues (1969, 1971) were among the first to explore this subject. They showed that by applying loads to rabbit tibiae diaphysis, dynamic (but not static) strains increased bone formation. However, they could not determine the physiological strains or the strains that the loading engendered (Ehrlich & Lanyon, 2002). Only with the development of strain gauges (the gold standard for measuring bone strain) in the mid-20th century was it possible to report different magnitudes of strain loads in bone tissue *in vivo* (Fritton et al., 2000; Hoshaw et al., 1997; Lanyon et al., 1975).

In fact, the concept of a mechanostat for bone adaptation to strain, first introduced by Frost in 1987 and then subsequently updated again in 2003, was one of the most significant contributions to musculoskeletal research (Frost, 1987, 2003). However, before explaining Frost's mechanostat theory (also referred to as the Utah paradigm; Frost 1987, 2001; Frost &

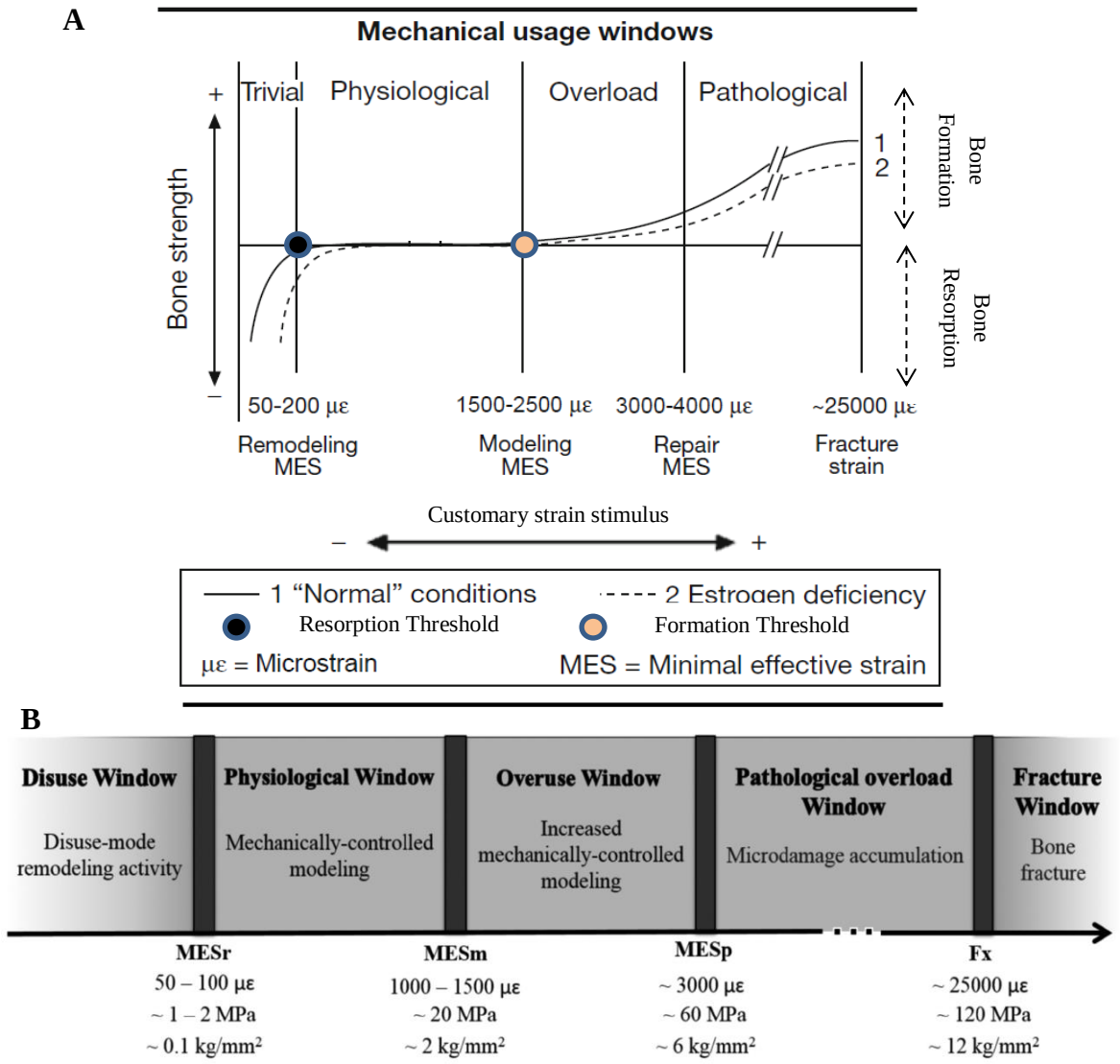
Jee, 1994), it is important to elaborate certain concepts related to it. For instance, when a force is applied to a bone, a stress is created and measured in units of pressure (force per cross-sectional area). This force causes a deformation in the bone tissue structure, which is measured as a strain, the ratio of the change in length to the original length. Due to the stiffness of bone tissue, strains are usually presented in microstrain units (με) as little deformation occurs (Burr & Allen, 2019).

Regarding the mechanostat theory, Frost proposed that the mechanical competence of bones is achieved and maintained by homeostatic mechanisms. Bone adaptation is dependent on mechanical strain thresholds or mechanical usage windows, where bone has various set points of minimum effective strain (MES) that govern whether bone mass is gained, maintained, or lost, determined by local (e.g., previous load-bearing), systemic (e.g., hormones), and external (e.g., diet) factors, as well as genetics and age (Rosa et al., 2015; Reginster & Burlet, 2006;Skerry 2006; Suominen, 2006).

Frost originally outlined MES for three stages of bone adaptation—remodeling, modeling, and microdamage—which create four mechanical usage windows. Later, Duncan and Frost stablished five mechanical usage windows (Duncan & Turner, 1995; Frost, 2003) with the same MES although with different strain values (Frost 2003; Figure 32).

Specifically, bone that is exposed to strains below the remodeling threshold (between 50–100 and 200 με), being in the disuse mode (also called trivial window), is removed and weakened by stimulation of intracortical and endosteal remodeling, losing bone mass due to resorption exceeding formation. Studies conducted during space flight (LeBlanc et al., 2000; Oganov et al., 2005) have revealed that this results in a net loss of bone over time.

Figure 32. *Mechanical usage windows for bone adaptation based on Frost's Mechanostat theory*.



Note. A. Mechanical usage windows defined by Frost's Mechanostat theory on bone adaptation to strain; B. Mechanical usage windows adapted by Duncan & Turner (1995) and Frost (2003). Reproduced and adapted from "Muscle training for bone strength" (p. 87), by Suominen, 2006, *Aging Clinical and Experimental Research, 18*(2), and from "From mechanical stimulus to bone formation: a review" (p.723), by Rosa et al., 2015, *Medical engineering & physics, 37*(8).

Strains from 100–200 to the modeling threshold (1000–1500 to 2500 με) represent the physiological window where the strains applied elicit homeostatic remodeling, maintaining the bone mass (remodeling may occur but with no net gain or loss). Frost believed that strain stimuli between remodeling and modeling thresholds (the physiological window) could define the region of natural remodeling or adaptation of bone to the typical peak voluntary mechanical loads that come from usual physical activities. In this area, there is equilibrium between bone formation and resorption cells. These strains can be easily attained with a variety of physical activity modalities, which highlights the importance of mechanical loading induced by exercise in promoting and maintaining bone health.

If mechanical loading increases and exceeds the modeling threshold, entering into the overuse/overload window (from 1000–1500 to 3000–4000 με), this results in an increase in bone formation, entailing an upregulation of osteoblast activity and net matrix deposition, therefore increasing bone mass and bone strength. Then a new modeling threshold is established. However, if mechanical strains exceed the microdamage threshold (also called repair threshold) located above 3000–4000 με, they can begin to cause bone microtrauma. If bone is exposed to repeated strains above the microdamage threshold in the pathological or overload window (from 3000–4000 to 25000 με), it can cause a range of nontraumatic fractures such as stress fractures (Basso & Heersche, 2002; Frost, 2003; van der Meulen, et al., 1993). Finally, fracture may occur at strains around 25000 με depending on bone quality and age (Frost, 1987, 2003; Jee, 2009), which is equivalent to a tension that stretches the bone by 2.5% or a stress around 110,353,801 N.m-2. This level of strain stimulus is highly unusual in daily and exercise activities (Frost, 1994).

Although it is widely believed that in a single individual, a single mechanostat threshold exists, this view is disproven by the fact that different bones require a specific strain magnitude to maintain bone mass. Therefore, various bones and bone tissues (cortical vs

trabecular) respond differently to decreases or increases in loading depending on the sensibility of the mechanostat (Pivonka, 2018).

Thus, to optimize bone health throughout a lifespan, it is necessary to engage in correct physical activity that produces appropriate levels of mechanical strains. Different strain levels have been reported from various types of physical activities to maintain or strengthen bone, such as walking (393–557 με), zigzag running (1147–1226 με), sprinting (2104 με), forward jumping (1600–3450 με), and vigorous exercise (~2000 με), which supports the mechanostat theory (Frost, 1987, 2003; Rosa et al., 2015). In addition, the mechanostat theory has also been verified in several experiments with animals (Jaworski & Uhthoff, 1986; Rubin & Lanyon, 1985; Skedros et al. 2001). However, several authors have criticized this theory for being phenomenological (Chen et al., 2010) in that it is only descriptive in nature and does not specify the mechanism behind the remodeling adaptation of bone (Carter & Beaupre, 2007; Pearson & Lieberman, 2004; Turner et al., 2002).

Finally, although the mechanostat theory provides the basis for the mechanical action on bone adaptation, focusing on the magnitude of loads imparted to bone as a central factor of this theory, there have since been numerous advances in the understanding of mechanisms underlying bone morphology (Pivonka, 2018; Robling , Duijvelaar et al., 2001; Srinivasan et al., 2002). It is now widely accepted that bone cells modulate their responses to dynamic mechanical stimuli through not only the load magnitude but also through various parameters such as the pattern (distribution/site-specific), rate, number, and frequency of loading (Daly, Dalla Via et al., 2019; Duncan & Turner, 1995; Kunnel et al., 2002). Other mechanical stimuli contributing to bone adaptation are discussed in later sections.

Nonetheless, understanding the mechanostat and mechanobiological regulatory factors involved in mechanosensation is essential to improve the ability to control bone adaptation based on physiological loading through different exercise modalities

iii. Three rules for bone adaptation

As a result of the experimental evidence about the influence of mechanical load on bone modeling and remodeling collected over the past four decades, mainly from animal models, Turner (1998) has proposed and developed three fundamental rules for bone adaptation (Burr et al., 2002): 1) Bone is driven by dynamic, rather than static, loading. 2) Only a short duration of mechanical loading is necessary to initiate an adaptive response. Extending the loading duration has a diminishing effect on further bone adaptation. Thus, short periods of exercise with sufficient magnitude or rate of strain and with rest periods between them are more effective osteogenic stimuli than a single sustained session of exercise. 3) Bone cells accommodate to a customary mechanical loading environment, making them less responsive to routine loading signals.

Regarding the first law, it is widely accepted that bone tissue is sensitive to rapid strain reversals as opposed to purely absolute load magnitudes (Hert et al, 1971; Liskova & Hert, 1971). That is because, as has been shown in animal models, strain stimulus inducing bone adaptation is dependent on strain magnitude and frequency (cycles per second), which implies that a static load has a frequency of zero, resulting in no effect on bone adaptation. Thus, strain magnitude and strain rate/loading frequency determine the level of bone adaptation to a mechanical stimulus (Turner, 1998). These factors must be considered in mechanical loading situations and would suggest that higher strain magnitudes, higher strain rates, higher loading frequencies, or the combination of all those conditions would stimulate bone adaptation better than the lower-level equivalent.

In addition, in connection with the second law, animal models have shown that increasing the number of loading cycles or duration beyond a certain threshold has no added benefit to the bone adaptation response. For instance, 36 loading cycles per day showed no greater statistical benefit in terms of bone adaptation than four to five cycles per day (Rubin & Lanyon, 1984; Umemura et al., 1997). Animal models have also revealed that load cycles divided into several discrete bouts, separated by several hours, are more effective than a single uninterrupted bout (Robling et al., 2002; Turner, 2003). These last experiments support the final law, illustrating that bone cells seem to be highly sensitive to the initial or abnormal loading stimulus, but once adapted to the new load, rate, or frequency, cells appears to desensitize and achieve steady state or mechanosensitivity, giving the impression of becoming saturated (Rubin & Lanyon, 1985).

It is necessary to consider the three rules for bone adaptation proposed by Turner when designing an exercise program to improve bone health.

iv. Young's modulus

In 1927, Leonhard Euler developed the concept of Young's modulus (Euler, 1960), which is the relationship between the external stress (force per unit area) applied to a solid object and the subsequent level of strain (proportional deformation) that occurs; in this way, Young's modulus is a measure of the intrinsic mechanical stiffness of the material.

As outlined above, a certain level of strain is required to initiate bone adaptation. Therefore, this property can be applied to bone as the presence of collagen in its composition gives it a somewhat elastic property, and it can be deformed under certain mechanical stresses before recoiling back to the original geometric shape. Numerous studies have found that Young's modulus in bone is highly dependent on the bone mineral density, bone volume, and trabecular thickness in micro- and macroarchitecture (Novitskaya et al., 2011). In fact,

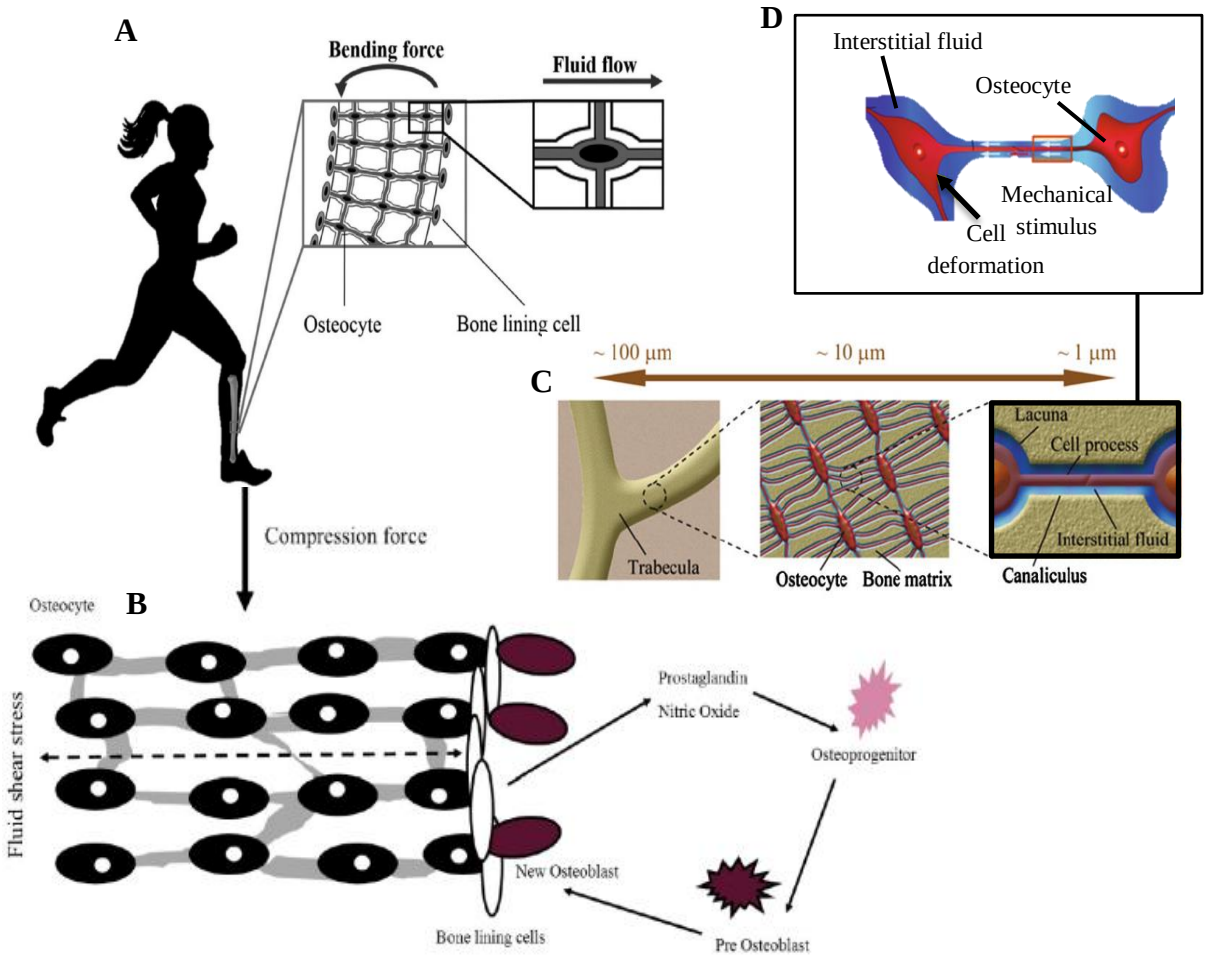
mechanical properties of both cortical and trabecular bone should be considered as mechanically different in terms of material properties (Rho et al., 1993). For instance, the force required to produce a deformation in the cortical bone is higher due to cortical tissue possessing more compressive strength and also mechanical stiffness than trabecular bone (with a higher Young's modulus, the greater is the stress force needed to deform the object; Amaral et al., 2002; Rho et al., 1993, 1998). Indeed, Rahal (2007) has indicated that cortical tissue could have over four times higher compressive strength than concrete.

v. Fluid flow stress

Along with the mechanostat theory, the three rules of bone adaptation, and the Young's modulus property, several mechanisms have also been proposed to explain how bone cells sense the mechanical stimulus to start bone adaption, which includes changes in hydrostatic pressure and electric fields resulting from electrokinetic effects with fluid flow and fluid-flow-induced shear stress. Recent research has started to support the role of interstitial fluid flow in bone remodeling.

Briefly, as a result of mechanical stress on bone, there is a deformation of the tissue (a strain) that produces interstitial fluid flow through the lacunar-canalicular network of bone, creating hydrostatic pressure gradients within the bone's matrix (Basso & Heersche, 2002). Internal hydrostatic pressures change, depending on external loading forces, which subsequently deforms the bone macrostructure and increases the internal fluid pressure. This fluid movement within the extracellular matrix of bone exerts a shear stress on bone-lining cells and osteocytes, which are three times more sensitive to relatively small extracellular fluid shear stresses than other endothelial bone cells, deforming the fluid flow and, thus, the osteocyte and dendritic processes (Bonewald, 2007; Figure 33).

Figure 33. *Bone fluid flow.*



Note. A. Mechanical strain inducing bone fluid flow; B. Cellular mechanism of mechanotransduction in response to compression forces and fluid shear stress; C. Trabecular bone, osteocytes and interstitial fluid flow in canaliculi; D. The osteocyte process within the canaliculi in response to mechanical stimulus. Reproduced and adapted from "From mechanical stimulus to bone formation: a review" (p.721), by Rosa et al., 2015, *Medical Engineering & Physics, 37*(8).

Therefore, the osteocytes appear to detect mechanical loading by the canalicular fluid flow generated by axial bending and initiate the signals to release the local products, which leads to division and differentiation of osteoprogenitor cells, beginning the production of new bone. Additionally, it is necessary to mention that shear stresses are proportional to the rate of fluid flow. Thus, as bone is loaded at a higher strain rate, fluid velocity and, consequently, shear stresses increase (Burr et al., 2002). In fact, several authors have shown that high levels of shear stress and fluid velocities are present at simulations of vigorous activity as this stimulus is closely linked with the mechanosensitivity of the osteocyte (Jacobs et al, 1998; Verbruggen et al, 2013).

In addition, the mechanisms of the shear stress produced by the fluid flow support the possible saturation effect that desensitizes bone tissue to repeated mechanical loading stimuli (Srinivasan & Gross, 2000). Thus, it has been shown that canalicular fluid responds maximally following the first loading cycle before gradually returning to a homeostatic environment with the application of multiple loading cycles.

vi. Beam theory

There are several more models and theories that explain how bone adaptation works in response to an external mechanical stimulus. Some of the better-known ones are Cowin's theory of adaptative elasticity, the model of trabecular bone adaptation at the continuum level (also called the Stanford model of daily stress stimulus), Huiskes's strain energy density model, mechanobiological models by Pivonka and colleagues, optimization models (also called cost-benefit models), and the beam theory (Drapeau & Streeter, 2006; Lieberman et al., 2001, 2003; Pearson & Lieberman, 2004; Pivonka, 2018).

The last one, the beam theory, is especially useful to explain how the long bone diaphysis models its responses to mechanical stimuli on the basis that bone diaphysis, under

externally loaded forces, performs in a similar manner to I-beams used for structural support in buildings. In this sense, this theory follows the principle that the distance that material is placed away from the center of a beam's cross-section, which makes for a stronger structure than material placed close to the center, can indicate the strength of the beam and its resistance to bending (Ruff, 2000a, 2000b; Ruff & Larsen, 1990).

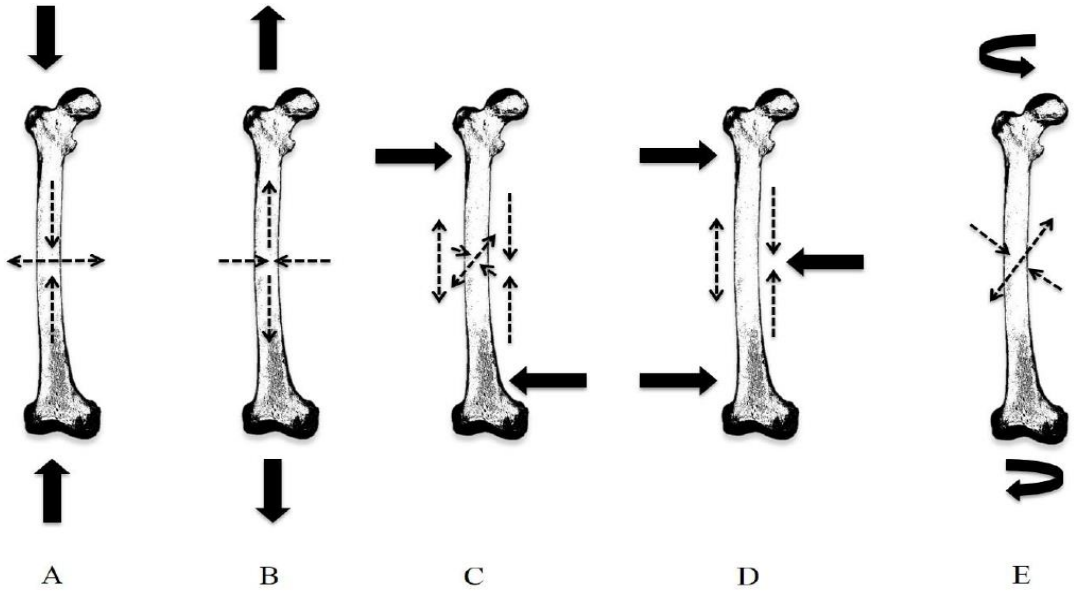
Adapting this theory to bone adaptation properties, the shape and size of the diaphysis are continually modified to maintain a balance between efficiency and strength as the largest amount of the osseous material is concentrated in the direction of the greatest loading stress (Carter, 1984; Rubin & Lanyon, 1984). Bones, like beams, can be physiologically loaded in five different directions or conditions (Figure 34), which often occur in combination: compression (negative elongation), tension (positive elongation), shear, bending, and torsion or twisted (Carter & Beaupré, 2007).

Compression and its opposite force, tension, act parallel to the longitudinal axis of the bone. While compressive forces shorten and widen the bone along the axis, tensile forces stretch the bone material, elongating it. Conversely, shearing and bending forces act on a plane perpendicular to the axis of the bone, causing lateral deformation, while torsion acts in all the planes. During human movement, these loading conditions occur in multiple planes and rarely appear isolated as they are produced by joint reaction, strains of muscle tendons on bone, or by the body mass in reaction to the ground (e.g., ground reaction forces).

Under these five mechanically loading conditions, bone experiences both stress and strain. As mentioned above, mechanical stress is the amount of force applied to an area, while strain is the amount of deformation of the material as a result of the force. Therefore, compressive stress results in negative or shortening strain, while tensile stress results in a positive or elongation strain. At the same time, shearing, bending, and torsion forces

represent a combination of compression and tension stress and thus result in both negative and positive strain.

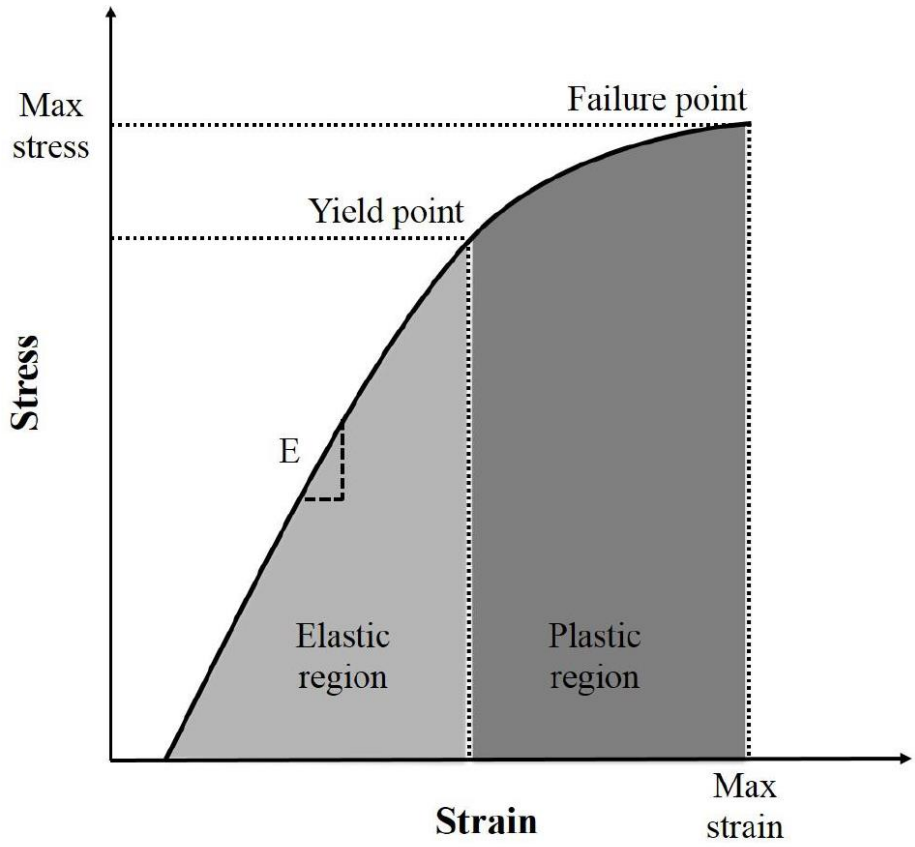
Figure 34. Loading conditions experienced by long bones.



Note. A. Compression; B. Tension; C. Shearing; D. Bending; E. Torsion. Dark arrows indicate the direction(s) of force applied to the bone during loading condition while dashed arrows indicate the directionality of strain from these forces. Reproduced from "Variation in Cortical Bone Distribution in the Aging Adult Appendicular Skeleton" (p. 44), by Gooding, 2017, *Doctoral dissertation*, University of Tennessee.

For any solid material, the ratio between stress and strain can be calculated as a stress-strain curve (Figure 35), where the slope of the curve, Young's modulus, represents the material's stiffness (Burr & Turner, 1999) and reflects the strength of the bone to resist stress before strain results in failure. This relationship differs depending on the loading condition applied, moisture content, age, health of the individual, and composition of the material, which, in bone, is inherently anisotropic (meaning that the collagen fibers within it are not all oriented in the same direction; thus, a single long bone will respond to stresses dissimilarly to other bone Currey 2006; Currey et al., 2009; Lieberman et al., 2003).

Figure 35. *Stress-stain curve for bone.*



Note. Under loading bone is able to resist deformation until the end of the material's ability (yield point) to return to its original shape (elastic region).When deformation past this point is considered unable to return to its original form (plastic region). When maximum strain and stress levels are reached, the material will fail. E= Young's modulus (slope of the curve) represents the bone's ability to resist stress before results in failure. Reproduced from *Skeletal tissue mechanics* (p. 121), by Martin et al., 1998, New York: springer

C. Measures and biomarkers of bone health

Bone health (also called bone strength) is the term used to define the bone's resistance to fracture. It is determined by both bone mass (also called bone density) and bone quality (also called bone structure; Camacho et al., 2016). This dissertation addresses aspects of each of these categories in the following sections.

i. Bone mass

- *Bone mineral density and and Bone mineral content*

Bone strength is dependent on many qualities of bone, of which bone mass, expressed mainly in BMD, is the most commonly measured and used for the diagnosis of osteoporosis (Blake & Fogelman, 2007; NIH Consensus on Osteoporosis, 2001). BMD refers to the amount of mineral matter per area or volume and is used as a predictor of osteoporosis and fracture risk (Weaver et al., 2016). While a number of bone-density measuring techniques are available, dual energy X-ray absorptiometry (DXA) is considered the gold-standard method of BMD assessment (Bonnick et al., 2010; Pivonka, 2018).

BMD is expressed by grams per area or per volume depending on the measurement tool used. BMD measured by DXA does not represent the volumetric density (grams per cubic centimeter) but rather the areal density (grams per square centimeter; Ott et al., 1997); thus, this is not an accurate measurement of the true BMD, which is mass divided by volume (density always implies volume). For this reason, the exact parameter of BMD determined by DXA is the areal BMD (aBMD), and it is estimated by dividing the bone mineral content (BMC) by the two-dimensional (2D) area of the site measured (Berger, 2002), in which the units given are grams per centimeter squared (g/cm^2).

BMC, which is the weight of the dry bone mass in grams, is measured by DXA from any selected part of the skeleton based on the levels of X-ray absorption. On the basis of the

proportion of light rays that pass through the soft tissue, as opposed to being blocked by minerals in the bone, computer software divides the amount of X-ray absorption by the surface area of the bone in each pixel of the scan and determines the BMD (Weaver et al., 2016). In addition to aBMD, volumetric bone mineral density also exists and consists of the estimation of vBMD through adding to the aBMD a projected postero-anterior lateral vertebral scan to measure vertebral width, height, and depth.

The aBMD value obtained by DXA is used as a suitable parameter for bone strength (r^2 = 0.59 to 0.88) as the actual strength of bone tissue cannot be evaluated in a living human and therefore must be estimated with noninvasive methods (Cheng et al, 1997). In addition, BMD measurement, although not totally representative of mechanical strength, is highly correlated with Young's modulus ($r = 0.69$; $P < 0.005$) and yield stress ($r = 0.64$; $P < 0.005$), therefore being a useful measure to show bone strength and stiffness (Gibson, 2005; Wachter et al., 2002).

Regarding the preferred or most relevant skeletal sites for monitoring aBMD, the lumbar spine L1–L4 (predominantly trabecular), the hip (mixed trabecularcortical, which encompasses the femoral neck, wards triangle, trochanter, shaft, and total hip aBMD measures), and the wrist (predominantly cortical) are the most common sites for DXA aBMD assessment (Pivonka, 2018). Among them, the femoral neck site is advocated by the International Osteoporosis Foundation (IOF) for the diagnosis of osteoporosis (Kanis et al., 2013), although analyses of multiple sites prone to fracture are recommended (Lee, Lee et al., 2014).

Current osteoporosis guidelines of three of the most representative organizations regarding bone—the North American Menopause Society (NAMS), the American Association of Clinical Endocrinologists (AACE), and the International Society for Clinical

Densitometry (ISCD)—are generally in agreement about preferred skeletal sites for scanning aBMD. For instance, NAMS indicates that the total hip is the preferred location for BMD testing, particularly in postmenopausal women (aged > 60 years) as spinal measurements may be unreliable (Management of postmenopausal osteoporosis: position statement of the North American Menopause Society, 2002). This organization proposes that the spinal measurements of BMD are especially useful in early postmenopausal women because this population tends to lose bone tissue faster in the spine than in the hip (trabecular bone loss happens faster and earlier than cortical bone).

On the other hand, AACE recommends BMD measurements at either the proximal femur or the lumbar spine (Hodgson et al., 2004), while ISCD recommends a spine scan as the preferred site, with the total hip as an alternative (Lenchik et al., 2002). However, all of them agree that measurements of BMD at peripheral sites such as the wrist or heel should not be used for diagnosis or monitoring the BMD, only for the assessment of fracture risk (Hodgson et al., 2004; Lenchik et al., 2002; Management of postmenopausal osteoporosis: position statement of the North American Menopause Society, 2002).

- *T-score and Z-score*

To standardize values from different bone densitometry scanners, results of aBMD are reported by DXA as either a T-score or Z-score, with both expressed as standard deviation (SD) units. T-scores are used for the diagnosis of osteoporosis and represent the number of SDs above or below the average aBMD value of a young and healthy adult reference population (T-score = [measured aBMD – young adult mean aBMD) / young adult population SD]; Kanis et al., 2008; Looker et al., 1998; Pivonka, 2018).

Specifically, the referent database is the mean femoral neck aBMD of healthy Caucasian (white) adult women (20–29 years of age) obtained from the National Health and

Nutrition Examination Survey III performed by WHO (Looker et al., 1998). This reference range allows researchers and clinicians to establish a comparison between their participants'/patients' aBMD and the aBMD of a normative healthy population through the T-score values. However, although this approach is recommend by the ISCD (Bianchi et al., 2010) for use in both men and women and is applied worldwide, it is not universally agreed upon, and there is some controversy regarding the usage of young Caucasian women as the reference group due to values being specific to gender (only women), ethnicity (only Caucasian), and site (only femoral neck; Bonnick et al., 2010; Hoiberg et al., 2007; Tenenhouse et al., 2000).

T-scores values are preferred for the aBMD measurement of men and postmenopausal women aged 50 and above and, thus, for diagnostic and classification osteoporosis in this population (Bonnick et al., 2010; Camacho et al., 2016). As such, a T-score of 0 indicates that the mean aBMD value in the specific skeletal site analyzed is the same as for the young, healthy reference population. A T-score strictly below 1, which means at least one SD below the mean aBMD value from the young reference population, is an indication of low bone mass, which can be categorized on the basis of the degree of bone mass loss: osteopenia if the T-score is between -1 and -2.5 and osteoporosis if the T-score is below or equal to -2.5. Subjects are considered to have normal BMD if their T-score is greater than or equal to -1 (Bonnick et al., 2010).

T-scores are usually calculated for the femoral neck and lumbar spine regions. In the case of the lumbar spine, measures are preferably reported from the L1–L4 segment, as supported by the ISCD (Baim et al., 2015), although sometimes values of L2–L4 are also reported by clinicians. Due to the highly variable rates of bone loss at different measurement sites, particularly with the aging process, lumbar and femoral neck regions can show discordance in their T-score values and bone mass classifications (Arlot et al., 1997).

On the other hand, Z-scores represent the number of SDs an individual's aBMD is above or below the mean aBMD of a matching age, sex, weight, and ethnic cohort (Allen & Krohn, 2014; Bonnick et al., 2010; Imel et al., 2014). As this value is an age-matched comparison, Z-scores are preferred over T-scores for the aBMD measurement of men and premenopausal women under the age of 50 (Baim et al., 2015). In this case, a Z-score two or more SDs below the reference aBMD mean is classified as below the expected range for age and suggests that advanced bone loss can be the result of other factors in addition to normal aging (secondary osteoporosis, while a Z-score within +/-2.0 SDs is determined as within the expected range for age (Camacho et al., 2016)

ii. Bone quality

The strong connection between BMD and bone strength has caused the diagnosis of osteoporosis and assessment of fracture risk to presently be based on the quantitative analysis of BMD by DXA. However, it is important to recognize that low BMD alone accounts for a maximum of 44% of fracture risk (Stone et al., 2003), which means that although DXA has been the most widely used clinical tool to assess bone strength by measuring BMD, it only provides partial information about bone strength and does not capture the other main component: bone quality (Bouxsein, 2003; Burr, 2004).

Bone quality is defined as the properties and characteristics of a bone that influence its resistance to fracture, but they are not related to measures of bone quantity or density (Chesnut & Rosen, 2001; Hernandez & Keaveny, 2006; Watts, 2002). There have been many discussions regarding the suitability of this term in the context of bone fracture risk assessment due to BMD measurements also containing the mineralization of bone matrix; consequently, it is not possible to separate BMD from bone quality (Pivonka, 2018; Sievänen et al., 2007).

Many bone characteristics have been hypothesized as potential factors of bone strength and quality (Burr, 2004; Chesnut & Rosen, 2001; Hernandez & Keaveny, 2006), and they can be classified into three main categories: bone structural properties, bone composition/material properties, and bone turnover rate (Klibanski et al., 2001). Properties of bone quality collected from different studies are summarized in Table 1.

Table 1. *Components of bone quality*.

Bone structural properties	
Macro-architecture	
Bone geometry	Cross-sectional area of the medullary cavity and cortical area
	Cross-sectional area of cortical area
	Bone cortex
	Distribution of cortical mass about the bone center
	Cortical thickness
	Trabecular number
	Trabecular thickness
Bone size	
Bone shape	
Spatial distribution	
Micro- architecture	
Lacunar	Lacunar number
	Lacunar morphology
Resorption cavity	Resorption cavity number
	Resorption cavity size
	Resorption cavity distribution
Mineral matrix	Mineral matrix distribution
	Mineral matrix alignment
Collagen	Collagen distribution
	Collagen alignment
Crystal	Crystal distribution
	Crystal alignment
Damage-accumulation	
Bone composition or material properties	
Mineralization	
Porosity	
Collagen traits	
Collagen cross-linking	
Crystallinity	
Micro-fractures or micro-damage	
Bone turnover or remodeling rate	
Bone resorption biomarkers	Collagen degradation products
	Non-collagenous proteins
	Osteoclastic enzymes
	Osteocyte activity markers
Bone formation biomarkers	Collagen synthesis products
	Non-collagenous proteins

Note: Information extracted and adapted from Allen et al., 2006, 2008; Bouxsein, 2005; Gamsjaeger et al., 2010; Griffith & Genant, 2008; Hernandez & Keaveny, 2006; Mashiba et al., 2001; Paschalis et al., 2005; Seeman, 2003; and Seeman & Delmas, 2006.

iii. Bone biomarkers

In addition to imaging techniques to assess bone mass or certain bone quality parameters, which provide a static measure of skeletal status, bone turnover markers (BTMs) are emerging as promising tools as they present information about the dynamic cell metabolism that occurs during the bone remodeling process with respect to bone formation and resorption. This could provide insight into the changes that the static skeleton (assessing it via DXA) may undergo in the future (Brown et al., 2009; Shetty et al., 2016). As shown above, bone remodeling rate assessment via BTMs is one of the main parameters to evaluate bone strength through bone quality as changes in the bone turnover rate could affect the quality of the bone tissue. They provide valid information about skeletal status that is independent from and complementary to other bone strength measurements, especially BMD (Johnell et al., 2002). In fact, a recent review has posited that BTMs measuring bone formation and resorption may offer an alternative monitoring strategy to BMD for bone health, especially for bone-loss treatment (Henriksen et al., 2011).

There are several advantages to testing BTMs over DXA in monitoring bone strength in normal or osteoporotic individuals, including that BTMs are noninvasive, relatively cheap, and allow the detection of changes in bone status earlier than DXA as they have the capability to detect changes in bone turnover rates after three to six months of applied therapy (such as physical exercise and antiresorptive or anabolic drugs), and even in some cases already after two weeks (Delmas et al., 2006; De Papp et al., 2007; Garnero, 1994; Kalaiselvi et al., 2013; Park et al., 2019; Pivonka, 2018; Shetty et al., 2016). Thus, one of the principal advantages of BTMs is that they can readily detect acute changes in bone cell metabolism (Park et al., 2019).

In the past, BTMs were primarily reserved for research, but with the recent refinements in methodology and a wider availability of reliable, sensitive, cost-effective, and

specific assays for BTMs, their use is increasing in clinical practice as a complement to the measurement of BMD in the management of osteoporosis (Shetty et al., 2016). However, it is important to take into account that BTMs are defined as nonspecific biomarkers of bone because they provide information about the whole-body skeletal turnover process as opposed to site-specific information on a particular bone region such as other measurements provide (Pivonka, 2018). In fact, there are other organs that may contribute to a specific BTM (Brown et al., 2009). Thus, not all BTM changes are bone-specific. The accuracy with which BTMs reflect the status of the bone remodeling process depends on, among other factors, their bone specificity as the ideal BTM is that which is not produced by any other tissue (Vasikaran, 2008).

Many BTMs are enzymes or proteins secreted by osteoblast and osteoclast cells during the bone remodeling cycle, although the majority are by-products originated during the synthesis or degradation of type-I collagen, due to this being the main protein (approximately 90%) that forms the organic matrix of bone (Eastell & Hannon, 2008; He et al., 2016; Liu & Webster, 2016; Naylor & Eastell, 2012; Shi et al., 2014). However, all BTMs can be easily determined through their concentration levels in blood (serum and plasma) and urinary samples, although the latter require corrections for creatinine values (Delmas et al., 2000; Eastell et al., 2018).

Generally, BTMs are classified into two major categories—bone resorption markers and bone formation markers—based on the metabolic process they are considered to reflect or the biological compartment to which they belong (Seibel, 2005; Cremers & Garnero, 2006; Leeming et al., 2006; Shetty et al., 2016). However, a lesser-known third category exists, consisting of markers of osteoclast regulatory proteins (Cremers & Garnero, 2006; Kuo & Chen, 2017; Leeming et al., 2006; Seibel, 2005). An overview of most BTMs is provided in Table 2 and Figure 36.

Table 2. *Bone turnover biomarkers.*

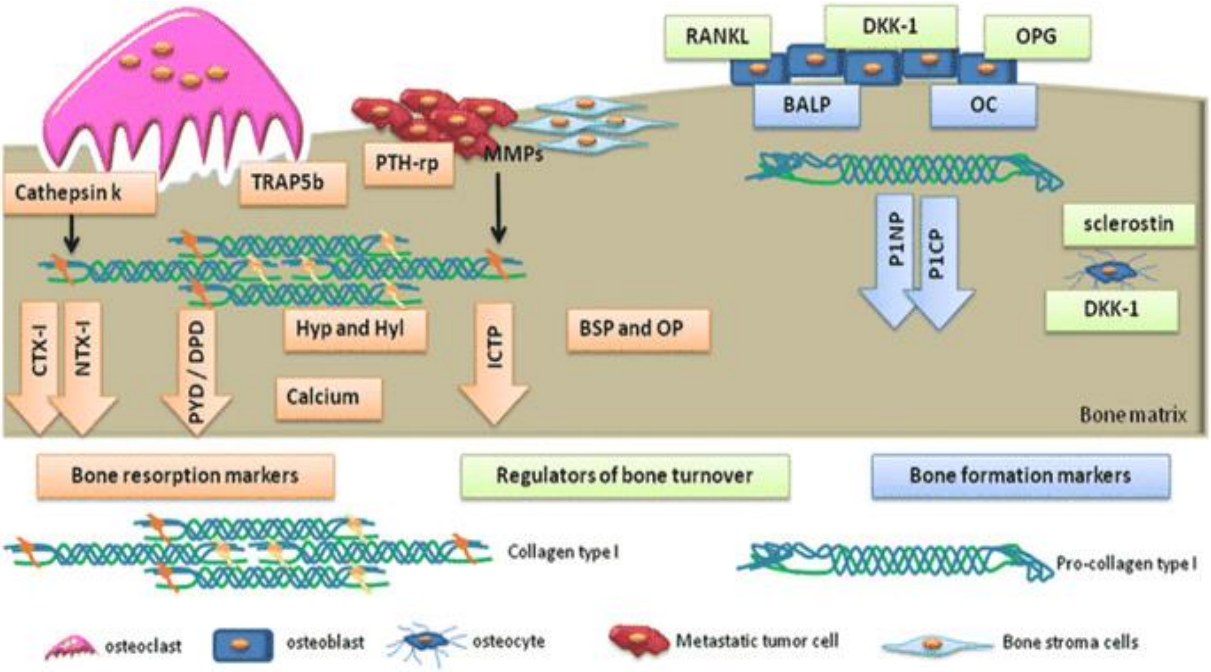
Bone Biomarker	Biological required sample	Assay or method	Biological variability		Reference values
			CVi	CVg	
Bone resorption biomarkers					
CTX-I	Urine, serum, plasma	ELISA, RAI, EIA	-	-	0.17–0.30 ng/ml // H: 50-70 pmolBCE/umol Cr, M: 50-70 pmolBCE/umol Cr (premonopausia), 28-190 pmolBCE/umol Cr (postmenopausia)
NTX-I	Urine, serum, plasma	ELISA, ECLIA	14.7	26.8	37 ± 15 nmol BCE/mmol Cr // H: 21 a 83 mol/eco/mmol Creat., M: 26 a 124 nmol/eco/mmol Creat. (postmenopausica) 17 a 94 nmol/eco/mmol Creat. (premenopausia)
ICTP or CTX-MMP	Serum	RIA	6.9	28.8	-
HYP	Urine	Bergman and Loxley method	-	-	34.7 mg/g creatinine
GHYL	Urine	HPLC	-	-	1.35 ± 0.82 mmol/mol
GGHYL	Urine	HPLC	-	-	1.93–6.07 μmol/L
PYD	Urine, serum	HPLC	18.6	24.8	28.8 μmol/mol creatinine // M: 16 a 37 nmol/mmol Creat, H: 12.8 a 25.6 nmol/mmol Creat
DPD	Urine, serum	Chemiluminescence immunoassay, EIA, HPLC, ELISA	13.1-23.5	26	11.3–22.3 nmol/L, 4.7 nmol/L, 4.4 nmol/L // H: < 2-7 nmol/mmol/Cr, M: < 2-5.6 nmol/mmol/Cr (premenopausia) 2-10 nmol/mmol/Cr
BSP	Serum	RIA	-	-	12.1 ± 5.0 μg/L, 8.0 μg/L
TRACP5b	Serum	EIA, ELISA	10.8	13.3	4.0 U/L, 3.40 ± 0.87 U/L // < 7 mU/mL
CTSK	Serum	ELISA	-	-	10.17 pmol/L
Osteoclast regulatory proteins					
RANKL	Serum	ELISA	-	-	0.08 pmol/L
OPG	Serum, EDTA plasma, citrate, lithium heparin plasma	ELISA	-	-	1.8 pmol/L
DDK-1	Serum	ELISA	-	-	34.3 pmol/L
Sclerostin	Serum	ELISA	-	-	29.5 pmol/L

Table 2. Continied

Bone Biomarker	Biological required sample	Assay or method	Biological variability		Reference values
			CVi	CVg	
Bone formation biomarkers					
PINP	Serum, EDTA plasma	RIA, ELISA, EIA	-	-	54.1 µg/L
PICP	Serum, EDTA plasma	RIA	8.6	17.6	97–116 ng/mL // H: 76 a 163 ng/mL, M: 69-147 ng/mL
Total ALP	Serum	Standard Technicon Auto-analyzer, Roche COBAS Integra 800, Olympus AU 5200 analyzer	-	-	113, >129, 64.8–79.7 U/L
bALP	Serum	EIA, IMRA, ELISA,	6.6	35.6	24.9–19.7 U/L, 66.4 ± 8.7 U/L // 0 a 35 U/L
OC	Urine, serum, lithium heparin plasma	ELISA, ECLIA, IMRA, EIA	9.1	30.9	4.1 ± 0.5 ng/mL, 16.16 ± 4.5 ng/mL // 2 a 22 ng/mL

Note. Bone resorption biomarkers: CTX-I: carboxyterminal cross-linking telopeptide of type I collagen, NTX-I: aminoterminal cross-linking telopeptide of type I collagen, ICTP or CTX-MMP: carboxyterminal cross-linked telopeptide of type I procollagen or CTX-matrix metalloproteinases, HYP; hydroxyproline, GHYL: galactosyl hydroxylysine, GGHYL: glucosylgalactosyl-hydroxylysine, PYD: pyridinoline, DPD: deoxypyridinoline, BSP: bone sialoprotein. TRACP5b: isoform 5b of tartrate-resistant acid phosphatase, CTSK: cathepsin K; Osteoclast regulatory proteins: RANKL: receptor activator of nuclear factor kappa-B ligand, OPG: osteoprotegerin, DDK-1: dickkopf-related protein 1: Bone formation biomarkers: PINP: aminoterminal propeptide of type I procollagen, PICP: carboxyterminal propeptide of type I procollagen, Total ALP: total alkaline phosphatase, bALP: bone alkaline phosphatase, OC: osteocalcin. CVi: intraindividual variability, CVg: interindividual variability, ECLIA: electrochemiluminescence immunoassay, EIA: enzyme immunoassay, ELISA: enzyme-linked immunosorbent assay, HPLC: high-performance liquid chromatography, IMRA: immunoradiometric assay, RIA: radioimmunoassay. Information extracted and adapted from Barba, (2011), Banfi et al., (2010), Civitelli et al., (2009), Eastel et al., (2018), Hlaing et al., (2014), Kuo and Chen (2017), Lorentzon et al., (2019), Romero-Barco et al., (2012) and Vasijaran et al., (2010).

Figure. 36. *Biochemical markers of bone turnover*.



Note. Reproduced and adapted from "Bone biomarker for the clinical assessment of osteoporosis: recent developments and future perspectives" (p.2), by Kuo and Chen, 2017, *Biomarker Research, 5*(1).

Despite there being a range of BTMs available to measure, in line with the recommendations of the IOF and the International Federation of Clinical Chemistry and Laboratory Medicine in 2010 (Maheshwari et al., 2009; Vasikaran et al., 2011), and also recently with the National Bone Health Alliance (NBHA) and the American Association for Clinical Chemistry (Bauer et al., 2012), serum C-terminal telopeptide of type-I collagen (CTX-I) and serum procollagen type-I N propeptide (PINP), as reference markers of bone resorption and formation, respectively, were measured in both projects of this PhD dissertation. Indeed, these two BTMs are the reference biomarkers also used in the current European guidance for the diagnosis and management of osteoporosis in postmenopausal women (Kanis et al., 2013) and in the consensus statement on the use of BTMs in the Asia-Pacific region (Wu et al., 2019). These organizations have proposed that all research studies

(interventional and observational) should include these two BTMs to increase the knowledge of the application of bone markers in clinical practice (Hlaing & Compston, 2014). The BTMs evaluated in this thesis are explained in more detail below.

- *Bone resorption markers*

Biochemical markers of bone resorption that are formed during the bone resorption phase of the bone remodeling process include (1) products from the degradation of type-I collagen, such as telopeptides of type-I collagen (carboxyl- [C-]terminal crosslinking: CTX-I, CTX-matrix metalloproteinases [CTX-MMP, also called ICTP] and amino- [N-]terminal crosslinking: NTX-I, hydroxyproline [HYP], hydroxylysine [HLys] glycosides [galactosyl hydroxylysine (GHYL) and glucosylgalactosyl-hydroxylysine (GGHYL)]) and pyridinium crosslinks (pyridinoline [PYD] and deoxypyridinoline [DPD]); (2) noncollagenous proteins such as bone sialoprotein (BSP); (3) osteoclastic enzymes such as isoform 5b of tartrate-resistant acid phosphatase (TRACP5b), cathepsin K (CTSK), or cathepsin L (CTSL); and (4) osteocyte activity markers (regulators of bone turnover) such as RANKL, osteoprotegerin (OPG), dickkopf-related protein 1 (DDK-1), and sclerostin (Banfi et al., 2010; Cremers & Garnero, 2006; Hu et al., 2013; Kuo & Chen, 2017; Roforth et al., 2014; Seibel, 2005; Shetty et al., 2016; Szulc & Delmas, 2008).

CTX-I and NTX-I are the amino- and carboxy-terminal fragments of type-I collagen that still have the crosslinkages attached (Khosla & Kleerkoper, 1999; Seibel, 1999). These two BTMs are fragments released from the telopeptide (end) region of type-I collagen following its enzymatic degradation. Both CTX-I and NTX-I are catabolized in the tubular kidney cells to smaller molecules that are also BTMs, such as HYP, HLys, PYD, and DPD (Szulc, 2012).

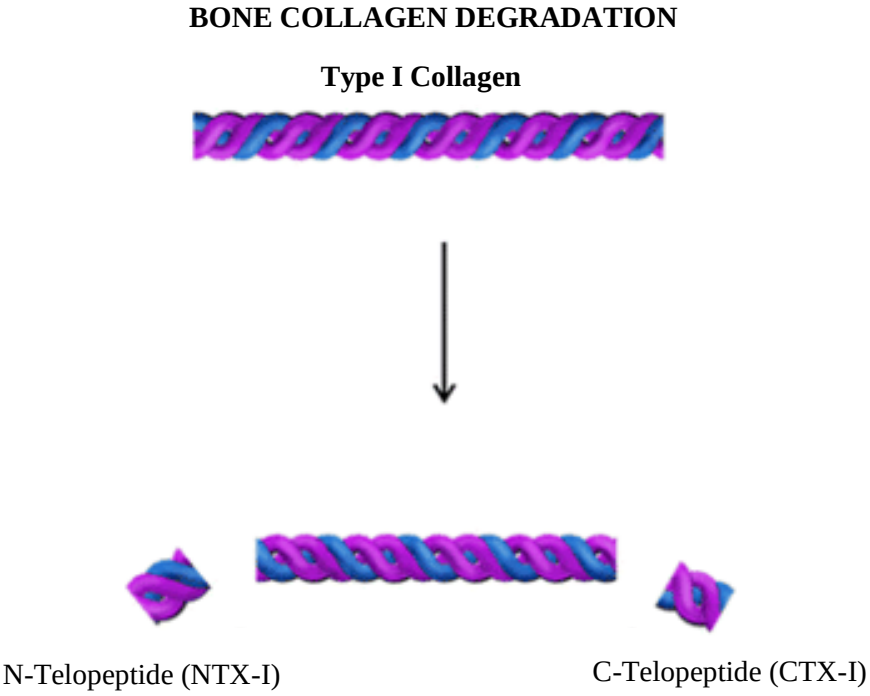
Among the resorption markers above, the most common are urinary levels of PYD and DPD, along with serum levels of NTX-I and CTX-I (Nuti et al., 2019). However, as CTX-I is considered by all the international and national organizations as the reference biomarker of bone resorption (Bauer et al., 2012; Hlaing & Compston, 2014; Maheshwari et al., 2009; Vasikaran et al., 2011; Wu et al., 2019), and was therefore chosen for the projects in this PhD dissertation, the following section focuses on this biomarker

─ β-isomerized form of carboxyterminal cross-linking telopeptide of type I collagen (β-CTx) ─

CTX-I was developed for the first time as a bone resorption marker in the 1990s (Fledelius et al., 1997; Hanson et al., 2010). This telopeptide is a metabolic nonhelical fragment of type-I collagen, released under cathepsin K cleavage (Cremers & Garnero, 2008; Shetti et al., 2016), which is composed of an octapeptide that contains crosslinking regions. Characteristically, CTX-I is crosslinked by bridges of PYD and DPD, which, following proteolytic degradation, are released into the blood and urine (Bonde et al., 1994). Thus, type-I collagen is degraded by cathepsin K first into the two long peptides of CTX-I and NTX-I crosslinks (depending on the crosslink-forming region with collagen molecules: amino- [N-]terminal or carboxyl- [C-]terminal) before further degradation into smaller molecules such as PYD and DPD (Herrmann et al., 2008; Figure 37).

Type-I collagen is subject to different age-dependent modifications such as isomerization and racemization due to its relatively long half-life (Banfi et al., 2010). These modifications are also present in collagen degradation products. For this reason, CTX-I circulates in its native (α) and β-isomerized forms (α-CTx and β-CTx, respectively).

Figure 37. *CTX-I and NTX-I formation from Type I Collagen in the bone collagen degradation process.*



Note. Reproduced and adapted from "National Bone Health Alliance Bone Turnover Marker Project: current practices and the need for US harmonization, standardization, and common reference ranges" (p. 2427), by Bauer et al., 2012, *Osteoporosis International*, *23*(10).

The native α-CTx form undergoes spontaneous β-isomerization in a process attributed to protein aging, where β-CTx represents mature type-I collagen. During this process, a translocation occurs of the peptide bond from the carboxyl group in position α to the carboxyl group in position β of the aspartic acid residue (Cloos & Fledelius, 2000; Fledelius et al., 1997).

In addition, both forms, α-CTx and β-CTx, with the continuous protein aging, may undergo post-translational modifications known as racemization, creating two new types: D- and L-forms (Szulc et al., 2012; Shetti et al., 2016). Thus, CTX-I molecules can be detected

in total as four different isoforms: the native form (α-CTx, also called a-L) and the three age-related forms, which are an isomerized form (β-L isomerized form, also called b-L), a racemized form (α-D native racemized, also called a-D), and an isomerized/racemized from (β-D isomerized racemized form, also called b-D; Cloos et al., 1998; Hlaing & Compston, 2014).

Simultaneous measurements of α-CTx and β-CTx forms, which represent the breakdown of recently synthesized collagen and aged collagen, respectively, have been proposed to calculate the α-CTx/β-CTx ratio as an index of very rapid bone turnover (Seibel, 2005). An increased ratio is associated with accelerated bone turnover, as has been described in individuals with bone metastases, Paget's disease, and in postmenopausal women with rapid bone loss (Garnero et al., 1997, Garnero, Bauer et al., 2008; Peris et al., 2006). However, the high interindividual variability (Cremers & Garnero, 2006), along with a lack of evidence to confirm its efficacy in different samples (urinary or serum; Herrmann & Seibel, 2008), makes further studies necessary to confirm the clinical utility of this ratio and determine whether it offers an advantage over other total CTX. For these reasons, this ratio is not evaluated in this dissertation.

Due to α-CTx being relatively more abundant than β-CTx in health or disease states in which newly formed collagen is present (such as in growing children, Paget's disease, or malignant bone disease; Fledelius et al., 1997; Garnero et al., 1997; Garnero, Bauer et al., 2008), along with β-CTx representing the degradation of mature type-I collagen rather than the degradation of immature collagen (α form), serum β-CTx was selected as a bone resorption biomarker in both projects of this study.

It is necessary take into account that, as with the other BTMs, the pre-analytic variability of CTX-I is high in certain conditions. In this case, serum CTX-I has been shown

to have a large circadian variation and is slightly affected by various conditions (e.g., age, gender, menopausal status), with a maximum level being observed at 5:00 a.m. and the minimum at 12:00 p.m. (Hannon & Eastell, 2000; Qvist et al., 2002). However, previous work has shown that acute fasting can significantly diminish the circadian variations (Christgau, 2000; Ju et al., 1997; Schlemmer & Hassager, 1999). In addition, serum CTX-I concentrations are also strongly influenced by food intake, substantially decreasing the postprandial levels of this resorption biomarker (20%) in comparison to the fasting state (Christgau, 2000). Hence, to avoid or at least reduce this pre-analytical variability, it is recommended to collect the blood or urine samples at the same time of day (morning) and in a fasting state (after the overnight fast) for their optimal clinical use (Clowes et al., 2002). These recommendations were followed in both projects included in this dissertation.

The clinical utility of the CTX-I lies in the fact that its elevated levels are associated with a high bone turnover (Camacho et al., 2016). In addition, previous studies have shown that its concentrations in postmenopausal women are significantly higher, being related to an increased rate of bone turnover and the risk of hip fracture (Garnero, Hausherr et al., 2009). Moreover, both serum and urinary levels of CTX-I have been found to be linked with an increased rate of bone resorption in individuals with hip and vertebral fractures (Kawana et al., 2002).

Finally, assays for detecting CTX-I in both serum and urine have been developed, including an electrochemiluminescence assay, a radioimmunoassay (RIA), ELISA, and an automated assay using antibodies (Bonde et al., 1994, 1996; Cremers & Garnero, 2006; Fledelius et al., 1997; Garnero et al., 2001; Risteli et al., 1993). Although CTX-I levels can be assessed in urine (a and b isoforms) and in serum (b isoform only; Seibel, 2005), and both serum and urinary CTX-I values are highly correlated ($r > 0.87$; Christgau et a., 1998), serum samples yield slightly more consistent results than urinary assays because the latter avoid the

need to correct for creatinine excretion, thereby minimizing variability (Herrmann & Seibel, 2008). Moreover, interindividual biological variability is also higher for urine CTX-I (23–48%) compared to serum CTX-I (15%; Seibel, 2005). This was an additional reason serum β-CTx was selected in this PhD dissertation to assess older women's bone resorption response to the exercise programs applied.

- *Bone formation markers*

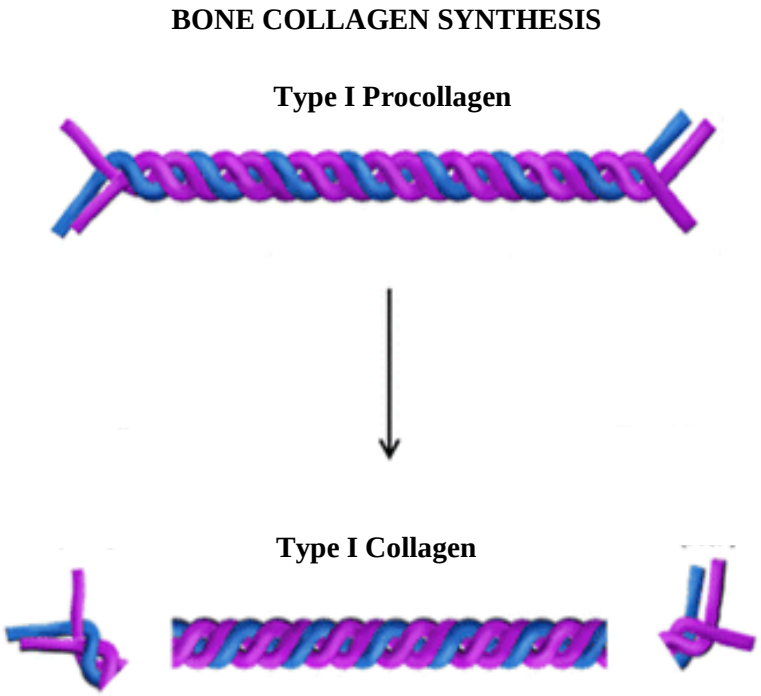
Bone formation markers are direct or indirect products of active osteoblasts expressed during different phases of their development (differentiation, extracellular matrix deposition, and maturation) and reflect different aspects of osteoblast function and bone formation (Shetty et al., 2016; Vasikaran et al., 2010). Several biomarkers available for the sensitive and specific assessment of the rate of bone formation can be categorized as (1) not specific bone proteins such as by-products of collagen synthesis (P1NP and procollagen type-I C-terminal propeptide [P1CP]); (2) osteoblast enzymes such as total alkaline phosphatase (ALP) and the bone-specific isoform of alkaline phosphatase (bALP); and (3) bone-matrix-specific proteins such as OC (Kuo & Chen, 2017; Shetty et al., 2016; Szulc & Delmas, 2008). As with the bone resorption biomarkers, this dissertation focuses on PINP, ALP, bALP, and OC as the BTMs assessed.

─ Aminoterminal propeptide of type I procollagen (P1NP) ─

Type-I collagen is the most important and abundant component of bone matrix (> 90%), which is derived from its precursor form, procollagen type-I molecule. Procollagen molecules are synthetized by fibroblast and osteoblast during bone formation. At each end of the molecule, procollagen type-I molecules contain amino (N)- and carboxy (C)-terminal peptide extensions, which are cleaved enzymatically during the extracellular process of conversion of procollagen to collagen and released into circulation, where they can be

measured as biomarkers of bone formation (P1NP and P1CP; Charles et al., 1994; Ebeling et al., 1992; Eriksen et al., 1993; Melkko et al., 1990, 1996; Parfitt, Simon et al., 2009; Figure 38). PINP is released into circulation as a trimeric form (derived from the trimeric collagen structure) and then is rapidly converted to its dimeric, monomeric, and fragmented forms as the original intact trimeric form is unstable at body temperature (Parfitt, Drezner et al., 2009; Samoszuk et al., 2008).

Figure 38. *PINP and PICP formation from Type I Procollagen in the bone collagen synthesis process.*



Note. Reproduced and adapted from "National Bone Health Alliance Bone Turnover Marker Project: current practices and the need for US harmonization, standardization, and common reference ranges" (p. 2427), by Bauer et al., 2012, *Osteoporosis International, 23*(10).

Although the majority of P1NP and P1CP is produced primarily from bone, type-I collagen and, consequently, PINP and PICP are not specific to bone because they are also synthesized in other nonskeletal tissues, mainly in the skin but also in cartilage, tendons, blood vessels, and dentine, as type-I collagen matrix is also present in these tissues (Garnero, Vergnaud & Hoyle, 2008; Liu et al., 1995; Seibel, 2005; Smedsrod, 1990). Nevertheless, circulating levels of these bone formation markers are mainly derived from bone due to skeletal tissues undergoing a higher rate of turnover than any other type-I collagen-containing tissues (Seibel, 2005; Szulc, 2012). Therefore, only a small amount of PINP and PICP come from nonskeletal tissues.

The fact that PINP is preferred to PICP as a clinical marker of bone formation (because, unlike PINP, PICP is cleared by the mannose receptor, which in turn can be regulated by thyroid hormones and growth hormone, thus complicating the interpretation in individuals with thyroid or pituitary dysfunction; Crofton et al., 1997; Smedsrod et al., 1990; Toivonen et al., 1998), along with the fact that PINP has been proposed as a reference bone formation marker by IOF due to its robust nature and dynamic response to treatment (Vasikaran et al., 2010, 2011) has caused PINP to be chosen rather than PICP as a bone formation biomarker for the projects in this dissertation.

Another reason this has been proposed as the reference bone formation marker is because it presents several advantages regarding the pre-analytical variability in relation to other biomarkers. Evidence has shown that the circulation levels of PINP are not significantly influenced by circadian variation, room temperature, and food intake; consequently, subjects do not need to be fasting (Clowes et al., 2002). In addition, PINP reliability has also been proven by low intraindividual variability and good assay precision (Vasikaran et al., 2011).

Moreover, among bone formation biomarkers, PINP has shown great potential as a sensitive and stable bone biomarker for the early detection of osteoporosis. Its clinical utility has been evidenced in postmenopausal women, where, after applying an antiresorptive treatment (such as bisphosphonates or estrogen), the blood concentrations of PINP were reduced by almost 80% (Bauer et al., 2006; Garnero, Vergnaud & Hoyle, 2008), and after three months of supplying anabolic agents (such as teriparatide), the levels increased by up to 200% (Black et al., 2003; Chen, Satterwhite et al., 2005; Ryder et al., 2010; Vescovi et al., 2008).

Finally, the presence of PINP can be determined in serum with either RIA or ELISA, electrochemiluminescence immunoassay analyzers, and automated methods (Lüftner et al., 2005; Garnero, Vergnaud & Hoyle, 2008). Immunoassays can detect either trimeric or monomeric forms.

– Alkaline phosphatase (ALP) and bone alkaline phosphatase (bALP) –

Bone formation can also be assessed by measuring ALP and bALP, enzymes produced by the osteoblast. ALP was the first BTM used for both a clinical and research setting when, in the 1920s, the assessment of enzyme activity in serum was first performed in patients with liver and bone diseases (Naylor et al., 2012; Shetty et al., 2016). ALP is a ubiquitous membrane-bound tetrameric ecto-enzyme present in the plasma membrane of the osteoblasts (Harris, 1990; McComb, 1979). Although its exact function is not completely clear, it plays an important role in osteoid formation and the bone mineralization process (Harris, 1990; McComb, 1979). During the maturation process of the newly formed osteoid, ALP is secreted by osteoblasts into the extracellular fluid, and its concentrations can be measured in serum (Vasikaran et al., 2010).

Total ALP activity in serum is a composite of four different isoenzymes produced by different genes: intestinal, placental, germ cell, and tissue nonspecific isoforms (McComb, 1979). The tissue nonspecific ALP gene encodes liver, kidney, and bone isoforms of ALP (Hlaing & Compston, 2014; Naylor et al., 2012). The proportions of these isoenzymes of the total ALP changes throughout life. During skeletal growth in childhood and adolescence, the bone isoform predominates (up to 90%), whereas in adults with normal liver function, bone and liver isoforms contribute 90–95% of total ALP and are present in approximately equal proportions (Burtis et al., 2012; Green et al., 1971; Magnusson et al., 1999). Thus, about half of the total ALP activity in serum in healthy adults is predominately of hepatic origin, and the other half derives from bone.

Therefore, total ALP could be an adequate marker to assess the bone formation in diseases that involve dramatic changes in bone turnover, such as Paget's disease, due to its lack of sensibility and specificity but not for situations with only subtle changes in bone metabolism as these can be osteopenic or osteoporosis conditions, wherein bALP affords greater specificity and sensibility to detect changes in the osteoblast function (Farley et al., 1981; Naylor et al., 2012; Vasikaran et al., 2008). In fact, some studies on osteoporosis patients have found a poor correlation between total ALP activity and bone formation indices determined by histomorphometry (Brown et al., 1987; Podenphant et al., 1987).

bALP is an enzyme located on the outer surface of osteoblasts and is one of the major regulators of the bone matrix mineralization and calcification process (Szulc et al., 2012). It hydrolyzes organic phosphates and pyrophosphate, which inhibits mineral crystallization and, thereby, provides inorganic orthophosphate, a substrate for the synthesis of hydroxyapatite (Orimo, 2010). Although total ALP is often used to evaluate and monitor patients with osteoporosis but without liver disease, due to its low cost and easy measurement, bALP is a more specific marker of bone formation than total ALP and is therefore more sensitive to

detecting the small changes in bone formation seen in lost bone mass conditions (Naylor et al., 2012). In fact, the production of bALP is correlated positively with bone formation rate as measured by histomorphometry (Parfitt, Drezner et al., 2009). Thus, the bALP isoenzyme is preferred over total ALP because of its higher sensibility and specificity to detect changes in the osteoblast activity (Seibel, 2005; Epstein, 1988; Garnero, 1993; Van Straalen et al., 1991).

In addition to its high sensibility and specificity, other advantages of using bALP include its sample stability, the wide availability of assays, and its low intraindividual variability (long circulatory half-life of 1–2 days; Hlaing & Compston, 2014; Kuo & Chen, 2017; Vasikaran et al., 2008).

There are different techniques to assess bALP in serum, and many methods have been developed to differentiate bALP from the liver isoform. The older semiquantitative methods involved heat inactivation, chemical inhibition by phenylalanine and urea, zone electrophoresis (agarose), wheat germ lectin or concavalin A inactivation, and neuraminidase inhibition (McComb, 1979). However, the reproducibility and precision of these assays were low because they showed a very high cross-reactivity between bALP and liver isoenzymes. The bALP isoenzyme is difficult to distinguish from the isoforms from liver because they are only different due to posttranslational glycosylation (Kuo & Chen, 2017). Nevertheless, a much better assessment of bALP was provided with the development of monoclonal antibodies in the late 1980s, which allowed the production of immunoassay specifics for bALP (immunoradiometric assay, HPLC; Burtis et al., 2012; Civitelli et al., 2009; Delmas et al., 2000; Panigrahi et al., 1994; Sharp et al., 2007). With the use of immunoassays over older methods, precision and reproducibility have improved greatly; however, even the immunoassays show significant cross-reactivity with the liver isoform (up to 15%; Magnusson et al., 2002).

─ Osteocalcin (OC) ─

As mentioned above, bone formation also can be assessed by measuring OC, also known as bone gamma-carboxyglutamic acid (GLA). Containing protein or bone-GLA protein, CO is a 5.8 kDa hydroxyapatite-binding and non-collagenous protein composed of 49 amino acids (Banfi et al., 2010; Civitelli et al., 2009; Kuo & Chen, 2017; Shetty et al., 2016). Moreover, OC is the most abundant non-collagenous protein in bone matrix (constituting approximately 15% of the non-collagenous bone matrix proteins; Brown et al., 1984; Dickson, 1993; Price, 1987) and comprises about 2% of total protein in the human body (Kuo & Chen, 2017; Lee et al., 2000). It is predominantly synthesized by mature osteoblasts and in small amounts in teeth by odontoblasts and hypertrophic chondrocytes (Hauschka et al., 1989) as its synthesis is stimulated by 25OHD (Hlaing & Compston, 2014).

Once synthesized, OC is found in the mineralized matrix of bone, but part of it is released into the bloodstream during the bone remodeling cycle. Thus, the OC serum levels are regarded as one of the bone formation markers (Naylor et al., 2012; Szulc et al., 2012).

OC contains three vitamin K-dependent gamma-carboxyglutamic acid residues, which are responsible for the calcium-binding properties of the molecule (Poser et al., 1980; Price, 1995). It contains three vitamin K-dependent glutamic acid residues, which are converted to GLA acid residues by vitamin K-dependent posttranslational carboxylation (Burtis et al., 2012; Ryder et al., 2010). This carboxylation process produces a structural molecular change responsible for the calcium-binding properties of the molecule (binding of OC with hydroxyapatite and mineralization of the bone matrix; Poser et al., 1980; Price, 1995). Thus, mineral binding of OC requires gamma carboxylation of the three glutamate residues of OC. Although the majority of OC after translocation is completely carboxylated, due to low activity of vitamin-K-dependent γ-glutamyl carboxylase, there are also noncarboxylated or

undercarboxylated forms of OC (Lee et al., 2000) that are not readily bound to hydroxyapatite and are released into the blood circulation (Takahashi et al., 2001).

Thus, the serum levels of OC represent a fraction of the total OC that has not bound with hydroxyapatite in the bone matrix because it has not been carboxylated or has been undercarboxylated (Lee et al., 2000). This circulating level of OC, which is considered a marker of bone formation, has a short half-life (5 min) in circulation and is rapidly degraded into fragments and cleared mainly by the kidneys and, to a lesser extent, by the liver (Hlaing & Compston, 2014). In addition, serum OC contains three types of fragments: intact OC, large (1–43) N-terminal midregion fragments, and several other smaller fragments (like C-terminal), each of which represents one-third of the circulating OC (Hlaing & Compston, 2014). The smaller OC fragments are thought to be derivative of osteoclastic bone resorption since the OC bound to hydroxyapatite in the mineralized matrix could also be released into circulation during the bone resorption process (Cloos & Christgau, 2004; Ivaska et al., 2004).

Regarding the clinical utility of OC, although it was discovered in 1976 and is known to be involved in the osteoid mineralization process, its precise function remains poorly understood (Seibel, 2005). Nevertheless, there is abundant evidence of the utility of OC as a bone formation marker (Hauschka et al., 1989). OC is a late marker of osteoblast activity, compared to synthesis of bALP and PINP (Brown et al., 2009), but serum levels of OC have been shown to reflect the intensity of bone formation rate, as was determined by quantitative bone histomorphometry and combined calcium balance/calcium kinetic studies, which found a positive correlation between the levels of serum OC and the histomorphometric parameters of bone formation (Brown et al., 1984; Charles et al., 1995; Delmas et al., 1985, 1986; Eriksen et al., 1993; Ureña et al., 1996).

In addition, the increased levels of undercarboxylated OC have been associated with hip fracture risk in elderly women (Vergnaud et al., 1997). Moreover, it has been demonstrated that the level of serum OC is highly correlated with the increase of BMD during bone formation treatment for osteoporosis **(**Kuo & Chen, 2017) and that the levels of OC are higher in postmenopausal women with osteoporosis than nonosteoporotic women (Singh & Kumar, 2015). For these reasons, OC has been widely used to assess the bone formation rate in exercise interventional studies.

However, several authors have observed that the clinical utility of OC can be limited by the presence of various types of OC-derived fragments circulating in the bloodstream as the smalls fragments could come from the bone resorption process, and there is a lack of analytical methods to recognize the different types of fragments (Bell, 1997).

Despite being a sensitive marker of bone formation, serum OC has limited clinical practice use due to its high biological, circadian, and assay variability (Seibel, 2005). In addition, the presence of different osteocalcin fragments in the serum and the instability of the intact molecule of OC may also negatively affect the reproducibility of repeated measures (Civitelli et al., 2009; Shetty et al., 2016). OC has a diurnal rhythm, with the highest concentrations at 4:00 a.m. and the lowest at 4:00 p.m. (Schlemmer & Hassager, 1999), so serum samples must be collected within a well-defined and consistent timeframe. Unlike other BTMs, circulating levels of OC are not significantly influenced by food intake, and, consequently, individuals do not need to be fasting for OC assessment (Schlemmer & Hassager, 1999). Nonetheless, serum levels of OC have been shown to be vulnerable to within-subject biological variability (12%; Garnero & Delmas, 1998), seasonal changes (concentrations are significantly higher in winter than summer and in spring than autumn; Douglas, et al., 1996; Woitge, et al., 1998), presence of renal dysfunction (Gundberg et al.,

1987), and several analytical factors (*in vitro* degradation, freeze-thaw cycles, and haemolysis; Diaz et al., 1984; Gundberg et al., 1985).

Lastly, available methods to assess OC include RIA, ELISA, chemiluminesence immunoassay, and automated assays (Cremers & Garnero, 2006; Power & Fottrell, 1991). Due to the heterogeneity of OC in the circulation and the varied specificity of the assays (intact, intact and N-terminal fragments, or intact and multiple fragments), discordant results are observed when different assays are used (Blumsohn et al., 1995), and presently, there is a lack of international standardization regarding which are the most clinically important fragments to measure.

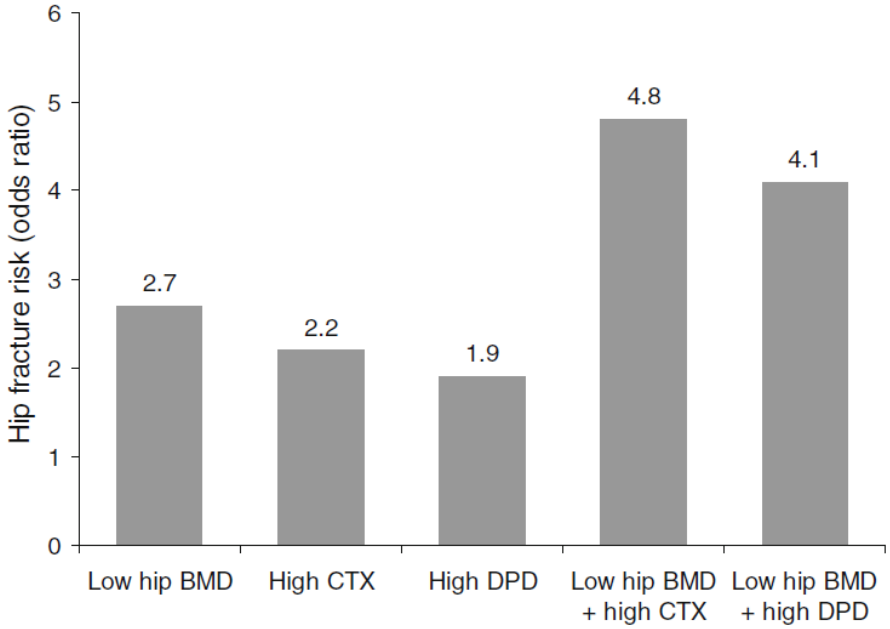
However, as intact OC is rapidly degraded *in vivo* and *in vitro* to N-terminal fragments of OC (Garnero et al., 1994; Riggs et al., 1986; Taylor et al., 1990), assays that detect both intact and N-terminal fragments of OC have been shown to be the most stable and reproducible because they are less susceptible to changes during storage (Delmas, et al., 2000; Lee et al., 2000; Swaminathan, 2001). Thus, assays that detect only intact OC are particularly affected by *in vitro* and *in vivo* degradation.

- *Clinical utility and variability of bone turnovers markers*

In the case of prediction, elevated levels of BTMs in early menopause can predict more rapid rates of bone loss than BMD (Chesnut et al., 1997; Garnero et al., 1999; Ross et al., 1998), with an 80% sensibility for detecting fast bone loss (> 3%/year) in the next two to 12 years, at least in at the forearm (not at the hip or spine; Delmas et al., 2000). However, BTM thresholds to prevent bone loss in menopausal and elderly subjects have not yet been defined, so the usefulness of BTMs in this sense is still debatable. What seems clearer is its utility in the prediction of fracture risk. Several prospective studies and recent reviews have suggested the use of BTMs as a predictor of fracture risk at vertebral and hip site fractures

(Garnero, Hausher et al., 2009; Gerdhem et al., 2004; Melton et al., 1997) in postmenopausal women independently of BMD (Garnero, Sornay-Rendy et al., 2009; Garnero et al., 2000) as increased levels of bone resorption markers were associated with increased fracture risk in women (Garnero et al., 2000; Figure 39).

Figure 39. *Association of BTMs and BMD with hip fracture risk in postmenopausal women > 75 years old.*



Note. CTX: carboxyterminal telopeptide, DPD deoxypyridinoline. Reproduced from "Bone turnover markers: understanding their value in clinical trials and clinical practice" (p. 845), by Civitelli et al., 2009, *Osteoporosis international, 20*(6).

The reason is because they reflect not only the increased bone loss but also the microarchitectural deterioration of bone tissue (Melton et al., 1997; Parfitt, 2002a, 2002b; Riggs & Melton, 2002). In addition, significant reductions in BTMs have also been associated with fracture risk reduction (Bauer et al., 2014; Eastell et al., 2011; Hochberg et al., 2002).

However, as with the prediction of bone loss, sufficient consensus has not yet been established for the cut-point of BTMs that increase fracture risk, and despite the ability to predict fractures independently of BMD, global data are not available to enable the use of bone markers as fracture risk assessment (FRAX) tools (Bonnick et al., 2010; Park et al., 2019) due to wide discrepancies in reference standards, measurement methods, and individual and geographical variations of BTMs (Diaz de Barboza et al., 2015). Although BTMs have not yet been demonstrated to make diagnostic and treatment decisions for osteoporosis, they are useful to provide early assessment of osteoporosis when the BMD measurement of DXA does not offer enough information to make the diagnosis. Therefore, interest in combining the use of BMD with DXA and BTMs has increased due to the potential to improve the early assessment of people with a high risk of osteoporosis, secondary osteoporosis, and other bone diseases (Bauer et al., 2012; Kuo & Chen 2017; Nuti et al., 2019; Park et al., 2019;Vasikaran et al., 2010).

Finally, one potential advantage of using BTMs in clinical practice is for monitoring osteoporosis treatment efficacy as they can detect the changes sooner than DXA (Delmas et al., 2000; Garnero et al., 1994). Particularly, changes in bone resorption markers occur within days or weeks of starting treatment, while the changes in BMD occur over months or years (Cho et al., 2020). Indeed, clinical trials have shown that early changes in BTMs are associated with long-term BMD changes in women taking anabolic (Bauer et al., 2006) or antiresorptive drugs (Greenspan et al., 2005). Moreover, BTMs could also potentially be used in making decisions to initiate therapy, monitor bone turnover when drug therapy is terminated, and monitor adherence and compliance to therapy (Camacho et al., 2016; Garnero et al., 2000; Glendenning, 2011; Johansson et al., 2014; Shetty et al., 2016; Srivastava et al., 2005; Vasikaran et al., 2011; Yoon & Yu, 2018).

As shown, there is a solid rationale for using measurements of BTMs as a tool in clinical settings. Nevertheless, it must be noted that although BTMs may have potential advantages over BMD measurements in clinical practice, their use is still limited mainly due to their high *in vivo* and assay variability (Biver, 2012; Seibel, 2005; Szulc et al., 2017; Vescini et al., 2016) and the lack of evidence-based thresholds for clinical decision-making (Camacho et al., 2016; Eastell & Szulc, 2017; Garnero, 2017; Kanis, Svedborn et al., 2014; Vasikaran et al., 2011). Perhaps the greatest challenge for the adoption of BTMs within the clinical setting is their potentially high variability, which has been reported to be greater for markers of resorption than of formation (Wichers et al., 1999). Factors determining the variability of BTMs are shown in Table 3.

Table 3. *Sources of variability in bone biomarkers*.

Source	Importance	Nature of effect
Uncontrollable sources		
1. Pre-analytical		
Biological causes		
Age	High	Age-related increase in BTMs until 3rd decade, then stable until menopausal increase in women & 8th decade increase in men
Gender	High	BTMs in people <50 years old are higher in men (although not supported by all studies), whereas >age 50 years women have higher BTMs than men
Ethnicity/race	Low	Small changes, such as lower OC in African Americans vs Caucasians
Menopausal status	High	BTMs increase within a few months after the last menstrual period
Pregnancy and lactation	Moderate	BTMs are increased during pregnancy; highest levels during third trimester, even higher postpartum
Fractures	High	BTMs increase after a fracture and remain elevated up to 1 year
Bed rest/immobility	Moderate	Bone formation markers decrease and resorption markers increase even in short term (7days)
Vitamin D deficit and secondary hyperparathyroidism	Moderate	BTMs are increased

Table 3. *Continued.*

Source	Importance	Nature of effect
Uncontrollable sources		
1. Pre-analytical		
Biological causes		
Diseases characterized by an acceleration of bone turnover: Primary hyperparathyroidism Thyrotoxicosis Acromegaly Paget's disease Bone metastases Hypogonadism in men (late onset hypogonadism, orchidectomy)	High	BTMs are increased
Diseases characterized by a dissociation of bone turnover: Cushing's disease Multiple myeloma	High	Some BTMs are increased and others decreased
Diseases characterized by a low bone turnover Hypothyroidism Hypoparathyroidism Hypopituitarism Growth hormone deficit	High	BTMs are decreased
Chronic diseases associated with limited mobility Stroke Hemiplegia Paraplegia Dementia Schizophrenia Depression Alzheimer's disease Sarcopenia Chronic immobilization in the homebound or institutionalized elderly	Moderate	Some BTMs are increased and others decreased
Associated diseasse Thyroid disease Liver disease Chronic renal disease Systemic inflammatory disease Diabetes Degenerative joint disease	Moderate	BTMs often increased (thyrotoxicosis, chronic kidney disease)

Table 3. *Continued*.

Source	Importance	Nature of effect
Uncontrollable sources		
1. Pre-analytical		
Exogenous causes		
Drugs Glucocorticoids Aromatase inhibitors Anti-convulsants Anti-epileptics Oral contraceptives Hormone replacement therapy Heparin Thiazide diuretics Vitamin K antagonist Gonadoliberin agonists Antiresorptive agents Anabolic agents	High	BTMs may be decreased (glucocorticoids, thiazide diuretics, heparin, antiresorptive drugs, oral contraceptives) or increased (aromatase inhibitors, anticonvulsants)
Geographical location	Low	Small changes amongst countries, usually explained by differences in lifestyle
Technical causes		
Sample integrity (haemolysis/multiple freeze–thaw cycles)	High	Some BTMs are increased and others decreased
2. Analytical		
Inter-laboratory variations	High	Some BTMs are increased and others decreased
Controllable sources		
1. Preanalytical		
Exogenous causes		
Circadian rhythm	High	Most striking for bone resorption markers. Generally highest during night and lowest in afternoon. Can be affected by calcium and disease
Seasonal variation	Low	Discordant findings. Elevated bone resorption during winter months has been reported
Menstrual variation	Low	Small decreases in bone resorption and increases in bone formation during luteal phase
Fasting status	High	Feeding results in a decrease in BTMs. For example, serum CTX-I decreases by 20% after breakfast
Food intake (Diet)	Moderate	Small reduction in BTMs immediately following calcium supplementation, CTX- I decreases after a meal
Physical activity and exercise	Moderate	Changes occur but depend on type, frequency and intensity of exercise and age of subjects
Tobacco smoking	Low	Discordant findings. Some BTMs are increased and others decreased

Table 3. *Continued*.

Source	Importance	Nature of effect
Controllable sources		
1. Preanalytical		
Exogenous causes		
Alcohol intake	Low	Discordant findings. Some BTMs are increased and others decreased
Technical causes		
Sample requirements (serum/plasma/urine)	Moderate	Some BTMs are increased and others decreased
Sample collection and transport (on ice/protection from light)	High	Some BTMs are increased and others decreased
Storage conditions of samples in lab (freezer temperature)	High	Some BTMs are increased and others decreased
2. Analytical		
Within-laboratory variations (appropriate reference ranges)	High	Some BTMs are increased and others decreased
3. Post-analytical		
Interpretation of results without taking pre-analytical and analytical variations into account	High	Some BTMs are increased and others decreased

Note. BTMs: bone turnover markers, CTX-I: carboxyterminal cross-linking telopeptide of type I collagen; OC: osteocalcin. Information extracted and adapted from), Hlaing et al., (2014), Lorentzon et al., (2019), Naylor et al., (2012), Shetty et al., (2016), Szulc et al., (2012) andVasikaran et al., (2010).

These strengths and weakness of BTMs in clinical practice have been considered by several organizations (NOF, NAMS, AACE, IOF, International Federation of Clinical Chemistry and Laboratory Medicine, and the NBHA), which have recognized that BTMs may provide valuable additional information to assist in the assessment of individuals with bone mass loss or high bone turnover (Hodgson et al., 2001; Position statement of the North American Menopause Society, 2002) and highlight the need to advance in the field of BTMs (Cosman et al., 2014; Schafer et al., 2010). However, these institutions provide differing recommendations for the clinical use of BTMs in risk assessment and in the monitoring of osteoporosis treatment (Vasikaran et al., 2010).

- *Reference values of bone turnover markers*

BTMs are not more widely used in clinical practice due to the wide variation of the reference values and the lack of consensus on normal reference intervals (Cho et al., 2020; Hu et al., 2013; Rathnayake et al., 2020), particularly for postmenopausal and elderly populations, where reports on the optimal BTM thresholds are controversial (Cho et al., 2020; Fisher et al., 2018; Hu et al., 2013; Rathnayake et al., 2020).

The majority of previous studies that have determined reference intervals (RIs) from serum β-CTx (Ardawi et al., 2010; Adami et al., 2008; Bae et al., 2012; de Papp et al., 2007; Eastell et al., 2012; Glover et al., 2008, 2009; Guañabens et al., 2016; Hu et al., 2013; Jenkins et al., 2013; Li et al., 2014; Michelsen et al., 2013; Suk et al., 2006), PINP (Ardawi et al., 2010; Adami et al., 2008; de Papp et al., 2007; Eastell et al., 2012; Glover et al., 2008, 2009), bALP (Ardawi et al., 2010; de Papp et al., 2007; Glover et al., 2008, 2009), or OC (Cho et al., 2020; Glover et al., 2008; Guañabens et al., 2016; Hu et al., 2013) was limited to cohorts of healthy premenopausal women. For males, β-CTx and PINP RIs have been established in Spanish men older than 50 (Olmos et al., 2010). However, only few studies have reported RIs for β-CTx (Boudou et al., 2009; Chen, Furtado et al., 2005; Cho et al., 2020; Garnero, Bauer et al., 2008; Gossiel et al., 2014; Hu et al., 2013; Lenora et al., 2007; Martínez et al., 2009; Michelsen et al., 2013; Trento et al., 2009; Zhao et al., 2011), PINP (Gossiel et al., 2014; Hu et al., 2013; Martínez et al., 2009; Michelsen et al., 2013; Zhao et al., 2011), bALP (Gossiel et al., 2014; Iki et al., 2004; Michelsen et al., 2013), and OC (Cho et al., 2020; Gossiel et al., 2014; Hu et al., 2013; Iki et al., 2004) BTMs in postmenopausal or elderly women, and these previous studies have reported large differences between pre- and postmenopausal concentrations in serum BTMs (Ardawi et al., 2010; Iki et al., 2004).

Rathnayake and colleagues have reported BTM RIs of intact and total OC, β-CTx, PINP, and bALP in different countries of East, South, and Southeast Asia (China, India, Japan, Korea, Pakistan) with a wide intercountry and intracountry variation (Rathnayake et al., 2020). From Europe, different studies have tried to establish the normative range of BTMs, especially for β-CTx and PINP, in healthy postmenopausal populations (Boudou et al., 2009; Garnero, Bauer et al., 2008; Gossiel et al., 2014; Lenora et al., 2007; Martínez et al., 2009; Michelsen et al., 2013; Trento et al., 2009). Among them, only one study has reported RIs for serum β-CTx and PINP concentrations in Spanish postmenopausal women (1,080) aged 44–93 years (63 ± 9); it reported RIs of 0.112–1.018 ng/mL for serum β-CTx and 19–100 ng/mL for serum PINP (Martinez et al., 2009). However, no RIs for bALP and OC have been found for postmenopausal or elderly Spanish women.

As seen in Table 4, RIs and mean or median values of all the BTMs show a high variability and are strongly dependent on the age, geographic area, ethnicity, and bone status (normal, osteopenia, and osteoporosis) of the population analyzed. Therefore, it is necessary to take these factors into account to analyze the results obtained in the present PhD dissertation.

Table 4. *Reference intervals of bone resorption and formation biomarkers in healthy postmenopausal and elderly women*

Bone biomarkers	Author	Contry	Age range	Sample size (*n*)	Median or mean	Reported reference interval (95%)
sβ-CTx (ng/ml)	Martinez et al., 2009	Spanish	44–93 (63 ± 9)	1,080	0.387	0.112–1.018
			50-60	-	0.405	-
			75	-	0.353	-
			>80	-	0.435	-
	Garneto et al., 2008	Germany	45–80	179	0.556	-
	Michelsen et al., 2013	Germany	60–64	114	0.32	0.23–0.51
			50–79	450	-	0.09–1.05
			60–75	250	-	0.080–0.990
			65–69	81	0.38	0.23–0.55
			70–74	55	0.37	0.26–0.60
			75–79	37	0.33	0.22–0.44
	Gossiel et al., 2014	UK, Germany, France	55–79	343	0.31	0.10–1.00
	Boudoy et al., 2009	France	46.2–67.0 (55.6 ± 5.7)	30	-	0.13–0.60
	Trento et al., 2009	Italy	54.6 ± 6.1	200	0.45: normal	-
			-	-	0.47:osteopenic	-
	Lenora et al., 2007	Sweden	75	601	0.312	-
	Chen, Furtado et al., 2005	Australia	>80	1,064* (men and women)	0.31	0.20–0.47
	Zhao et al., 2011	Beijin	47–108	1,724	0.439: total	-
			-	-	0.503:	-
			-	-	osteoporotic	-
			-	-	0.457: osteopenic	-
					0,39: normal	
	Hu et al., 2013	Shangai	60–64	51	0.441	0.307–0.584
			65–69	70	0.471	0.356–0.585
			70–74	77	0.431	0.297–0.565
			75–79	66	0.384	0.284–0.482
	Cho et al., 2020	Korea	60–75	174	0.463	0.110–1.040

Table 4. *Continued.*

Bone biomarkers	Author	Contry	Age range	Sample size (*n*)	Median or mean	Reported reference interval (95%)
sPINP (ng/ml)	Martinez et al., 2009	Spanish	44–93 (63 ± 9)	1,080	47.7:normal 50.5: osteoporotic	19–100 -
	Michelsen et al., 2013	Germany	50–79	450	-	18.2–102.3
			60–64	114	47.4	35.2–59.8
			65–69	81	45.1	30.7–57.8
			70–74	55	42.4	30.8–63.3
			75–79	37	38.5	28.3–52.3
	Gossiel et al., 2014	UK, Germany, France	55–79	343	49.7	21.2–116.4
	Zhao et al., 2011	Beijin	47–108	1,724	56.7: total	-
			-	-	62.4: osteoporotic	-
			-	-	58.4: osteopenic	-
			-	-	52.8: normal	-
	Hu et al., 2013	Shangai	60–64	51	47.07	34.78–59.36
			65–69	70	50.61	38.11–63.11
			70–74	77	50.04	37.94–62.13
			75–79	66	45.44	35.60–54.47
bALP (ng/ml)	Michelsen et al., 2013	Germany	50–79	450	-	8.1–31.6
			60–64	114	16.2	13.3–20.4
			65–69	81	15.8	12.8–18.8
			70–74	55	15.8	12.7–21.4
			75–79	37	16.1	11.8–18.1
	Gossiel et al., 2014	UK, Germany, France	55–79	343	14.1	7.2–27.6
	Iki et al., 2004	Japan	>50	1,083	15.7	-
sOC(ng/ml)	Gossiel et al., 2014	UK, Germany, France	55–79	343	24.5	12.7–47.4
	Hu et al., 2013	Shangai	60–64	51	26.40	20.28–32.60
			65–69	70	25.57	22.90–28.22
			70–74	77	26.50	20.82–32.17
			75–79	66	24.11	18.85–29.37
	Cho et al., 2020	Korea	60-75	174	20.25	3.8–38.0
	Iki et al., 2004	Japan	>50	1,083	8.4	-

Note: *Sample size includes men and women. sβ-CTx: serum β-isomerized form of CTx; sPINP: Procollagen type I N propeptide; bALP: bone alkaline phosphatase; sOC: serum osteocalcine.

iv. FRAX® tool

While the assessment of BMD is an important factor to consider in the assessment of bone strength, there are other clinical risk factors that can have a large influence on future fracture risk (Kanis et al., 2008; Kanis, Oden et al., 2009). On this basis, the FRAX® tool was developed by the WHO Collaborating Centre for Metabolic Bone Diseases in Sheffield, United Kingdom, and launched in 2008 (www.shef.ac.uk/frax/; Kanis et al., 2008) to evaluate the fracture risk of individuals. This tool integrates the weight of clinical risk factors for fracture risk on the basis of the global epidemiology data from 12 cohorts of men and women with approximately 250,000 person-years, 60,000 patients, and over 5,000 fractures, which was later confirmed in 11 additional cohorts (Kanis et al., 2007; Silverman, 2006) to provide estimates of the probability of fracture.

A total of 10 clinical risk factors that predict fracture risk were identified and included in the FRAX® tool: age, sex, body mass index (BMI), previous fractures, parental history of fractures, current smoking, use of glucocorticoids, rheumatoid arthritis, causes of secondary osteoporosis, and alcohol intake > 3 units per day. Secondary causes of osteoporosis include inflammatory bowel disease, untreated hypogonadism, organ transplantation, immobility, type-1 diabetes, and thyroid disorders (Kanis et al., 2008). These clinical risk factors are largely independent of BMD (Hillier et al., 2011; Kanis, Hans et al., 2011; Kanis et al, 2012; Kanis, Johanson et al., 2014; Lewiecki et al, 2011). For this reason, FRAX can be used with or without the inclusion of BMD values, although it is convenient to introduce them because BMD of the proximal femur remains the primary component of fracture risk estimation (Kanis et al, 2008).

The FRAX® algorithms, which use Poisson regression that includes age, country-specific life expectancy, and current relative risk (Hernlund et al., 2013), compute the individual country-specific 10-year probability of a major osteoporotic fracture (clinical

spine, forearm, hip, or shoulder fracture) and hip fracture in men and women between 40 and 90 years of age (Kanis, Melton et al., 2009). To date, the FRAX® tool (which is not a diagnostic tool but was designed to optimize diagnostic and treatment decisions) has been endorsed by both the IOF and NOF and is now available for 71 countries in all continents and has been incorporated into many regional and country guidelines.

However, it is important to note that FRAX® also has a number of limitations. For example, it does not incorporate other risk factors of fractures with proven evidence such as those associated with BTMs, fall events, lower dietary calcium intake, vitamin D deficiency, lower levels of physical activity, previous osteoporosis treatment, or the use of different drugs such as anticonvulsants or aromatase inhibitors (Gambacciani & Levancini, 2014; Shetty et al., 2016). In addition, several clinical risk factors involve no account of dose response when there is evidence that the risk associated with the use of glucocorticoids (van Staa et al., 2001, 2002), the number of prior fractures (Kanis, McCloskey et al., 2011; Lindsay et al., 2001; Lunt et al., 2003), smoking (Kanis, Johnell et al., 2004; Law & Hackshaw, 1997), and excess alcohol consumption (Kanis, Johansson et al., 2004) rises with increased exposure. Moreover, the FRAX® calculation model does not consider lumbar spine BMD (only the femoral neck) or the number and severity of vertebral fractures, and it underestimates future fracture risk as it reports risk for only major and hip fractures, which comprise approximately half of all fragility fractures. Nevertheless, the FRAX® tool is easy to use, and its simplicity is appropriate for primary care.

D. Osteopenia and osteoporosis

Osteoporosis is a growing major global clinical and public health problem due to it is associated with an increased risk of fracture which can lead to disability, loss of functional independence, pain, and increase morbidity and mortality (Reginster & Burlet, 2006). Osteoporosis impacts on quality of life of the people whose suffer it, being more common in

women than men, especially in postmenopausal and older women, and also impacts on social and economic health systems of the countries (Bonnick et al., 2010). In the following sections, osteoporosis will be explorer further.

i. Definition, diagnosis and types

The first recognition of its pathological appearance was in 1835 by Lobstein (Lobstein, 1835) who applied the term osteopenia because literally means "loss of porous bone" (Greek: osteo means "bone", poros means "passage, pore", penia means "loss") (Kwan, 2015).

It is currently possible to find multiple definitions of osteoporosis, but the most accepted are those of the NIH and WHO. The widely accepted definition of osteoporosis was developed by the NIH panel in 2000 as "a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture" (NIH consensus, 2000). The WHO definition also continues to be widely applied due to its diagnostic utility because it is based on the level of the BMD (g/cm2) measured by DXA and previous hip fracture (Kanis, 1994). According to the WHO definition, a BMD T-score of 2.5 SD or more below the average value for young, healthy adult Caucasian women (a T-score of $\leq$ 2.5 SD) constitutes a diagnosis of osteoporosis, while a BMD T-score between -1.0 and -2.5 SD is classified as osteopenia (low bone mass). In practice, sex and race-specific T-scores are typically used (Kanis, 1994).

Moreover, NAMS has supported the definitions above and added that BMD T-score levels for diagnosing osteoporosis or osteopenia must be present in at least one of these anatomical regions: total hip, femoral neck, or lumbar spine (at least two vertebral levels measured in the posterior-anterior projection, not the lateral projection; Bonnick et al., 2010). In addition, distal one-third radius bone density may be considered as a diagnostic site, but

the relationship between the BMD T-score at this site and fracture risk is not clear (Bonnick et al., 2010).

Nonetheless, it is necessary to take into account that the previous definitions do not cover the full spectrum of bone strength because they do not consider bone quality or microarchitecture. Bone strength is dependent on many qualities of bone and reflects the integration of two main features, bone density and bone quality. From bone density, BMD is the best single predictor of bone strength, accounting for 60–85% (Pivonka, 2018). Consequently, BMD is the most commonly used measure to diagnose osteoporosis (NIH, 2001; Post et al., 2010; Weinstein, 2000; WHO, 1994, 2001). However, bone quality, which includes bone geometry, shape, degree of mineralization, collagen structure, heterogeneity of bone microstructure, bone structure, bone tissue composition, microarchitecture, rate of bone turnover, mineralization, hydroxyapatite crystal size, connectivity of trabeculae, and microdamage, and which is also part of bone strength, is not used to assess the presence of osteoporosis because it is difficult or impossible to measure in clinical practice at this time (Bonnick et al., 2010; Bouxsein, 2003; Burr, 2004; NIH, 2000).

Regarding the diagnosis of osteoporosis, DXA is the gold-standard diagnostic tool used to identify patients with it (Blake & Fogelman; WHO, 1994). Based on the approach of WHO, the T-score value of BMD is necessary for an accurate identification of osteoporosis in both sexes. T-score is obtained by subtracting the mean BMD of the young, healthy adult population from the measured femoral BMD and dividing by the SD of the normal population: T-score = (measured BMD – young healthy adult mean BMD) / young healthy adult population SD. A T-score below -1 is an indication of low bone mass; osteopenia is present if the T-score is between -1 and -2.5 and osteoporosis if the T-score is below or equal to -2.5. A T-score value higher than -1 is defined as normal bone density (Kanis et al., 1994,

2002, 2008; Palacios et al., 2009; Table 5). Each decrease in SD has been calculated to represent 12% of bone loss (Ibáñez, 2003).

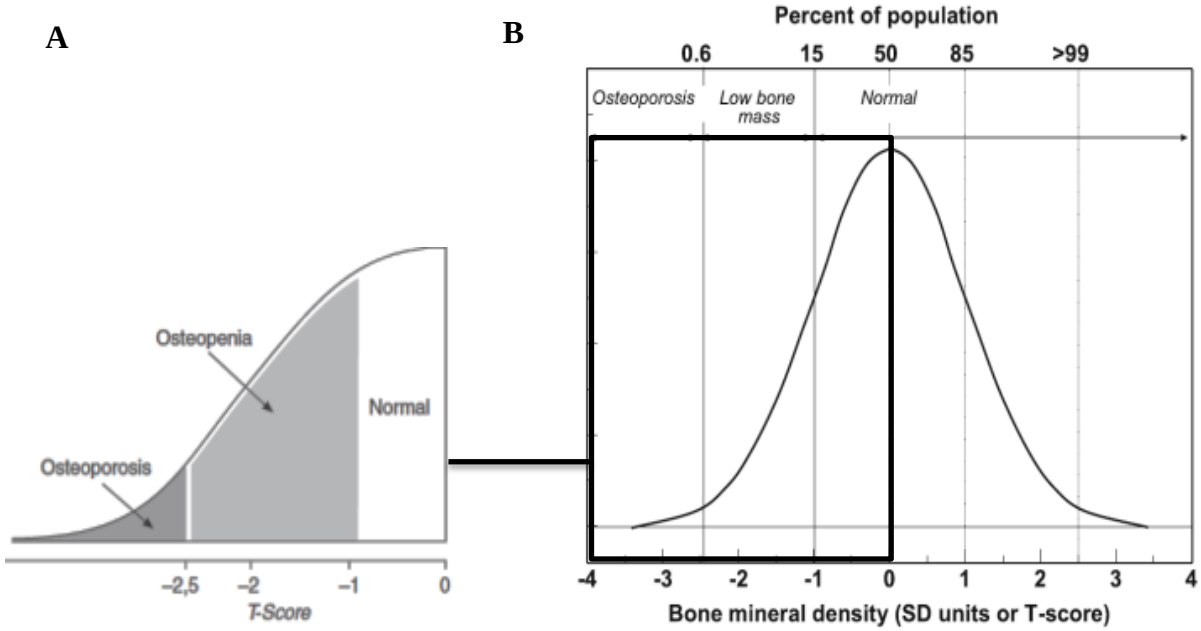
Table 5. *Diagnosis criteria for osteoporosis by WHO.*

Condition	Diagnostic criteria
Normal	BMD < 1SD of a young healthy adult reference value
Osteopenia	1 < BMD < 2.5 SD below that of a young healthy adult reference value
Osteoporosis	BMD ≥ 2.5 SD below that of a young healthy adult reference value
Severe osteoporosis	• BMD ≥ 2.5 SD below that of a young healthy adult reference value • With 1 or more fractures

Note: WHO: World Health Organization; BMD: bone mineral density; SD: standard deviation. Adapted from Palacios et al. (2009) and Kanis et al. (2008).

Specifically, the BMD reference value of the young, healthy adult population comes from the mean femoral neck BMD obtained from the National Health and Nutrition Examination Survey III reference data (Looker, 1998), where young (20 to 29 years old), healthy, Caucasian (non-Hispanic white) women is the reference population for both men and women, as recommended by the ISCD (Bianchi et al., 2010; Figure 40). However, there is some controversy regarding the usage of young Caucasian women as the reference group, and several organizations have proposed using ethnic-specific and gender-specific reference data (Hoiberg et al., 2007; Tenenhouse et al., 2000).

Figure 40. *Distribution and threshold of BMD.*



Note. A. Distribution of BMD in young healthy Caucasian women in SD units; B. Threshold values for normal, osteopenia and osteoporosis. Reproduced and adapted from "Osteoporosis in the European Union: medical management, epidemiology and economic burden" (p. 6), by Hernlund et al., 2013, *Archives of Osteoporosis, 8*(1).

In addition to diagnosis through densitometry, osteoporosis can be diagnosed clinically if there is a low-trauma (e.g., fragility) fracture in the absence of other metabolic bone disease, independent of the BMD T-score value. Thus, people with osteopenia or low bone mass but with previous fractures in spine, hip, pelvis, proximal humerus, or distal forearm should be diagnosed with osteoporosis and considered for treatment since they are also at an increased risk for future fractures (Camacho et al., 2016). As a new clinical diagnostic method, the NBHA has even proposed that osteoporosis may also be diagnosed in patients with osteopenia and increased fracture risk using FRAX® country-specific thresholds (Siris et al., 2014), an idea supported by the AACE (Camacho et al., 2016).

As mentioned, despite the strong connection between BMD and bone strength, osteoporosis diagnosed based on bone density alone seems to miss a large proportion of individuals with low bone strength. In fact, current research has indicated that 80% of all trauma fractures occur in nonosteoporotic individuals with normal or somewhat reduced BMD (Jarvinen et al., 1999; Sievanen, 2000; Siris et al., 2004). In addition, low BMD (osteporotic and osteopenic conditions) alone accounts for a maximum of 44% of the fracture risk (Stone et al., 2003). These findings highlight the need to capture bone quality for proper bone strength assessment. For instance, small changes in cortical and trabecular structure can lead to large increases in bone strength independent of changes in BMD (Jarvinen et al., 1999; Sievanen, 2000).

The biomechanical community is continuously developing new approaches to estimate bone strength. In addition to DXA, quantitative computed tomography (QCT) scanning may be used to provide further clinical details of bone structure (Clarke & Khosla, 2010), while conventional magnetic resonance imaging (MRI) can be used to overcome projection errors, as in the case of sagittal obliquity and scoliosis (Palacios et al., 2009).

From the pathological perspective, osteoporosis can be categorized into two main types: primary and secondary. Primary is usually linked to bone loss due to aging and gender, while secondary is associated with medical disorders (e.g., malabsorption) or medications (e.g., glucocorticoids) that adversely affect skeletal health (Bonnick et al., 2010; Lau & Guo, 2011; Palacios et al., 2009). Primary osteoporosis can be further classified into three subtypes: juvenile, type I or postmenopausal osteoporosis, and type II or senile osteoporosis (Burr & Allen, 2019; Nuti et al., 2019; Raisz, 1997). Juvenile osteoporosis indicates a form found in childhood and adolescence, which is mostly due to genetic mutations (Nuti et al., 2019). Postmenopausal osteoporosis occurs in females within 15 to 20 years after menopause, while senile osteoporosis occurs in older adults of both sexes (Grynpas, 2003; Kanis, 1994).

There is another type called idiopathic osteoporosis, caused by unknown reasons (Lau & Guo, 2011; Palacios et al., 2009).

ii. Pathophysiology

The principal underlying mechanism of osteoporosis is an imbalance between bone resorption and bone formation (Raisz, 2005). In normal bone remodeling, bone resorption is balanced by bone formation. However, in postmenopausal osteoporosis, there is an increase of bone turnover and a high rate of loss of trabecular bone, particularly in the vertebrae due to estrogen deficiency after menopause. In fact, after menopause, bone resorption increases by 90%, whereas bone formation also increases but only by 45%, as assessed by markers of bone resorption and formation (Garnero, Hausherr et al., 2009).

Lower circulating levels of serum 17β-estradiol, primarily in the early years after menopause (a decrease by 85–90% from the mean premenopausal level; Khosla et al., 1997), are related to the loss of estrogen-mediated inhibition of bone resorption without a fully compensatory increase in bone formation (Riggs et al., 1998).

The cellular and molecular mechanisms by which estrogen deficiency leads to bone loss are (1) the increase of the RANKL (Lacey et al., 1998), which leads to increased osteoclast recruitment and activation and decreased osteoclast apoptosis; (2) the decrease of the receptor OPG secreted by osteoblast cells, which neutralizes the RANKL through its receptor, RANK (Hsu et al., 1993; Simonet et al., 1997); and (3) the decrease of T-lymphocytes and B-lymphocytes, which also neutralize RANKL (Clowes et al., 2005; Eghbali-Fatourechi et al., 2003). Thus, estrogen deficiency leads to an alteration in the RANKL/OPG ratio that favors bone resorption. In addition, an increase in the levels of the parathyroid hormone (PTH) secretion in a later menopause phase (hyperparathyroidism

status) is another important factor in postmenopausal bone loss due to a correlation between the levels of the PTH and the levels of bone resorption markers (Clarke & Khosla, 2010).

Type-II osteoporosis is more related to a reduction in bone formation rates than an increase in bone turnover and also to a decrease in vitamin D produced by the kidneys (Grynpas, 2003; Kanis, 1994) as vitamin D deficiency is associated with increased serum PTH levels (Clarke & Khosla, 2010; Holick, 2007). The decrease in bone formation has generally been attributed to lowered paracrine production of growth factors (Marie et al., 1993) and/or decreased growth hormone (Giustina et al., 1998; Ho et al., 1987) and IGF-1 levels (Bennett et al., 1984; Boonen et al., 1999; Pfeilschifter et al., 2000).

ii. Prevalence

In an aging society, the prevalence of osteoporosis and osteopenia continues to increase progressively, particularly in older adults (Reginster & Burlet, 2006). It is estimated that over 200 million people worldwide currently have osteoporosis (Cooper, 1999), and the prevalence is expected to rise with the increasing lifespan and aging population (Cummings & Melton, 2002).

Wade and colleagues (2014) have analyzed the country-specific osteoporosis prevalence in those aged 50 or older in nine industrialized areas: the United States, Canada, Australia, Japan, and five European countries (France, Germany, Italy, Spain, and the United Kingdom). They have found that osteoporosis prevalence at the total hip or hip/spine ranged from 9 to 38% for women and 1 to 8% for men, with a total of 49 million individuals affected. For females, osteoporosis prevalence ranges from 9 to 15% (France and Germany, respectively) based on total hip BMD and from 16 to 38% (United States and Japan, respectively) when spine BMD data were included. Approximately 30% of postmenopausal

and older women are affected by osteoporosis in Western societies (Palacios et al., 2009; Table 6).

Table 6. *Prevalence of osteoporosis based on BMD at total hip and at total hip or spine in those aged 50 years older.*

Country	Total hip		Total hip or spine	
	Prevalence (%)		Prevalence (%)	
	Males	Females	Males	Females
USA	2	14	4	16
Canada	2	11	3	18
France	2	15	8	32
Germany	2	15	8	33
Italy	2	12	8	30
Spain	**2**	**12**	**8**	**30**
UK	1	9	7	27
Japan	4	14	6	38
Australia	2	10	6	22

Note: Data reproduced and adapted from Wade et al. (2014).

Regarding Spain, osteoporosis affects approximately 12% of females (1,011,971) and 2% of males (121,452) based on total hip BMD, or 30% (2,537,629) and 8% (539,295) of women and men, respectively, based on total hip or spine BMD. As can be seen, the prevalence of osteoporosis in the lumbar spine is higher than in the total hip both in men and women. In fact, these results are in accordance with the data shown by Díaz and Moro (2006), who found that in Spain, the prevalence of osteoporosis in the lumbar spine was 22.8% and in the femoral neck 9.1% in women over 50.

According to the EPISER study of the prevalence of rheumatic diseases in the Spanish population, osteoporosis currently affects one in four women and one in eight men from the age of 50. In those over 70, one in two women and one in four men will have osteoporosis (Redondo, 2014). In the report by Hernlund and colleagues (2013) about the medical management, epidemiology, and economic burden of osteoporosis in the European

Union, the estimated number of men and women with osteoporosis based on femoral neck BMD in 2010 in Spain was 6.8% and 22.6%, respectively, which represents 5.4% of the total population. Table 7 shows the osteoporosis prevalence in all of Europe.

Table 7. *Prevalence of men, women and total population over 50 years with osteoporosis (defined as a T-score of −2.5 SD or less at the femoral neck).*

Country	Prevalence (%)		
	Male	Women	Total
Austria	6.5	22.2	5.5
Belgium	6.6	22.4	5.6
Bulgaria	6.4	20.9	5.6
Cyprus	6.2	19.3	3.7
Czech Republic	6	20.4	5.0
Denmark	6.5	21.1	5.1
Estonia	6.2	22.2	5.8
Finland	6.4	21.5	5.7
France	6.7	22.5	5.5
Germany	6.6	22.6	6.1
Greece	6.9	22.3	5.7
Hungary	6.2	21.1	5.5
Ireland	6.2	20	3.7
Italy	6.9	23.4	6.3
Latvia	6.1	22.3	5.8
Lithuania	6.1	21.7	5.3
Luxembourg	6.1	21	4.3
Malta	5.9	19.8	4.9
Netherlands	6.3	20.8	4.9
Poland	5.8	20.1	4.8
Portugal	6.7	22	5.6
Romania	6.2	20.5	4.8
Slovakia	5.7	19.4	4.2
Slovenia	6.6	21.5	5.4
Spain	**6.8**	**22.6**	**5.4**
Sweden	6.9	22.4	5.6
UK	6.7	21.9	5.2
EU27	6.6	22.1	5.5

Note. Data reproduced and adapted from Hernlund et al. (2013).

Accounting for the total population with low bone mass (osteopenia and osteoporosis) in the United States alone, an estimated 54 million individuals, 55% of the population over age 50 (10.2 million have osteoporosis, and 43.4 million have osteopenia), present this condition (Looker et al., 2012; National Osteoporosis Foundation, 2014). This number is expected to increase to 71.2 million in 2030, according to the Cosman et al. (2014).

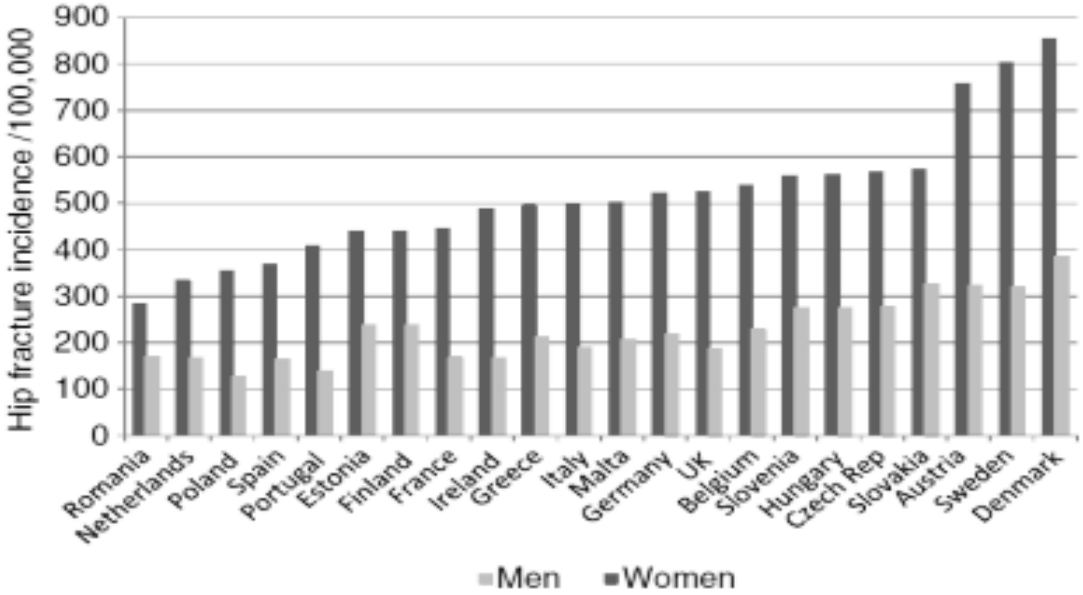
In the Valencian community, contradictory findings have been discovered. Quiles et al. (2008) have shown that in 822 women of Gandia between 45 and 69 years of age, the prevalence of osteoporosis was 11.7% and for osteopenia 28.7%. On the other hand, Reig (2009) has found a prevalence of 32% of osteoporosis and 50% of osteopenia in postmenopausal females over 50 in Valencia City.

The increase in the global prevalence of osteopenia and osteoporosis leads to an increment in the prevalence of osteoporotic fracture risk and osteoporotic fractures cases (also called fragility fractures). By 2040, an estimated 319 million adults aged 50 or more worldwide will be at high risk of osteoporotic fracture (Odén et al., 2015). Currently, osteoporosis causes more than 8.9 million fractures annually worldwide (1.6 million at the hip, 1.7 million at the forearm, and 1.4 million vertebral fractures), approximately 1,000 per hour (Hernlund et al., 2013). In fact, it is estimated that worldwide, one in three women and one in five men over 50 will sustain an osteoporotic fracture during their lifetime (Cooper, 2010; Reginster & Burlet, 2006; Wright et al., 2014), and the annual incidence of hip fracture worldwide is predicted to reach 8.2 million by 2050 (Cummings, 2002). Other authors have cited worse data, with one in two women (46–50%) and one in four men (20–22%) affected by this medical condition (Brewer et al., 2011; Hernlund et al., 2013; van Staa et al., 2001).

In Spain, the incidence of fractures in adult women in 2010 was 30,030 in hip, 19,155 in vertebra, 25,155 in forearm, and 65,070 other fractures (Hernlund et al., 2013). Although

the highest fracture rates are in Western regions since one-third of all osteoporotic fractures occur in Europe (Hernlund et al., 2013), the Spanish population registered one of the lowest hip fracture rates in Europe (incidence/100,000) among men and women above 50 (Figure 41).

Figure 41. *Hip fracture incidence/100,000 in men and women above 50 years standardized to the European population.*



Note. Reproduced and adapted from "Osteoporosis in the European Union: medical management, epidemiology and economic burden" (p. 55), by Hernlund et al., 2013, *Archives of Osteoporosis, 8*(1).

iii. Health care costs

Importantly, osteoporosis and its major consequence, minimal trauma fractures, place an enormous burden on the economy and healthcare systems of all countries. The cost of treating osteoporosis and its fractures has been estimated at $19 billion annually in the United States alone (Cosman et al., 2014) and $7.4 billion in Australia (Palacions et al., 2009). These figures are expected to increase due to the ever-rising costs associated with the aging

population (Hernlund et al., 2013; United Nations Department of Economic and Social Affairs, 2017).

In Europe, the cost of osteoporosis, including pharmacological intervention, was estimated at €37 billion (representing 3% of the healthcare spending; Hernlund et al., 2013). Costs of treating incident fractures comprised 66% of this cost, long-term fracture care 29%, and pharmacological prevention 5% (Hernlund et al., 2013). From the specific cost of the fractures, hip fractures represented 54%, other fractures 39%, and vertebral and forearm fractures 5% and 1%, respectively (Hernlund et al., 2013).

In Spain, it is estimated that the cost of osteoporosis in million € was 2,842 in 2010 and will increase to 3,680 in 2025, which represents an increase of 30% in 15 years (Hernlund et al., 2013). This cost is 2.8% of the entire healthcare spending. In addition, fracture cost per capita in Spain constitutes €68 (in Europe €75), while the cost of the first-year treatment of the hip, vertebral, forearm, and other fractures per capita is estimated as €9,421; €2,349; €1,076; and €7,112, respectively (in Europe, €13,816; €3,380; €989; and €7,652; Hernlund et al., 2013).

iv. Clinical risk factors

As a polyfactorial bone disorder, osteoporosis is affected by many factors that have been identified. However, it is important to distinguish between risk factors for osteoporosis and risk factors for osteoporotic fracture. For osteoporosis, risk factors can be categorized as fixed and modifiable. Major fixed and modifiable risk factors for osteoporosis are listed in Table 8.

Table 8. *Risk factors of osteoporosis.*

Fixed	**Risk factors examples**
Genetics	Variations in the DARC gene, osteogenesis imperfecta, Bruck syndrome, osteopetrosis, high-bone-mass syndrome, osteoporosis-pseudoglioma syndrome, von Buchem disease, sclerosteosteosis, familial expansile osteolysis, juvenile Paget's disease, hypophosphatasia, hemochromatosis, thalassemia, Ehler–Danlos syndrome, Gaucher's disease, glycogen storage disease, homocystinuria, Marfan syndrome.
Age	Advanced (40-50 years and above)
Sex	Female
Race/ethnicity/ancestry	White, Asian
Family history of osteoporosis	Parents, brothers or sisters with osteoporosis
Menopausal state	Postmenopausal
Body size	Small body and bone sized, height loss
Disorders	Predisposition to low bone mass Cystic fibrosis Muscular dystrophy
Modifiable	**Risk factors examples**
Nutrition (levels of protein, calcium, phosphorus, Magnesium, Fluoride, Vitamin D, Zinc, Cooper, Boron, Manganese, Strontium, Silicon, Potassium, Vitamin C, Vitamin K, Vitamin A, Vitamin Bs)	Anorexia nervosa Calcium and vitamin D deficiencies General malnutrition Idiopathic hypercalciuria High-caffeine diet High-sodium diet
Physical activity	Low level or lack of physical activity, previous and current physical activity
Body mass	High levels of body fat (overweight and obesity), low BMI and body weight.
Drug use	Smoking (current or former) Ethanolism (excess alcohol intake)
Medication	Long-term use of certain anticonvulsants (eg, phenytoin) Oral or intramuscular use of glucocorticoids for more than three months. Intramuscular medroxyprogesterone Immunosuppressives (eg, cyclosporine) Gonadotropin-releasing hormone agonists or analogues. Anti-retrovirals

Table 8. *Continued.*

Modifiable	**Risk factors examples**
Medication	Thiazolidinediones Excessive thyroxine doses Cytotoxic agents Aromatase inhibitors Heparin Anticoagulants (AVK) Blood thinners Oral contraceptives Proton pump inhibitors Selective serotonin Re-uptake inhibitors
Hormones	Low levels of sex steroids, high levels of parathyroid hormone, high levels of serotonin
Growth factors	Low levels of GH, IGF-1, IGF-2 and growth factors
Muscular factors	Low level of muscle mass, low levels of muscle function, a decrease muscle cross-sectional area, low levels of muscle strength.
Circulating factors	Low level of cardiorespiratory fitness, inadequate blood supply, inadequate blood flow, inadequate blood circulation, cardiovascular system altered.
Nerve factors	Alterations in nerve system, alteration in the innervation of skeletal system.
Glial factors	Alterations in Schwann cells.
Systemic conditions and disorders	Endocrinopathies (cortisol excess, Cushing's syndrome, hypogonadism, hyperthyroidism, primary hyperparathyroidism, type 1 diabetes mellitus, thyrotoxicosis) Gastrointestinal diseases [Billroth I gastroenterostomy, chronic liver disease (eg, primary biliary cirrhosis), malabsorption syndromes (eg, celiac disease, Crohn_s disease), total gastrectomy, inflammatory bowel disease) Rheumatic conditions (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, scleroderma) Other disorders and conditions (chronic renal disease, cancers, lymphoma and leukemia, inflammatory diseases, chronic obstructive pulmonary disease, immobilization).

Note. Information extracted from Bonnick et al. (2010); Clarke & Khosla, 2010; Hernlund et al. (2013); Huang & You-Qiang, 2015; Imel et al. (2008); Knaw, 2015; Nuti et al. (2019); Stewart & Ralston, 2000; Papaioannou et al. (2009); Watts & Manson, 2017; Weaver et al. (2016).

For osteoporotic fractures, a total of 10 risk factors were identified after WHO performed a meta-analysis of the relationship of clinical risk factors and fracture, analyzing global epidemiology data from 12 cohorts (approximately 250,000 person-years, 60,000 patients, and over 5,000 fractures) and confirmed in 11 additional cohorts (Silverman, 2006). The 10 risk factors identified were age (50 to 90 years), sex, weight, height, low femoral neck BMD, prior fragility fracture, parental history of hip fracture, current tobacco smoking, long-term use of glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis, and alcohol intake of more than two units a day (WHO, 2009). These 10 factors were then used to create the platform called FRAX to calculate the 10-year risk of major osteoporotic fracture (hip, spine, shoulder, and wrist; Bonnick et al., 2010).

v. Osteoporotic fracture

Osteoporosis is the main bone disorder of the skeletal system, but osteoporotic fractures are the important end result due to their devastating consequences. However, the definition of an osteoporotic fracture is not straightforward. The definition with most consensus considers osteoporotic fracture as all fractures from low-energy trauma, defined as "a fall from a standing height or less, or trauma that in a healthy individual would not give rise to fracture" (Borgstrom et al., 2006). From this approach, the vast majority of forearm or hip fractures are fragility fractures (Kanis et al., 2001, 2002). However, several scientists do not agree with this definition since osteoporotic individuals are more likely to fracture than their normal counterparts following high-energy trauma as well (Kanis et al., 2002). In addition, this idea is also based on the imperfect correlation between low-energy fractures and low BMD that has been documented (Kanis, Johnell et al., 2004; Kanis et al., 2008).

Independent of the approach selected, what is clear is that fractures due to osteoporosis represent a costly public health issue and a serious concern for older adults because of the disability and increased mortality risk they cause (Black & Rosen, 2016). This

problem is especially crucial in postmenopausal women, where osteoporotic fractures are more common than breast cancer, myocardial infarction, and stroke combined (Singer et al., 2015). In addition, after the first fragility fracture, the risk for subsequent fractures more than doubles in the next six to12 months, persisting for the next 10 years (Bliuc et al., 2015; Sobolev et al., 2015). Table 9 shows how the FRAX 10-year probability of a major osteoporotic fracture in women with a previous fracture increases with age in European countries with higher populations (Hernlund et al., 2013). Moreover, 40% of the people who suffer a hip fracture will be institutionalized or unable to walk independently, 60% will still require assistance a year later, and one in three will die within 12 months (Cooper et al., 1993; Magaziner et al., 1990).

Table 9. *FRAX 10-year probability (%) of a major osteoporotic fracture in women with a previous fracture.*

Country	Age (years)							
	52	57	62	67	72	77	82	87
Spain	3.7	4.6	6.2	9	13	18	24	24
Italy	7.4	8.5	11	15	19	24	30	31
Germany	7.1	7.8	10	14	18	23	29	31
France	5.5	6.3	8	11	16	22	30	36

Note: Data extracted from Hernlund et al. (2013).

Osteoporotic fractures may occur in almost all skeletal bones, but the most common locations are the vertebral column, hip (specifically the proximal ends of femur), proximal humerus, and forearm (specifically the fracture of the distal end of the radius, called Colles fracture; Hernlund et al., 2013; Nuti et al., 2019; Eurostat, 2011; Wilson et al. 1994). However, other fractures after the age of 50 are also related, at least in part, to low BMD and should be regarded as osteoporotic (Diez-Perez et al., 2011; Hooven et al., 2009; Kanis, Johansson et al., 2004), such as fractures of the pelvis, tibia, or ribs. It is also necessary to take into account that while the most frequent cause of fractures of long bones (femur, humerus, and radius) is the low- or high-energy trauma due to falls, it is more difficult to

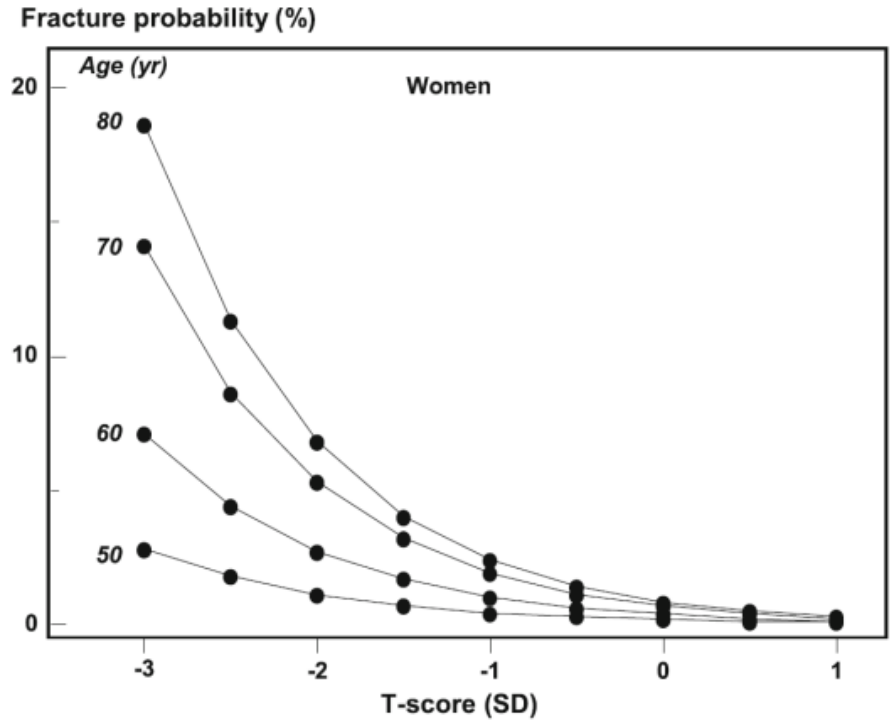
determine the cause of the osteoporotic fractures of the vertebral bodies, which is the reason they often go undiagnosed (Nuti et al., 2019).

The vast majority of osteoporotic fractures occur in elderly women (Hernlund et al., 2013). It is estimated that that a 50-year-old white woman has a 50% lifetime risk of any osteoporotic fracture and a 15 to 20% risk of hip fracture (Black & Rosen, 2016), showing about twice as high a risk of sustaining any fracture than men (Hernlund et al., 2013), although there are variations among different fracture sites (x5 higher risk at forearm and x2 higher risk at spine than men). Osteoporosis is responsible for an estimated 90% of all spine and hip fractures in white American women ages 65 to 84 (Joseph et al., 1988). However, most postmenopausal women with fractures do not have BMD values corresponding to osteoporosis, but they show low BMD values, and most of them are categorized as osteopenic (Siris et al., 2004).

In general, lower levels of BMD are associated with a higher risk of fracture, particularly at the hip, making this a strong risk factor for fracture (Black & Rosen, 2016). The ability to predict fragility fractures by the levels of BMD is comparable to the use of blood pressure to predict stroke or serum cholesterol to predict myocardial infarction (Hernlund et al., 2013). Prospective studies have indicated that a decrease of one SD in BMD represents a 10 to 12% decrease in BMD, and the risk of fracture increases by a factor of 1.5 to 3.0 for each SD decrease in BMD (Borgstrom et al., 2006; Kanis & Gluer, 2000; Marshall et al., 1996; Figure 42). This phenomenon depends on fracture type and measurement (Kanis & Gluer, 2000; Marshall et al., 1996), but the most closely related is when BMD is used to predict the fracture risk at that same site (Bonnick et al., 2010). For instance, at the hip, the fracture risk increases 2.6-fold for each SD decrease in age-adjusted BMD (Cummings et al., 2006; Kanis & Gluer, 2000; Marshall et al., 1996), while the risk for spine fracture increases 2.3-fold for each SD decrease in age-adjusted BMD at the lumbar spine (Kanis & Gluer,

2000). In addition, T-score BMD value of the total hip can predict the risk of suffering any fracture, with an increase of 1.6-fold for each SD decrease at the hip (Bonnick et al., 2010).

Figure 42. *Relationship between BMD at femoral neck expressed as a T-score and 10-year hip fracture probability in women according to age.*



Note. Reproduced from "Osteoporosis in the European Union: medical management, epidemiology and economic burden" (p. 20), by Hernlund et al., 2013, *Archives of osteoporosis, 8*(1).

Focusing on hip fractures, about one-third of elderly individuals fall annually, with the result that 5% will sustain a fracture, and 1% will suffer a hip fracture (Hernlund et al., 2013), with this type of osteoporotic fracture accounting for less than 20% of osteoporotic fractures worldwide (Strom et al., 2011). It has been estimated globally to occur 1.25 million times annually (338,000 in men and 917,000 in women) and is predicted to increase 240% in women and 310% in men from 1990 to 2025 (Gullberg et al., 1997). The risk of hip fracture

has been shown to increase exponentially with age, mostly above 70, and especially in women, who are two times more likely than men to fracture their hips after 50 (Melton et al., 1993).

Despite the total percentage of osteoporotic fractures that represents, hip fracture is the most serious and devastating osteoporotic fracture in terms of morbidity, disability, and mortality (Melton & Cooper, 2001). Up to 20–25% of patients die in the first year following hip fractures (with higher rates in urbanized countries; Harvey et al., 2010; Woolf & Pfleger, 2003), whether directly or indirectly through the medical consequences that they can cause (Bonnick et al., 2010; Cooper et al., 1993; Cummings & Melton, 2002; Klop et al., 2014; Leibson et al., 2002). Even if the person survives, 50% will have some long-term loss of mobility, which can ultimately result in a dependent living situation and a poor quality of life (Black & Rosen, 2016; Bonnick et al., 2010). The reduction of functionality and mobility may also decrease one's healthspan (Sernbo & Johnell, 1993).

Finally, the type of hip fracture must also be taken into account. Trochanteric fractures (intratrochanteric: extracapsular fracture) are more characteristically osteoporotic and are also more commonly associated with a prior osteoporotic fracture than those that occur in the femoral cervix (subcapital or transcervical: intracapsular fracture; Michaelsson et al., 1999). In addition, the increase in sex-specific and age-specific risks for hip fracture is also greater for trochanteric than cervical fractures (Michaelsson et al., 1999), but both types have in common that more than 95% occur as a consequence of a fall (Beck et al., 2017). Therefore, strategies to optimize bone strength and reduce fall risk, such as exercise training or physical activity programs in older adults, especially postmenopausal women, must be developed to more effectively prevent fractures.

Moreover, vertebral fractures are the most common osteoporotic fracture with a prevalence of 15% in women aged 50–59 and 50% in women above age 85 (Costa et al., 2013; Diacinti & Guglielmi, 2010; Melton et al., 1993), although these fractures are less well documented than hip fractures because they rarely require hospitalization and therefore often go undiagnosed. Some clinical details that can suggest a vertebral fracture are prolonged use of corticosteroids, age, structural spinal deformity, loss of height > 6 cm, and a distance between the last rib and the iliac crest < 2 fingers. It is therefore advisable to carefully evaluate the presence of dorsal kyphosis, progressive loss of height, or dorso-lumbar pain to detect possible vertebral fractures (Nuti et al., 2019).

It has also been found that this kind of fracture increases linearly with age, although more slowly after menopause than hip fractures (Bonnick et al., 2010). However, the rate increases exponentially during later life, with a significant percentage of vertebral fractures occurring in osteopenic older men and women, especially in a woman's mid-70s (Bonnick et al., 2010; Iñiguez-Ariza & Clarke, 2015; Muschitz et al., 2009). Vertebral fractures are especially important in subjects with osteoporosis because they tend to indicate a decrease in bone strength earlier than any other skeletal locations due to the vertebrae having more trabecular than cortical bone. Since trabecular tissue is affected earlier than cortical in osteoporosis, vertebrae become at a high risk of fracturing (Chen et al., 2013).

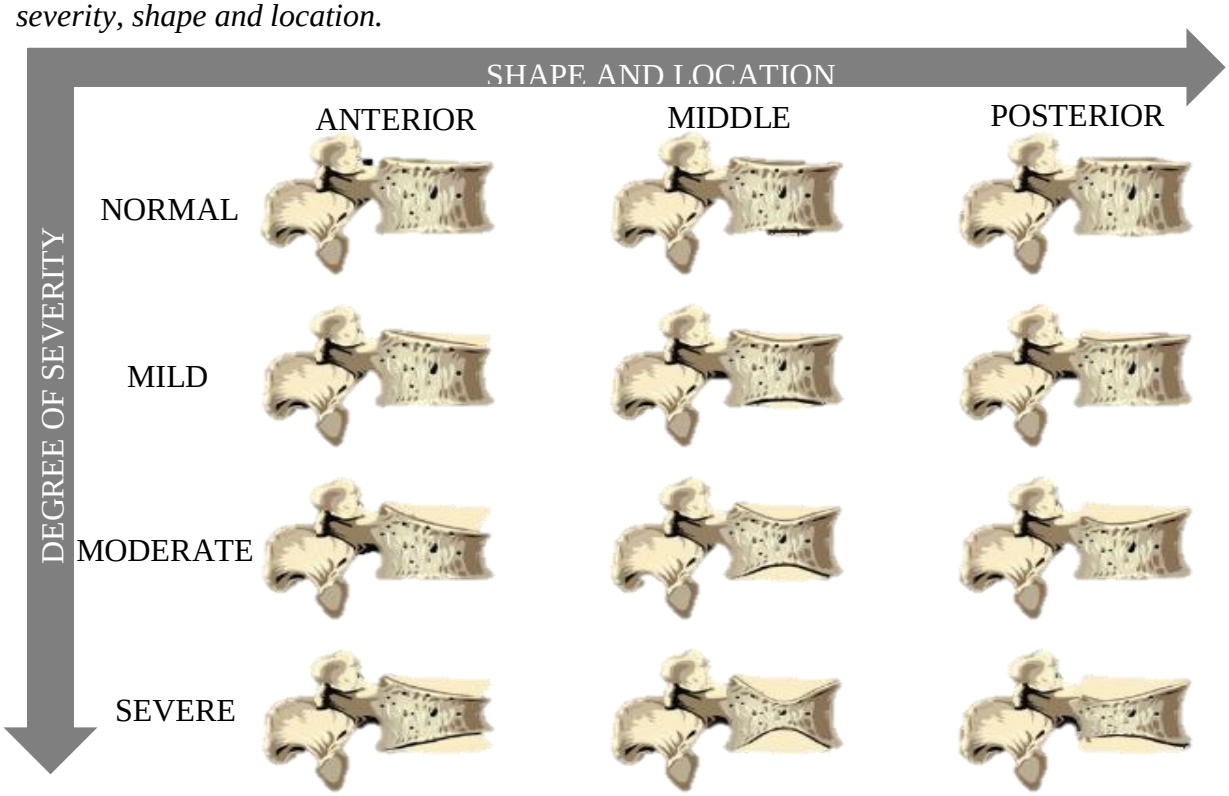
Vertebral fractures, as with hip fractures, are associated with an increased risk of death and are also very strong predictors of further fracture at the spine and elsewhere (Black & Rosen, 2016; Johnell et al., 2001; Klotzbuecher et al., 2000; Kotowicz et al., 1994; Lindsay et al., 2001; Watts & Manson, 2017). Moreover, vertebral fractures may cause substantial chronic pain, loss of height, and kyphosis (abnormal curvature of the thoracic spine). Spinal pain and deformity can greatly restrict regular movement and lung function or cause digestive problems (Silverman et al., 2001). Osteoporotic fractures can also take a high psychological

toll as well (Gold, 2001). Both hip and vertebral osteoporotic fractures produce changes in pain, mobility, body image, and independence that can have a strong impact on mood and self-esteem (Black & Rosen, 2016; Bonnick et al., 2010; Hernlund et al., 2013).

In the same way with hip fractures, vertebral osteoporotic fractures can be classified according to shape as wedge fractures (in which there is anterior or posterior height loss), crush fractures (involving compression of the entire vertebral body), and biconcavity (where there is a central compression of the end-plate regions with a relative maintenance of the anterior and posterior heights; Hernlund et al., 2013). According to the degree of severity, vertebral fractures can be classified as mild (20–25% height loss), moderate (25–40% height loss), or severe (> 40% height loss; Genant et al., 1996). Figure 43 shows the different vertebral fractures.

Finally, it is necessary to note that not all fractures have the same pathogenesis. As mentioned above, most of the fractures are associated with reduced BMD (osteopenia or osteoporosis); however, in terms of bone remodeling, it has been documented that women with osteoporotic fractures may have high, normal, or low rates of remodeling. Women with fractures can have a negative balance owing to increased resorption, reduced bone formation, or both, while other women with fractures may not have a negative balance in bone remodeling (Arlot et al., 1990; Brown et al., 1994; Eriksen et al., 1990). This heterogeneity suggests that all individuals with osteoporotic fractures should not be treated in the same way.

Figure 43. *Classification of spinal fractures and deformities in base on the degree of severity, shape and location.*



Note. Reproduced and adapted from "Comparison of semiquantitative visual and quantitative morphometric assessment of prevalent and incident vertebral fractures in osteoporosis" (p 986), by Genant et al., 1996, *Journal of Bone and Mineral Research, 11*(7).

vi. Treatments

In recent years there have been significant advances in the management of osteoporosis, especially with respect to the development of pharmacological and lifestyle interventions to reduce bone fracture risk. The aim of all osteoporosis treatments is to reduce or prevent bone fractures by avoiding modifiable risk factors, such as smoking, excessive alcohol intake, and poor levels of physical activity. Treatments also seek to either improve, maintain or at least reduce the bone loss associated with modifiable factors and non-modifiable factors, like age or sex.

Despite advances, problems persist in answering the question of who should receive osteoporosis treatment.A management strategy focused on lifestyle approaches may be all

that is needed for individuals who are at low risk for osteoporotic fracture. However, the US NOF and the NAMS recommend including pharmacologic treatment of osteoporosis for the following populations: (1) individuals with hip or spine fractures thought to be related to osteoporosis; (2) those who have BMD values consistent with osteoporosis at the lumbar spine, femoral neck, or total hip region (e.g., a BMD SD of 2.5 or more below the young normal mean and a T score of -2.5 or lower); (3) those with a BMD SD between 1 and 2.5 below the young normal mean (osteopenia) and whose 10-year risk based on the FRAX calculator is 20% or more for major osteoporosis-related fracture (i.e., hip, forearm, humerus, and clinical vertebral fracture combined) or 3% or more for hip fracture (Bonnick et al., 2010; Cosman et al., 2014). For men with prostate cancer undergoing adjuvant hormonal block therapy and women with breast cancer, a history of previous osteoporotic fractures and chronic glucocorticoid therapy (prednisone doses equivalent to ≥ 5 mg/day),such a high risk of fracture appears that the decision to initiate pharmacologic therapy may be ruled out by the need to acquire densitometric values (Nuti et al., 2019).

Regarding the pharmacologic treatment approach to osteoporosis, there are several approved drug therapies that can be distinguished according to the following characteristics: specific sites and modes of action, mechanisms of action, dosage regimens, route of administration (oral, intravenous, nasal), degrees of efficacy, and effectiveness (Black & Rosen, 2016; Close et al., 2006). Furthermore, these therapies can be classified into two basic categories: anti-catabolic agents (previously referred to as antiresorptive) and anabolic agents (Riggs & Parfitt, 2004). These two classes of drugs act through opposite effects on the bone remodeling process. Anti-catabolic drugs inhibit osteoclast-mediated bone loss, thereby reducing bone turnover (Chesnut & Rosen, 2001; Greenspan et al., 1998; Rodan, 1998b; Russell et al., 1999). Anti-catabolic agents are also associated with a moderate increase of bone mass, resulting from the increased mineralization of the bone matrix (Pivonka, 2018). In

contrast, anabolic agents boost bone mass by increasing bone remodeling and stimulating bone formation that is greater than bone resorption, thus creating a positive bone turnover (Lindsay et al., 1997; Neer et al., 2001; Zhou et al., 2003).

The current drugs that have been approved for the treatment of osteoporosis in the USA by the US Food and Drug Administration and in Europe by the European Medicine Evaluation Agency are shown in Table 10. From all of them, parathyroid hormone peptides (Teriparatide and PTH 1–84) remain the only approved anabolic agents for stimulating new bone formation (Iñiguez-Ariza & Clarke, 2015). Four anti-catabolic agents (alendronate, risedronate, zoledronic acid, and denosumab) are generally considered as initial options for most patients who are candidates for treatment because of their evidence of having "broad spectrum" antifracture efficacy (hip, spine, and nonvertebral fracture risk reduction; Camacho et al., 2016).

Table 10. *Drugs Approved in USA and Europe for the Treatment and Prevention of Osteoporosis.*

Drug class and agent	Where it is approved?	Route of administration	Dosing regimen	Type of fracture risk prevention	Approved use for osteoporosis
			Isolated therapies		
Biphosphonates					
Alendronate (Fosamax)	USA, EU	Oral	35–70 mg/wk or 5-10 mg once daily	Vertebral, non-vertebral, hip	Treatment and prevention
Risedronate (Actonel, Atelvia, generic form)	USA, EU	Oral	35 mg/wk or 150 mg/mo (in a single dose or in two 75-mg doses on consecutive days)	Vertebral, non-vertebral, hip	Treatment and prevention
Ibandronate	USA, EU	Oral and intravenous	Oral: 150 mg/wk; intravenous: 3 mg every 3 mo	Vertebral	Treatment and prevention
Zoledronic acid (Reclast, generic infusion form)	USA, EU	Intravenous	5 mg/yr	Vertebral, non-vertebral, hip	Treatment and prevention
Neridronate	EU	Intravenous	100mg in 10 days	Only for osteogenesis imperfecta	Treatment
Etidronate	USA, EU	Oral	400 mg/day for 2 weeks every 3 mo	Only for Paget's disease	Treatment
Clodronate	EU	Oral	800 mg/day	Vertebral	Treatment
Biologic					
Denosumab (Proplia)	USA, EU	Subcutaneous	60 mg every 6 mo	Vertebral, non-vertebral, hip	Treatment

Table 10. *Continued*.

Drug class and agent	Where it is approved?	Route of administration	Dosing regimen	Type of fracture risk prevention	Approved use for osteoporosis
			Isolated therapies		
Anabolic or parathyroid hormone peptides					
Teriparatide or PTH 1–34 (Forteo)	USA, EU	Subcutaneous	20 μg/day	Vertebral, non-vertebral	Treatment
PTH 1-84	USA, EU	Subcutaneous	1000 μg/day	Vertebral, non-vertebral	Treatment
Calcitonin (Miacalcin, Fortical)	USA	Intranasal	200 IU/day	Vertebral	Treatment
Selective strogen-receptor modulators (SERM) also known as estrogen agonist/antagonist					
Raloxifene (Evista)	USA, EU	Oral	60 mg/day	Vertebral	Treatment and prevention
Bazedoxifene	USA, EU	Oral	20 mg/day	Vertebral and non-vertebral	Prevention
Estrogens					
Conjugated equine estrogen	USA	Oral	0.15–1.25 mg/day	Vertebral, non-vertebral, hip	
17β-estradiol	USA	Oral and transdermal	Oral: 0.025–0.10 mg/day; transdermal: 2 times/wk	No data from randomized trials	
Ultra-low-dose 17β-estradiol	USA	Oral	0.014 mg/day	No data	

Table 10. *Continued*.

Drug class and agent	Where it is approved?	Route of administration	Dosing regimen	Type of fracture risk prevention	Approved use for osteoporosis
			Isolated therapies		
Selective tissue estrogenic activity regulator (STEAR)					
Tibolone	EU	Oral	1.25-2.5 mg/day	Vertebral and non-vertebral	Prevention
Hormone replacement therapy					
Estrogen-only	USA	Oral and transdermal	0.625 mg/day	Vertebral, non-vertebral, hip	Treatment and prevention
Estrogen-progestin	USA	Oral and transdermal	0.625 mg/day	Vertebral, non-vertebral, hip	Treatment and prevention
Estrogen-tibolone	USA	Oral and transdermal	0.625 mg/day	Vertebral, non-vertebral, hip	Treatment and prevention
			Combination therapies		
Strontium ranelate (Protelos)	USA, EU	Oral	2g/dy	Vertebral, non-vertebral, hip	Treatment and prevention
Alendronate and estrogen therapy	USA	Oral	Combination dosages	No data from randomized trials	Treatment and prevention
Risedronate and estrogen therapy	USA	Oral	Combination dosages	No data from randomized trials	Treatment and prevention
Teriparatide and estrogen therapy.	USA	Oral and subcutaneous	Combination dosages	No data from randomized trials	Treatment and prevention
Teriparatide and biphosphonates	USA	Oral and subcutaneous	Combination dosages	No data from randomized trials	Treatment and prevention

Table 10. *Continued*.

Drug class and agent	Where it is approved?	Route of administration	Dosing regimen	Type of fracture risk prevention	Approved use for osteoporosis
			Combination therapies		
Teriparatide and biphosphonates	USA	Oral and subcutaneous	Combination dosages	No data from randomized trials	Treatment and prevention
Teriparatide and denosumab	USA	Subcutaneous	Combination dosages	No data from randomized trials	Treatment and prevention
Bazedoxifene with conjugated estrogens [defined as tissue selective estrogen complex (TSEC)]	USA	Oral	Combination dosages	No data from randomized trials	Treatment and prevention
			New therapies		
Cathepsin K inhibitors					
Odanacatib	-	Oral	50mg/day	In phase II study	-
ONO-5334	-	Oral	300mg/day	In phase II study	-
Anabolics					
PTHrp Analogue (Abaloparatide)	-	Oral and subcutaneous	80 μg/day	In phase II study	-
Anti-sclerostin antibodies					
Romosozumab (Evenity)	USA	Subcutaneous	210mg/mo	In phase IV study	Treatment
Blosozumab	-	Subcutaneous	125mg/wk	In phase II study	-

Table 10. *Continued*.

Drug class and agent	Where it is approved?	Route of administration	Dosing regimen	Type of fracture risk prevention	Approved use for osteoporosis
			New therapies		
Anti-DKK1 antibodies					
BHQ880	-	Subcutaneous	10 mg/kg	In phase I study	-

Note. Data extracted from Bonnick et al. (2010), Camacho et al. (2016), Iñiguez-Ariza and Clarke (2015), Nuti et al (2019), Solomon et al (2016).

Most of the drugs in Table 10 have only been approved for the treatment of postmenopausal osteoporosis. In fact, alendronate, risedronate, zoledronic acid, teriparatide, and strontium ranelate are the only approved drugs for the treatment of osteoporosis in men **(**Hernlund et al., 2013). In addition, alendronate, risedronate zoledronic acid, etidronate and teriparatide are also approved for the prevention and treatment of glucocorticoid-induced osteoporosis (Lekamwasam et al., 2012). For more information about the pharmacologic agents, such as the mechanisms of action, side effects or efficacy studies, see the following articles: Black and Rosen, 2016; Bonnick et al., 2010; Camacho et al., 2016; Gambacciani and Levancini, 2014; Herlund et al., 2013; Iñiguez-Ariza and Clarke, 2015; Nuti et al., 2019.

A number of new approaches are being explored for the prevention of fractures, particularly in postmenopausal women (Canalis, 2010). These approaches include cathepsin K inhibitors, transdermal PTH peptide formulations, antibodies to Wnt antagonists (e.g., sclerostin), and drugs that act on calcium sensing receptors (Cosman et al., 2010; Hoeppner et al., 2009; Kumar et al., 2010; Stoch et al., 2009).

Pharmaceutical agents are the first line of treatment for osteoporosis because they can reduce the risk of fractures by approximately 20% to 60%, depending on the agent used, patient population, and adherence (Daly, Dalla Via et al., 2019). However, experts have recently highlighted "a crisis in the treatment of osteoporosis" because prescriptions and adherence to pharmacology regimens have decreased in recent years (Khosla & Shane, 2016). In fact, only 20% of postmenopausal women that experience an osteoporotic fracture receive the appropriate follow-up treatment (Kanis, McCloskey et al., 2014). If they do receive the correct treatment, only between 25% and 81% continue following it after 6 months to 1 year, depending on the therapy. Thus, adherence to therapy is poor (McCombs et al., 2004; Tosteson et al., 2003; Segal et al., 2003).

An additional issue with pharmaceutical agents is that the drugs have no effect on other key fracture risk factors. These factors include dynamic balance, coordination, overall functional performance, muscle strength, and muscle power. As these factors have all been associated with risks for falls and factures (Cawthon et al., 2008), they highlight the importance of identifying non-pharmacological therapies for osteoporosis prevention and treatment. One of the most important non-pharmacological therapies that has been recommended is the application of physical exercise programs.

Alongside pharmacological agents non-pharmacological interventions, or lifestyle approaches, are necessary in the prevention and management of osteoporosis. All individuals, particularly postmenopausal women and older adults, regardless of their bone density or clinical risk factors for osteoporosis should be encouraged to obtain adequate calcium and vitamin D intake. They should also consume a balanced diet, participate regularly in weight-bearing, resistance and balance exercise, avoid tobacco use, limit their alcohol consumption, and institute fall prevention measures in relation to environmental factors (e.g., avoid carpet edges, slippery or uneven flooring, inadequate footwear; Bonnick et al., 2010; Howe, Rochester et al., 2011; Hopewell et al., 2018; Prentice, 2004; Watts & Manson, 2017).

In terms of nutrition, adequate calcium and vitamin D intake are prescribed as strategies to optimize peak bone mass and maintain bone health throughout life (Nuti et al., 2019). Calcium is a nutrient that has acute antiresorptive effects on bone tissue and downregulates the bone remodeling process (Daly et al., 2014). Nonetheless, daily calcium intake tends to decline with advancing age (Ervin et al., 2000). For example, the intestinal absorption of calcium becomes reduced in older women (Ireland & Fordtran, 1973). In most older adults a vitamin D deficiency also appears in part due to a clinical condition that contributes to a decline in calcium absorption (Holick et al., 2005; Lips et al., 2001). An

estrogen deficiency in postmenopausal and older women also appears to result in an increase of urinary calcium excretion (Heaney et al., 1999).

The main factor influencing calcium intake is the amount of calcium ingested through dietary sources. In postmenopausal women age 60 and older, milk and its derivatives provide 80% of the total calcium intake, making dairy a major contributor of dietary calcium (Wang et al., 2008). To a lesser extent, pulses, almonds, and some vegetables (spinach, cabbage, and turnips) are also a source of calcium (Nuti et al., 2019). Despite the high availability of calcium in these dietary sources, the average calcium intake among older adults and postmenopausal women, particularly from places with less hours of natural light such as Canada or the USA, is about half of what is recommended, with a median of approximately 600mg per day (Alaimo et al., 1988; Ervin et al., 2004; Statistics Canada, 2004). This dietary deficiency may contribute to secondary hyperparathyroidism and negative calcium balance (Nuti et al., 2019).

The recommended daily calcium requirements depend on age and certain conditions (Table 11). Most of the organizations (the AACE, NOF, IOM Endocrine Society) recommend that women aged 51 years or older consume 1,200 mg of calcium per day (Ross 2011), and they state that there is no extra benefit in the consumption of amounts in excess of 1,500 mg per day (Bauer, 2013; Bonnick et al., 2010; Bolland et al., 2011; Moyer, 2013; Prentice et al., 2013; Reid & Bolland, 2012). In fact, an excess of calcium intake may be harmful, as it may increase the risk of non-oxalic kidney stones, cause vascular calcification, and create cardiovascular issues (Nuti et al., 2019). The upper limit of tolerable intake of calcium for adults has been established by NAS, citing the limit to be at 2,500 mg per day (Bonnick et al., 2010).

Table 11. *Recommended daily calcium requirements at different ages and under different conditions.*

Age	Sex	Calcium requirements (mg/day)
0-6 mo	M + F	200
6-12 mo	M + F	260
1-5 yr	M + F	700-800
6-10 yr	M + F	800 – 1,200
11-24 yr	M + F	1,200 – 1,500
25-50 yr	M + F	1,000
Pregnant or nursing	F	1,200 – 1,500
Postmenopausal women receiving estrogen therapy	F	1,000
Postmenopausal women without estrogen therapy	F	1,200 – 1,500
50-65 yr	M	1,000
65+ yr	M	1,200
65+ yr	F	1,200 – 1,500

Note. Mo: months; yr: years; M: male; F: Female. Adapted from National institutes of Healt (1994), National Academy of Sciences (1997), Osteoporosis Canada (2002), Nuti et al. (2019) and Ross et al. (2011).

Although studies have suggested that dietary calcium may be preferred over calcium obtained from supplements (Silverman et al., 2008; Watts & Manson, 2017), calcium supplements may be needed for individuals whose diets do not supply sufficient calcium (Watts & Manson, 2017). However, the optimal intake and utility of calcium supplements concerning the reduction of fracture risk and the increase of BMD is controversial. Supplementation of calcium intake has been shown to slightly increase BMD in women after the onset of menopause and in women with deficient dietary intakes (Nuti et al., 2019). A recent meta-analysis has also reported that obtaining calcium solely through supplements produces only a slight reduction in fracture risk (15% of total fractures and 30% of hip fractures), particularly in the elderly population (Nuti et al., 2019; Weaver et al., 2016). The most convincing evidence of the efficacy of calcium supplementation in fracture prevention

have been shown when administered in combination with vitamin D and in combination with anti-resorptive or osteoanabolic drugs (Nuti et al., 2019, Laurent, 2018).

Calcium also plays an important role in the effects of exercise on bone mass in older adults. Findings from different studies have proven that insufficient intake of calcium can compromise the skeletal response to loading and that exceeding daily calcium requirements do not appear to result in greater exercise-induced skeletal gains (Lanyon et al., 1996; Prince et al., 1995). The threshold level of calcium required to optimize the osteogenic responses to exercise has been reported to be at least 1,000 mg per day (Daly et al., 2014). However, more evidence is needed to support this claim. Adequate levels of calcium are needed to maintain bone mass, reduce fracture risk, and optimize the osteogenic effect of exercise in older adults and particularly in older women.

Along with calcium, vitamin D is recognized as an important component of any osteoporosis prevention regimen because adequate intake of vitamin D is also necessary for maintaining bone health. Vitamin D is commonly characterized as a vitamin, although it is more of a steroid prohormone (Bonnick et al., 2010). Vitamin D is essential in the physiologic regulation of calcium and phosphorus due to its ability to stimulate intestinal absorption of these minerals that enable normal mineralization of bones (Heaney, 2009; Harrison et al., 1991; Rizzoli et al., 2014; Veldurthy et al., 2016). Vitamin D may be obtained from dietary sources, such as oily fish (like salmon and mackerel), animal fats, liver, eggs, milk and dairy products, fortified foods (vitamin D_3) or some vegetables (mushrooms; Agostini et al., 2018; Gunton et al., 2015; Nuti et al., 2019). However, diet provides only about 10% to 20% of the daily requirement of vitamin D (Agostini et al., 2018; Gunton et al., 2015; Nuti et al., 2019).

As mentioned above, vitamin D is more of a hormone than a vitamin. The reason for this distinction is because 80% of the daily requirement of vitamin D comes from endogenous subcutaneous synthesis in human body as a result of sunlight exposure (Cianferrotti et al., 2015). Skin exposure to ultraviolet B rays (wavelength 290 to 310 nm) stimulates the conversion of 7-dehydrocholesterol into vitamin D_3 in the liver to 25OHD (Agostini et al., 2018; Gunton et al., 2015). This endogenous synthesis depends on multiple factors, such as the intensity of solar radiation **(**Agostini et al., 2018), the use of sunscreen (sunscreen protection eight or higher blocks the production of vitamin D by 97.5%; Holick, 2002), skin tone (a darker tone results in less production), geographic location, time of day, calendar season, and age (NOF, 2014). Additionally, older women who are frail and with chronic illness, housebound, or institutionalized and live in northern latitudes are at high risk for vitamin D deficiency (NOF, 2014). Hypovitaminosis D is also known to be a considerably widespread condition in the elderly population because aging decreases the capacity of human skin to produce vitamin D, in particular 7-dehydrocholesterol (MacLaughlin & Holick, 1985; Nuti et al., 2019). This permanent vitamin D deficiency is associated with increased bone turnover and bone loss and is caused by a decrease in intestinal calcium absorption that lowers serum calcium and consequently leads to increased PTH (Dobnig et al., 2008; Ginde et al., 2009; Girgis et al., 2013). Thus, this condition may exacerbate osteoporosis in postmenopausal women and older adults. Furthermore, low levels of vitamin D can also produce secondary hyperparathyroidism, reduce muscle strength and muscle function, and increase the risk of falls and fractures. Low vitamin D levels are also associated with sarcopenia and disability in the elderly with (Girgis et al., 2013; Rizzoli et al., 2014).

To evaluate a person's overall vitamin D status, it is necessary to assess for a specific form of vitamin D, namely 25OHD. This precursor of calcitriol synthetized in the liver is the major circulating form of vitamin D and is considered the best biomarker to assess a person's

vitamin D status (Agostini et al., 2018). The NOF recommends measurement of 25OHD in individuals at risk for vitamin D deficiency (NOF, 2014). However, it is important to note that a new steady state of 25OHD is not achieved until at least three months after a new dose of vitamin D has been applied (usually three to six months after the start of supplementation; Bonnick et al., 2010; Nuti et al., 2019). The current indications of plasma 25OHD levels from the AACE and US Endocrine Society are shown in Table 12.

Table 12. *Interpretation of plasma levels of 25OHD.*

nmol/L	ng/mL	Interpretation
< 25	< 10	Severe deficiency
25–50	10–20	Deficiency
50–75	20–30	Insufficiency
75–125	30–50	Ideal range
125–375	50–150	Possible side effects
> 375	> 150	Intoxication

Although what the optimal 25OHD level is remains controversial, the AACE and US Endocrine Society define vitamin D sufficiency as having plasma 25OHD greater than or equal to 30 ng/mL (≥75nmol/L). This measure was chosen on the basis of studies that have shown the following evidence: (1) the presence of lower PTH levels when plasma 25OHD levels are at 28 to 45 ng/ml (70-110 nmol/L; Heaney, 2004); (2) the observation that secondary hyperparathyroidism becomes increasingly common as 25OHD levels fall below 30 ng/mL (Chapuy et al., 1997); and (3) the finding that calcium absorption efficiency stabilizes at concentrations at or above approximately 32 ng/ml (80 nmol/L; Heaney, 2004). Evidence about the safety and optimal upper limit of plasma 25OHD is not conclusive, but it seems that levels above 50 ng/ml (> 125 nmol/L) are associated with potential adverse effects (Binkley et al., 2007; Camacho et al., 2016; Ross et al., 2011). The US Institute of Medicine has proposed another classification. It defines adequate plasma 25OHD levels as

concentrations above 20 ng/mL (> 50 nmol/L), insufficient levels as concentrations between 12 to 20 ng/mL (30 to 50 nmol/L), and deficient 25OHD levels as concentrations less than 12 ng/ml (< 30 nmol/L; Francis et al., 2015; Ross et al., 2011).

Due to the widespread condition of hypovitaminosis D in elderly populations, there is a frequent need for vitamin D supplementation in old age (ergocalciferol or cholecalciferol, namely Vitamin D_2 or Vitamin D_3). Supplementation has been proven as useful in the prevention of fractures and BMD loss in the elderly. However, there is no consensus on the recommended daily vitamin D intake. Many scientific organizations (IOF, the US Endocrine Society, the NOF NAMS) recommend a vitamin D intake of 800 to 1,000 IU per day for older adults at increased risk for fractures and vitamin D deficiency (Bischoff-Ferrari, 2019; Cosman et al., 2014; Dawson-Hughes et al., 2010; Holick et al., 2011). The Institute of Medicine (now the National Academy of Medicine) recommends doses of 600 to 800 IU per day, while for those at increased risk of osteoporosis they recommend an intake of 1,000 to 2,000 IU per day (Watts & Manson, 2017). In addition, recent results have suggested that doses greater than 1,000 IU per day, or even 4,000 IU per day, may be necessary for older adults (Arora et al., 2015; Baron et al., 2015). As often happens with optimal doses, there is also controversy in establishing a safe upper limit of vitamin D intake. While the National Academy of Sciences (NAS) has established an upper limit of safe intake for vitamin D as 2,000 IU/day (NAS, 1997), other authorities, such as the Institute of Medicine, consider this amount to be overly conservative (Hathcock et al., 2007). They suggest the safe upper limit for the general population to be an intake of 4,000 IU/day (Ross et al., 2011). Doses greater than 10,000 IU/day may be associated with risks of hypercalcemia and hypercalciuria (Bonnick, et al., 2010).

If the administration of high vitamin D doses (boluses) is deemed appropriate in treatment, for instance in individuals with malabsorption or obesity, those on medications that

affect vitamin D metabolism and older adults with a high vitamin D deficiency are recommended to not exceed 100,000 IU per week (14,000 IU/d) because of the increased bone resorption, fractures and falls that have been seen at this level of higher dosage. Significantly, only the weekly administration of doses equivalent to 50,000 IU (or 5,000 IU/d) of Vitamin D_2 or D_3 over a period of two to three months have been proven to be effective in restoring values to normal levels in adults with a severe vitamin D deficiency (Holick et al., 2005, 2013; LeBoff et al., 2008; Nuti et al., 2019; Wimalawansa, 2012). This regimen should be followed by maintenance therapy of 1,000 IU to 2,000 IU daily, or equivalent doses administered weekly or monthly (Holick et al., 2005, 2013; LeBoff et al., 2008; Nuti et al., 2019; Wimalawansa, 2012). It is also necessary to take into account that to rapidly obtain adequate serum levels of 25OHD, supplementation with vitamin D_3 is preferred over vitamin D_2, and orally administered supplements are more effective than intramuscular applications (Nuti et al., 2019).

Regarding the specific effects of vitamin D supplementation on BMD, studies have found that, on average, effects are modest – only small increases have been observed in hip BMD (1%) but not in other skeletal sites (Jackson et al., 2006; Camacho et al., 2016; Nuti et al., 2019; Rahme et al., 2017). In addition, there is evidence that the effect of vitamin D supplementation on BMD increases when it is at doses of at least 800 IU/d and combined with both a serum 25OHD concentration greater than 60 nmol/L as well as adequate levels of dietary calcium (at least 1,000 mg/d; Bischoff-Ferrari et al., 2012). Studies have also found that doses of vitamin D at 400 to 700 IU/d in combination with supplemental calcium can reduce the rate of bone loss in postmenopausal and older women (Dawson-Hughes et al., 1990; Jackson et al., 2006). However, it seems that high percentages of fat (i.e., being overweight) can decrease this positive effect in elderly populations (Rahme et al., 2017).

The findings from RCTs and meta-analyses on the anti-fracture effect of vitamin D have been inconsistent. It seems that the benefits of vitamin D supplementation depend heavily on both compliance and dose. A meta-analysis of studies on postmenopausal women (mean ages 71 to 85 years) found a significant reduction in both hip and non-vertebral fractures with vitamin D supplementation at doses greater than or equal to 700 to 800 IU/day (Bischoff-Ferrari et al., 2005). In addition, a critical review of four recent meta-analyses has reported that vitamin D supplementation is only shown to prevent fracture risk among older adults (65 years or more), including older adults at risk of vitamin D deficiency and fractures, when given at doses of 800 to 1000 IU daily (or the equivalent weekly or monthly dose) with good adherence (Weaver et al., 2016) and in combination with calcium. This meta-analysis found a significant 30% reduction of hip fractures and a 15% reduction of total fractures from a daily combined intake of vitamin D and calcium (Weaver et al., 2016). However, no effects have been reported when vitamin D supplementation is applied without calcium or administered to adults age 50 years and older without vitamin D deficiency or osteoporosis (Bolland et al., 2018; Zhao, Zhang & Zhang, 2017). In addition to the skeletal effects of vitamin D, some studies have also found that vitamin D supplementation with daily doses greater than 700 to 800 IU improve muscle strength (Bischoff, Stähelin, Dick et al., 2003) and balance (Pfeifer et al., 2000; Bischoff-Ferrari et al., 2006), and reduce the risk of falling (19% to 23% reduction in older adults; Bischoff-Ferrari et al., 2004, 2009).

Vitamin D plays a vital role in musculoskeletal health regulating calcium-dependent functions of muscle, such as mitochondrial function, contraction and insulin sensibility (Broe et al., 2007). Vitamin D also appears to optimize the effect of dietary protein on skeletal muscle anabolism (Rizzoli et al., 2014). In addition, vitamin D modulates bone-muscle crosstalk through the effects it exerts on a range of bone and muscle derived hormones, such as osteocalcin, sclerostin, IL-6, and myostatin (Gunton et al., 2015). Finally, as occurs with

calcium, vitamin D deficiency can alter the osteogenic effect of exercise-induced mechanical loading on bone tissue by reducing the osteoblast activity that produces osteopontin and osteocalcin, which are used in the process of bone matrix mineralization (Lanske et al., 2014).

Along with calcium and vitamin D levels, it is also necessary take into account other macro- and micronutrients, such as protein, vitamin K, and magnesium in the prevention of BMD loss and fracture risk. In the past a high dietary protein intake had been reported to possibly have adverse effects on bone health because of a potential increase in urinary calcium excretion and acid production (calciuric effect; Kerstetter, 1990). However, there is now evidence indicating that increased dietary protein intake has a favorable effect on minimizing bone loss in elderly populations, particularly when calcium intake is adequate (Darling et al., 2009; Hannan et al., 2000; Mangano et al., 2014; Rapuri et al., 2003). Additionally, increased dietary protein intake has been found to reduce risk of hip fracture in both genders in patients with inadequate intake (Nuti et al., 2019). These effects of higher protein intake on bone health can be attributed to multiple factors, such as enhanced intestinal calcium absorption, suppressed PTH levels, increased IGF-1 concentrations, and improved strength and muscle mass. All these effects may improve the osteogenic effect via increased loading on bone (Calvez et al., 2012). Recommendations concerning dietary protein intake for the general population are 0.8 g/kg/d (Joint WHO/FAO/UNU Expert Consultation; 2007). However, because intake levels are usually lower in elderly populations, the European Society for Clinical Nutrition and Metabolism has proposed a daily recommended amount of 1.0 to 1.2 g/kg/d as being optimal for a healthy older individual (Deutz et al., 2014; Volpi et al., 2013).

Lastly, data regarding magnesium and vitamin K supplementation in the prevention and treatment of postmenopausal and senile osteoporosis are inconclusive (Camacho et al.,

2016; Mutlu et al., 2007; Nieves, 2005; Odabasi et al., 2008). Nonetheless, severe deficiency of both micronutrients can result in hypocalcemia and resistance to vitamin D (Bonnick et al., 2010).

E. Age-related changes in bone tissue

i. Bone mineral density and aging

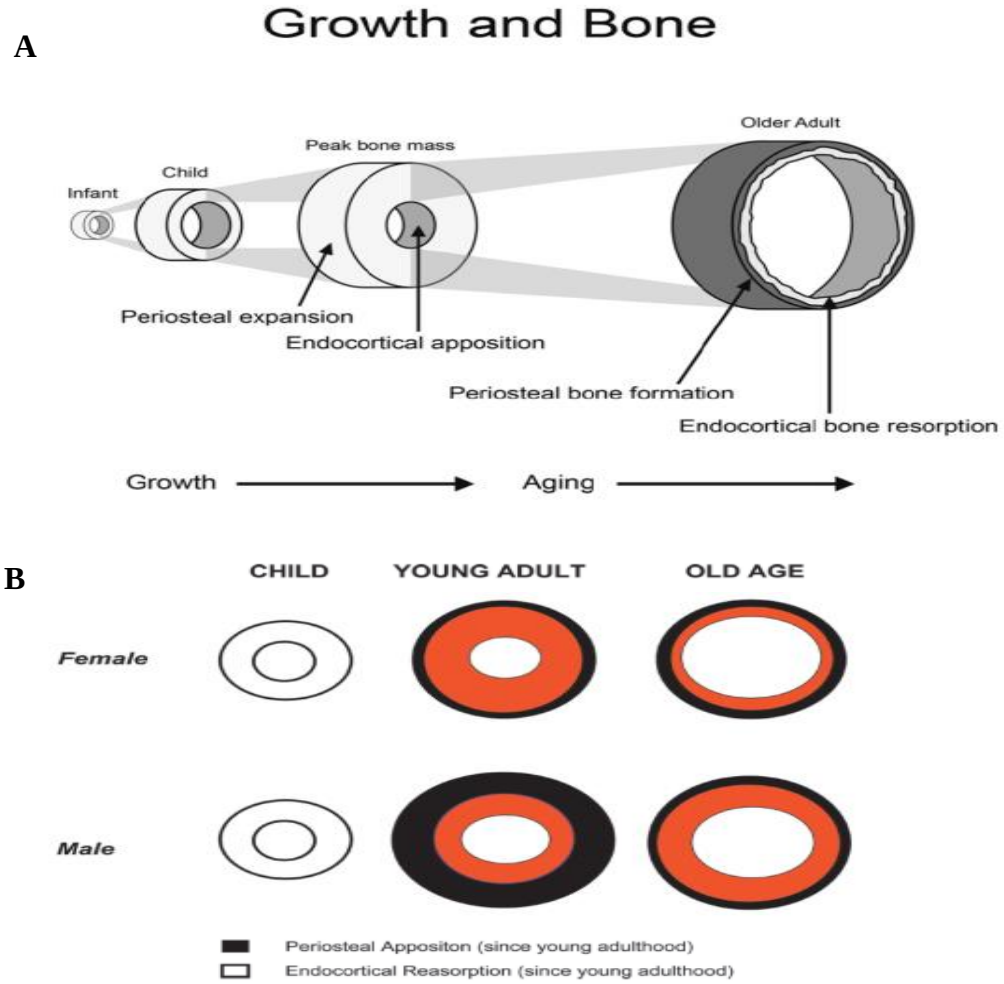
The amount of bone mineral tissue acquired from birth to adulthood follows different age- and sex-specific patterns. These patterns are crucial to understanding the subsequent bone loss that occurs at older ages.

Bone mass develops during childhood from ages 7 to 11. With the onset of puberty and adolescent growth spurts in height and weight, the peak of bone mineral accretion is reached shortly after the peak of height – peak velocity in BMC being attained 0.5 to 1 year after peak height velocity (Weaver et al., 2016; Wang et al., 2005). In fact, in boys of European ancestry the peak bone mineral accretion rate occurs at 12.5 years (± 0.90), and in girls it occurs at 14.1 years (± 0.95; Bailey et al. 1999). BMC accrual occurs on average 1.5 years earlier in girls than in boys due to their earlier sexual maturation (Bailey et al. 1999; Wang et al., 2005). Importantly, between 25% and 50% of the peak bone mass of adulthood is accrued over the 4-year period of the adolescent growth spurt (Baxter-Jones et al., 2011; Pivonka, 2018). In females, this accrued amount represents double the amount of BMC that will be lost during the post-menopausal period from ages 50 to 80 years (Arlot et al., 1997). The bone loss during the same ages is less pronounced in men.

The sex differences in bone strength and size are established during puberty. In boys there is a greater expansion, and periosteal modeling places the cortical tissue further from the axis of the long bones, while in girls the cortical bone mass remains closer to the axis (Schoenau et al., 2002; Seeman, 2001). In addition, girls tend to increase bone formation and

suppress bone resorption at the endocortical surface due to the increased levels of estrogen during puberty (Wang et al., 2004, 2005, 2006). These differences result – in general terms – in better geometry and – in absolute terms – greater bone mass for boys, similar cortical thickness for both sexes, and higher cortical area related to muscle area for pubertal girls (Schoenau et al., 2000; Figure 44).

Figure 44. *Changes in bone structure and geometry throughout the lifespan.*



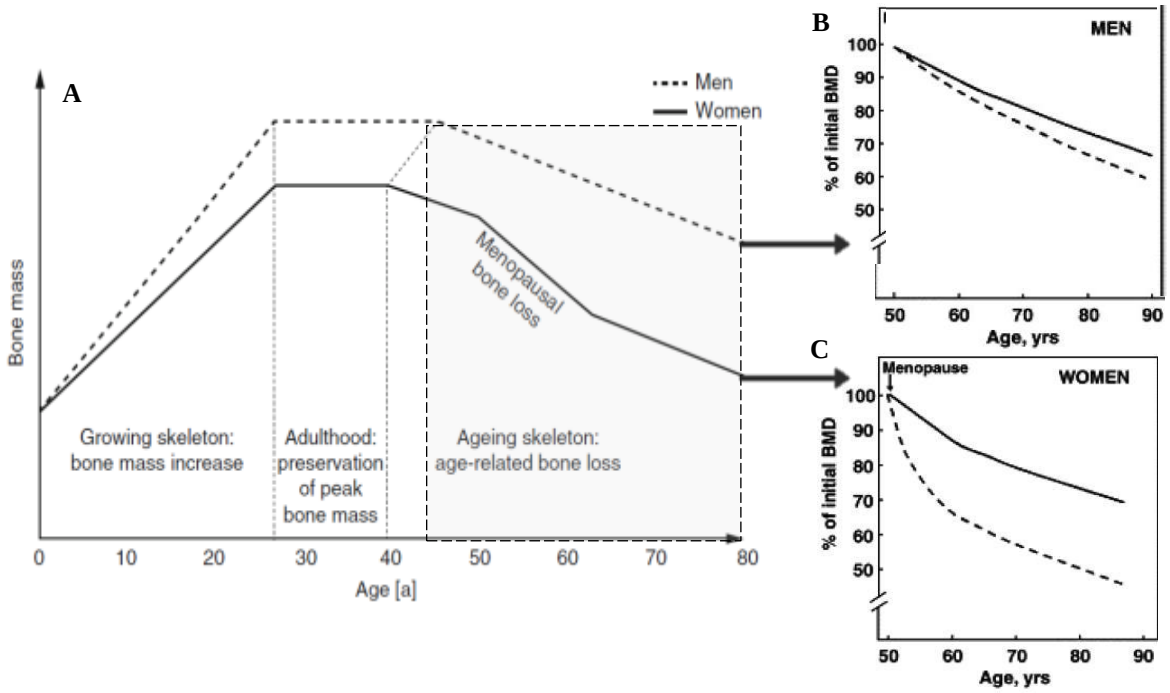
Note. A. Changes in bone structure throughout the lifespan; B. Changes in bone geometry in women and men during the periods of childhood, young adulthood and senescence. Reproduced and adapted from "The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations" (p 1284), by Weaver et al., 2016, *Osteoporosis International*, *27*(4), and from

The peak of bone mass is achieved in men and women during the third decade of life (depending on the specific skeletal site; Bonjour, 1994). Under normal conditions, the process of bone loss in both sexes starts after this plateau in young adulthood from ages 30 to 39 years. Bone loss then begins at relatively slow rates at around the age of 40 (Knaw, 2015), appearing as a decline in aBMD and vBMD of both appendicular and axial bones (Ensrud et al., 1995; Jones et al., 1994; Riggs et al., 2004). The decline in bone mass becomes evident around 50 years of age, and it becomes particularly pronounced in women during menopause, due to bone resorption increases associated with estrogen withdrawal **(**Suominen, 2006). During this period, bone mass losses can range from 0.7% to 1% per year in both sexes. However, pre-menopausal women and especially post-menopausal women can lose up to one to three percent of bone mass per year (Greenspan et al. 1994; Ilich et al., 2014; Mazess et al. 1987). At the older ages (eighth and ninth decades), the rate of bone loss increases again (Ensrud et al. 1995; Riggs et al. 1981). Bone loss in both genders becomes similar at this point (Kelly et al., 2009), although some authors have indicated that the decrease in bone mass is still higher in women in this period of life (Riggs et al., 2004, Figure 45).

Notably, the bone loss process does not occur at the same rate in trabecular and cortical bone tissue. Cortical tissue remains stable in women until menopause, and its stability continues somewhat later in life for men, but it then decrease in both sexes. In fact, the loss of cortical bone is less rapid than the loss of trabecular bone until around the age of 60 (6 to 10 years after menopause), when bone loss becomes more aggressive and continues for the rest of one's life (Clarke & Khosla, 2010). By contrast, the loss of trabecular bone tissue begins as early as the third decade and continues throughout life, with accelerated loss around the time of menopause in women (Khosla, 2013). Thus, women start losing trabecular and cortical BMD more rapidly and earlier than men at around the age of 50 (onset of menopause), which is when women experience a dramatic deficiency of gonadal sex steroid

secretion (Clarke & Khosla, 2010). In absolute terms, the majority of bone loss (70-80%) comes from the cortical compartment (Bala et al., 2015), because about 80% of the skeleton is cortical (Zebaze et al., 2010). However, in relative terms, the loss of trabecular bone is greater than cortical bone (Bala et al., 2015).

Figure 45. *Bone mass across the lifespan.*



Note. A. Bone mass across the lifespan. B. Age-related changes in bone mass in men after 50 years of age C. Age-related changes in bone mass in women after menopause. Reproduced and adapted from "Physiology of bone loss" (p. 15), by Clarke and Khosla, 2010, *Radiologic Clinics, 48* (3).

It has been estimated that between young adulthood and death women lose on average about 50% of their trabecular bone tissue and about 30% of their cortical bone from the whole skeletal system, while men lose roughly 30% and 20%, respectively (Riggs & Melton, 1992). In particular, during women's lives they can lose an average of 58% of bone mass in the femoral neck and 42% in the vertebrae (Riggs et al., 1982). In contrast, the mean bone loss of males only arrives to 38% and 10% in femoral neck and vertebrae, respectively (Riggs

et al. 1982). As can be seen, average decreases in trabecular and cortical BMD at central sites (spine and hip) are greater in women than in men, which is consistent with menopausal-induced increases in bone turnover and bone porosity. However, the bone losses at peripheral sites are quite similar between both sexes (-24% in women and -26% in men; Khosla, 2013).

With aging, net loss in BMD in both men and women is characterized by a high remodeling rate that results in a negative balance and is caused by the osteoclast activity surpassing osteoblast activity (Looker et al., 1998). In addition, with aging the differentiation potential of bone marrow stem cells also decreases due to different factors (Khosla & Riggs 2005). The influence of hormones on age-related bone loss in women and men has been clearly identified and is caused in large part by gonadal sex steroid deficiency (e.g., estrogen deficiency from menopause, testosterone deficiency from andropause, and adrenal androgens deficiency from adrenopause; Clarke & Khosla, 2010; Leboff & Glowacki 1999). Others factors such as vitamin D deficiency, age-associated sarcopenia, and secondary hyperparathyroidism can also play key roles in the bone loss process (Clarke & Khosla, 2010).

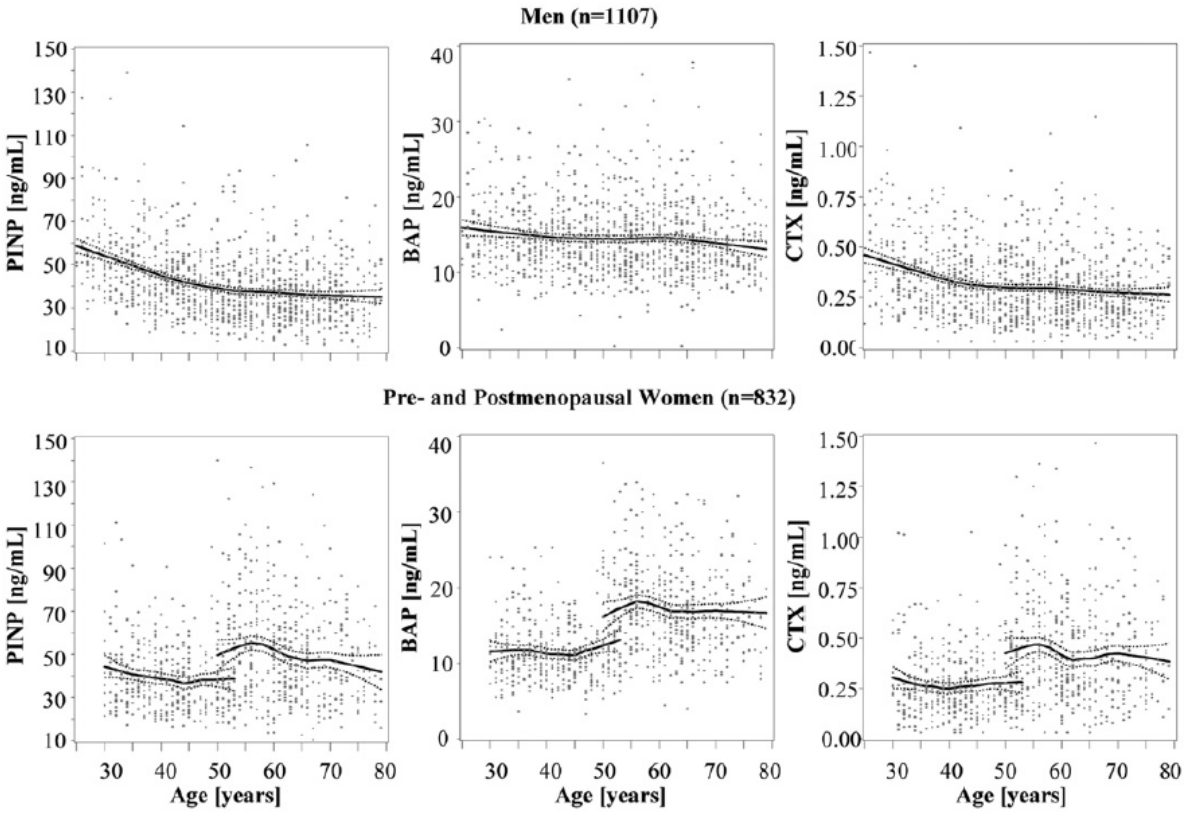
Regarding age-specific typical bone changes, aging is linked to complete loss of trabecular plates, trabecular thinning and loss of connectivity in the case of bones, namely trabecular – vertebrae, distal radius, and tibia **(**Suominen, 2006). In long bones, which are predominantly composed of cortical tissue, aging is manifested in cortical porosity, especially in women, because endocortical resorption begins to exceed periosteal apposition (Semman, 2003). Furthermore, a relevant difference between the aging bone loss process of men and women exists due to women primarily losing bone via decreases in trabecular numbers by complete loss of trabeculae. Men, in contrast, principally undergo trabecular thinning (Khosla, 2013).

The data discussed above shows that postmenopausal and older women are at significantly increased risk of osteopenia, osteoporosis, and fracture than men. The reason is due to the severe effects of menopause on the loss of bone mass, which is evidenced by the fact that 80% of osteoporotic patients are women. In addition, women also present lower levels of muscle mass and strength than men, increasing the risk of falls, fracture, bone loss, and disability. Thus, the management of training programs to prevent bone loss and the adoption of a regular exercise routine as a habit is imperative to women at all stages of life, but particularly after menopause. The need to know what can be the best training program to prevent and treat bone loss in older women drove the development of this PhD dissertation.

ii. Bone turnover markers and aging

There are age and gender specific differences in BTMs during the aging process. After the peak of bone mass has been reached in women under 30 years of age, they then continue to develop higher levels of BTMs (the higher bone turnover rate) between the ages of 30 to 35 years, as they have not yet reached skeletal maturity (Glover et al., 2008; Hu et al., 2013). After this period, all BTMs begin to decrease as age increases until age 44. Next is a time stable concentration until 49 years of age. The levels of the bone resorption marker β-CTx and the bone formation markers PINP, OC, and bALP then increase abruptly due to menopause at 50 years old (in Europe the median age of natural menopause is about 54 years; Hu et al., 2013; Dratva et al., 2009). In women older than 60 years of age, BTMs are relatively stable but begin to show small decreases in concentration after 75 years of age (Michelsen et al., 2013). Thus, serum concentrations of BTMs are markedly higher in postmenopausal women than in premenopausal women. In fact, some authors have reported levels of β-CTX to be 79% to 138% higher in postmenopausal women than in premenopausal women, and levels of OC to be around 37% to 71% higher (Garnero, Grimaux et al., 2009; Iki et al., 2004: Figure 46).

Figure 46. *Age-related changes in bone formation and bone resorption markers in men and women (pre and postmenopausal).*



Note. Reproduced from "Reference intervals for serum concentrations of three bone turnover markers for men and women" (p. 402), by Michelsen et al., 2013, *Bone*, *57*(2).

By contrast, in men the concentrations of BTMs decrease with age, reaching their lower levels at ages 56 to 60 years (Szulc et al., 2001). In the sixth decade of life, the levels of BTMs, particularly the bone resorption marker β-CTx, increase quickly, which is consistent with the findings from the loss of BMD and with the fact that the age of onset of osteoporosis in men is 10 years later than in women (Hu et al., 2013). The reason for later onset could be that men finish growing and achieve the peak of bone mass later than women (Gundberg et al., 2002). Furthermore, the gonadal sex steroid deficiency (andropause) in men occurs around 10 years after the average onset of menopause in women. At older ages BTMs levels stabilize and a plateau appears (Michelsen et al., 2013).

F. Methods to assess bone health

i. Methods to assess bone mineral density

Whilst a number of bone density measuring techniques are available, DXA scans are currently the gold standard of BMD assessment in both research and clinical fields (Hans & Baim 2017; Lewiecki & Binkley 2017; Subramaniam et al. 2018; WHO, 2004). Moreover, DXA scans are the most utilized method to assess bone mass in the vast majority of studies and are the tool used to diagnosis osteoporosis in clinical practice (Blake & Fogelman, 2010; WHO, 2004). In addition, DXA scans can also be considered the gold standard in assessing fracture risk (Hans & Baim 2017; Lewiecki & Binkley 2017; Subramaniam et al. 2018).

DXA was first introduced in the late 1980s and early 1990s (Chun, 2011). It relies on low-dose x-ray technology that assess the attenuation of x-ray beams as they pass through different tissues with varying density (Weaver et al., 2016). A DXA scan creates a 2D projection of bone from a defined area, and thus provides an estimate measure of the BMD in the areal selected: the aBMD (g/cm2) (Beck, 2003; Weaver et al., 2016; WHO, 2004). The DXA technology is ideal because it is rapid (less than 10 minutes), widely available, precise, and safe, as DXA scans deliver only a very low dose of ionization (~0.03 to 15 μSv; Thomas et al., 2005). Furthermore, DXA scans are preferable because other techniques which construct a three-dimensional (3D) image use much higher levels of ionizing radiation (1.5 to 2.5 mSv; Adams, 2009; Krug et al., 2010).

The two most common sites for DXA aBMD assessment are the lumbar spine (L1–L4) and the total hip (Cummings et al., 1993; Johnell et al., 2005; Stone et al., 2003). The femoral neck of the hip is the gold standard measure for the diagnosis of osteoporosis and for the assessment of fracture risk according to the IOF (Kanis et al., 2013). These three axial areas, total hip, femoral neck, and lumbar spine, are preferred over peripheral sites (distal

one-third radius, calcaneus, tibia, finger) for the assessment of aBMD and the risk of fracture according to the WHO and the AACE (Camacho et al., 2016). However, peripheral measurements can also be used when axial sites are not available (Camacho et al., 2016). Possible cases include individuals with whom femoral or lumbar evaluation is not possible or not accurate, patients that are severely obese, or patients that suffer from primary hyperparathyroidism **(**Nuti et al., 2019). Axial sites may also be used when DXA availability is limited, particularly for the assessment of fracture risk that is not for diagnosis or monitoring (Hodgson et al., 2004; Lenchik et al., 2002; Siris et al., 2001). Other body regions, such as Ward's triangle or an individual vertebra, have not been validated for the diagnosis of osteoporosis or fracture risk (Camacho et al., 2016), and are therefore not recommended for use in this aim. The measurement of aBMD at different sites, however, can be useful when the objective is the evaluation and monitoring of a therapy's efficacy.

The accuracy of aBMD DXA readings can be influenced by a variety of factors that need to be taken into account. From a technical point of view, variability in BMD measurements depends on the type of device used (e.g., Hologic DXA or Lunar scanners). Other technical factors include the intra- and inter-observer variability, the technician variability, errors in the use of ethnic-specific or sex-specific databases, failure to carry out appropriate adjustment or recalibration of the software, and the between-center variations (Blank et al., 2006; Camacho et al. 2016; Maghraoui et al., 2006).In addition, inadequate training of the technician in DXA testing and interpretation, failure to exclude extra-skeletal calcifications, inadequate knowledge of how to eliminate fractured vertebrae, positioning errors (of the region of interest as well as the as the patient) or non-adherence of the recommendations of the ISCD to measure at least 2 consecutive vertebrae, particularly after of age of 65 due to interference of extra-skeletal calcifications, osteoarthritis signs or

vertebral fractures after this age, could also influence the accuracy of the DXA results (Camacho et al., 2016; Nuti et al., 2019).

It is important to note that DXA does have some limitations. The 2D technique of DXA implies an inability to measure the depth component of bone, including bone geometry, macro- and micro-architecture, and porosity properties of bone strength, which are independent of aBMD (Augat & Schorlemmer, 2006; Macdonald et al., 2011; Sornay-Rendu, 2007). In addition, one of the major limitations of DXA is that it cannot identify the proportions of cortical and trabecular bone tissue (Kuo & Chen, 2017; Pivonka, 2018).

When aBMD is measured by DXA the variation in bone strength is not fully explained. Current research indicates that despite aBMD being a good predictor of population fracture risk (Kanis et al., 2008), up to 80% of all low-trauma fractures occur in individuals who are not osteoporotic but have normal or reduced BMD (osteopenia; Jarvinen et al., 1999, 2005; Sievanen, 2000), reaching 50% only in women (Nguyen, Eisman et al., 2007). This finding highlights the limitations of DXA to provide information about major determinants in bone strength, such as structure, shape, and size of bone (Griffith & Genant 2008; Kanis et al., 2008; Tawara et al., 2010; Perilli et al., 2012). Another limitation of DXA is its potential to overestimate aBMD because it does not differentiate aBMD from non-bone hyperdensities caused by foreign bodies or from aortic calcifications, which can also be located at the lumbar spine (Adams, 2013).

Despite these limitations and their variable influence on the results, DXA is still the preferred imaging technique to assess aBMD, estimate fracture risk, and to diagnose osteoporosis. The reason for this preference is that aBMD assessed by DXA linearly correlates and accounts for 60% to 70% of bone strength (Adams, 2013; Bouxsein et al., 1995; Lotz et al., 1991). Moreover, the overall reproducibility of DXA measurements has

been tested successfully with phantom measurements (Shepherd et al., 2005). For these reasons, DXA technology was the method selected for the studies performed in this PhD dissertation assessing the aBMD of the lumbar spine and hip.

Several other techniques are available for measuring BMD at different skeletal sites. These techniques include single-energy x-ray absorptiometry (X-ray), radiographic absorptiometry, dual photon absorptiometry, quantitative ultrasound (QUS), MRI, QCT for hip and spine, peripheral quantitative computed tomography (pQCT) for tibia and radius, and high resolution pQCT (HR-pQCT; Camacho et al., 2016; Pivonka, 2018).

Recently, 3D imaging techniques, such as MRI and the different modalities of computed tomography, provide supplementary information of bone strength and make it possible to assess bone quality (microarchitecture and geometry). For example, QCT provides the vBMD (g/cm3) measurement of trabecular and cortical compartments; identifies the 3D geometry of the bone (e.g., total bone area, periosteal and endosteal circumference); gives the structural strength in bending, compression, and torsion (e.g., cross sectional moment of inertia, section modulus, strain–strength index, axial–strength index); and portrays the micro-architecture of the bone tissue. The information from a QCT thus gives a more accurate and holistic estimation of bone strength (Bandirali et al., 2015; Baum et al., 2013; Johnston et al., 2014; Krug et al., 2010; Weaver et al., 2016). Other parameters such as medullary volume and cross-sectional area could be obtained by QCT to better assess the quality of bones (Black et al., 2008). Newer HR-pQCTs allow for better understanding of the microstructure level of the bone, as well as the cortical porosity and the trabecular plate (e.g., trabecular thickness and trabecular numbers; Adams et al., 2014; Pivonka 2018). HR-pQCTs also provide a high-resolution 3D image using a relatively low radiation dose (3 to 5 μSv) compared to total body QCT scans (Geusens et al., 2014).

Among the rest of the methods, QUS is the most applied technique, along with MRI and pQCT, for examining bone condition and fracture risk. Notably, QUS was the first technique to not use ionizing radiations (Conversano et al., 2015; Kuo & Chen, 2017; Pisani et al., 2014). This technique provides the parameters of speed and attenuation, which are indirect indices of structural integrity and bone mass. However, as it does not represent a direct measurement of BMD, QUS cannot be used for the diagnosis of osteoporosis (Nuti et al., 2019).

All of the imaging techniques still have some limitations, such as high cost, limited accessibility, bulky equipment and lack of diagnostic cutoff points that impede their use in common research and clinical settings.

ii. Methods to assess bone turnover rate

For assessing the turnover rate of bones, bone histomorphometry is the gold standard. However, bone histomorphometry is an invasive technique. It also requires a laboratory specialist's interpretation, and it cannot be used many times in the same individual (Eastell et al., 2018). Other techniques, such as calcium balance or tracer kinetic, can also be applied to analyze bone turnover, but they use radioisotopes, which are time consuming, and a specialist is still necessary for interpreting the results (Eastell et al., 2018).

The appearance of BTMs for assessing bone turnover rate has brought a great change in the field. Due to this new method, results can be analyzed and interpreted by non-specialist health-care professionals. The method is inexpensive. It can be applied in a large population, and it can be conducted using easily accessible samples (blood or urine; Eastell et al., 2018). In addition, BTMs have been validated in both healthy and osteoporotic individuals against gold standard methods, such as bone histomorphometry and tracer kinetics (Eastell et al., 1988; Eastell et al., 1997).

A variety of automated and manual assays are available for the analysis of BTMs in research and clinical purposes. These assays include RIA, immunoradiometric assay (IMRA), EIA, chemiluminescent immunoassay (CLIA), electrochemiluminescence immunoassay (ECLIA), ELISA, and HPLC (Rathnayake et al., 2020; Shetty et al., 2016). The assays' inter- and intra-assay variability is usually low, with the coefficient of variance (CV) typically within 5% to 10% (Eastell et al., 2018; Lemming et al., 2006). Of all the assays, ELISA is the most widely used. Automated standardized assays are the methods recommended by international organizations due to intra- and inter-assay CVs being lower when automated immunoassays are used (Maet et al., 2016; Rathnayake et al., 2020; Shetty et al., 2016; Zhang et al., 2015; Zhao et al., 2011).

G. Exercise-related effects on bone health

Currently, pharmaceutical agents targeting BMD continue to be the standard therapy treatment for low bone mass. Pharmaceutical agents are used because they can reduce the risk of fractures by approximately 20% to 60%, depending on the drug used. Agents with bisphosphonates are seen as the first line of treatment (Rachner et al., 2011). Despite the strength of evidence in favor of pharmaceutical treatments, their potential side effects after long-time use, such as upper gastrointestinal effects or osteonecrosis of the jaw (Daly, Dalla Via et al., 2019; Kennel & Drake, 2009; Miller & Derman, 2010), high cost, poor adherence, and low long-term compliance (Kothawala et al., 2007; Rabenda et al., 2008) make the identification of non-pharmacological therapies necessary for osteoporosis prevention and treatment. In fact, a panel of experts has recently highlighted a crisis in the treatment of osteoporosis because both adherence and prescription to pharmacotherapy agents have decreased in recent years, corroborating the need for new therapies (Khosla & Shane, 2016).

Additionally, drug treatments have no effects on other key risk factors for fractures, such as weak muscle strength and power, reduced balance or coordination joint flexibility

agility, and limited overall functional performance. In the last years exercise training has emerged as an effective alternative to drug treatments in the improvement of bone strength. Moreover, exercise training is the only strategy that can also improve all modifiable fracture risk factors, especially in postmenopausal and older women (Daly, Giannoudis et al., 2019; Kemmler et al., 2015).

Over the last four decades, epidemiological and clinical trial research has been examining the effect of exercise training programs to attenuate the decline of bone mass in advancing age (Ayalon et al., 1987; Bembem et al., 2000; Bilek et al., 2016; Brentano et al., 2008; Daly et al., 2020; Kemmler et al., 2012; Nelson et al., 1994). In general, evidence suggests that regular physical activity has a positive osteogenic response on bones (Kannus et al., 1995; Welten et al., 1994).

It is important to note that not all forms of exercise have the same positive effects on BMD. Because of this fact, studies that have evaluated the role of exercise programs on bone-related variables in elderly people have obtained conflicting results. For example, prolonged aerobic training activities, such as swimming, cycling, and walking, are commonly known for their beneficial effect on all body systems. In the case of the bone system this common belief is incorrect. Empirical evidence suggests that none of the prolonged aerobic activities provide enough stimulus to create bone (Martyn-St James & Carroll, 2008b; Rector et al., 2008; Taaffe et al., 1995). As recently highlighted in a meta-analysis of intervention studies in pre- and postmenopausal women (Borer et al., 2007), the problem is that these low-impact non-weight-bearing exercises, especially regular walking and swimming, are still frequently prescribed to prevent osteoporosis (Hong & Kim, 2018). Despite their benefits on cardiometabolic factors and aerobic fitness, they produce insufficient stimulus to optimize bone strength. Notwithstanding, other physical exercises, such as multi-directional weight-bearing and moderate- to high-impact activities (hopping, jogging, jumping), progressive

resistance exercise (alone or in combination with other activities) have been shown to maintain and improve the aBMD in postmenopausal women and older adults (Allison et al., 2015; Bailey et al., 2010; Beck et al., 2017; Marques, Mota, Machado et al., 2011). Among these other sports, resistance training and combined exercises seem to be the most promising interventions to maintain or increase aBMD in this population (Hong & Kim, 2018; Howe, Shea et al., 2011; Shojaa et al., 2020; Zehnacker et al., 2007; Zhao et al., 2015).

A number of reviews, systematic reviews, and meta-analyses have been conducted on exercise's effects on aBMD in different sites of older adults (Benedetti et al., 2018; Cadore et al., 2005; Gómez Cabello et al., 2012; Guadalupe-Grau et al., 2009; Hong & Kim, 2018; Jepsen et al., 2017; Kemmler et al. 2017; Lau et al., 2011; Marin-Puyalto et al., 2018; Marques, Mota & Carvalho, 2011; Mcmillan et al.,2017; Merriman et al., 2009; Nickander et al., 2010; Nordstrom & Hogstrom, 2011; Simas et al., 2017; Slatkovska et al., 2012; Souza et al., 2020). The vast majority of these trials have been conducted in postmenopausal and older women due to their higher prevalence of osteopenia and osteoporosis. This fact makes it possible to find numerous systematic reviews and meta-analyses that have investigated the effects of different types of exercise on bone strength in this population segment (Berard et al., 1997; Bonaiuti et al., 2002; Borer, 2005; Daly, Dalla Via et al., 2019; Dionello et al., 2016; Fratini et al., 2016; Hamilton et al., 2010; Howe, Shea et al., 2011; Kelley, 1998, 2002, 2006, 2012; Kim et al., 2016; Lee et al., 2007; Liu et al., 2017; Ma et al., 2013; Ma, Liu et al., 2016; Martyn-St James & Carroll, 2006, 2008a, 2008b; Marín-Cascales, Alvaraz, Ramos-Campo & Rubio-Arias, 2018; McMahon et al., 2017; Oliveira et al., 2016; Polidoulis et al., 2011; Rahimi et al., 2020; Rutherford et al., 1999; Sañudo et al., 2017; Schmitt et al., 2009; Segev et al., 2018; Shojaa et al., 2020; Sun et al., 2016; Wallace & Cumming, 2000; Wayne et al., 2007; Wolff et al., 1999; Xu et al., 2016; Zehnacker et al., 2007; Zhao et al., 2015; Zhao, Zhang & Zhang, 2017).

Results in general confirm that exercise may have a positive influence on the skeletal system by increasing or at least maintaining aBMD at different sites. Benefits depend on the type of exercise. Aerobic or ground reaction forces exercises include four different weight-bearing exercises: high-impact loading exercises (vertical jumping, rope jumping, fast running, etc.), low-impact loading exercises (slow jogging, walking, etc.), odd-impact loading exercises (step or aerobic classes, bounding, agility exercises, etc.), and combined loading exercises (impact exercises mixed with strength/resistance training); resistance, strength training, or power training alone, also called joint reaction force exercises; whole body vibration exercises, aquatic exercises, Tai-chi, combined (usually weight-bearing exercises plus strength training), and multi-component exercises (usually weight-bearing exercises, strength training and balance or flexibility). The parameters of the applied exercise regimen [intensity (low, moderate, high), repetitions, sets, rest, number of exercises, frequency of exercise sessions (≤ 2 or more than two), duration of exercise sessions (10 to 90 min), the level of bone mass of subjects (normal, low or very low), the length of the training period (short: <6 months; medium: six to 12 months, or high: > 12 months), the bone site measured (lumbar spine, femoral neck, trochanter, whole body, total hip), the compliance of the subjects with the training program, the statistical analysis performed and the years after menopause (early or later post-menopausal women) lead to contrasting results (Berard et al., 1997; Howe, Shea et al., 2011; Kelley et al., 2002; Kim et al., 2016; Marques, Mota & Carvalho, 2011; Martyn-St James & Carroll 2008a, 2008b; Rahimi et al., 2020; Souza et al., 2020; Wallace & Cumming, 2000; Zhao et al., 2015).

Kelley et al. (2012) have shown that different reaction force exercises can improve lumbar spine aBMD and femoral neck BMD in postmenopausal women (standard mean difference [SMD] for lumbar spine: 0.179; 95% CI = -0.003 to 0.361; SMD for femoral neck: 0.208; 95% CI = 0.102–0.474). However, Nikander et al. (2010) did not find any significant

effects of exercise on bone strength from any training program. Marques, Mota and Carvalho (2011), in contrast, found that exercises significantly increased femoral neck BMD and lumbar spine BMD in older women (weighted mean differences [WMD] for femoral neck: 0.014; 95% CI = 0.003 to 0.025); WMD for lumbar spine: 0.012; 95% CI = 0.002 to 0.022). Nonetheless, in the meta-analysis by Lau et al. (2011) the authors found no significant effects of whole-body vibration exercises in older women.

In one of the most complete Cochrane Reviews in the field, Howe et al. (2011) reported that, in general, exercise improved trochanter BMD (SMD: 1.03; 95% CI = 0.56 to 1.49) and lumbar spine (SMD: 0.85; 95% CI = 0.62 to 1.07) in healthy postmenopausal women. Regarding ground or joint reaction force exercise, the study showed a statistically significant difference of exercise minus control group benefit of 0.85% in lumbar spine BMD, but no significant change in femoral neck BMD (-0.08%). This review also suggested that a combination of different types of exercise had a significant effect on BMD at the lumbar spine, femoral neck and trochanter. Howe et al. (2011) also found that jumping, jogging and whole-body vibration had a significant effect on BMD at the trochanter and total hip compared to the control groups. They also observed that Tai chi and walking had a significant effect on BMD at the spine and wrist compared to the control groups. In addition, the authors found that resistance exercise had a significant effect on BMD at the femoral neck and lumbar spine compared to the control groups.

A meta-analysis by Martyn-St James & Carroll (2008a) also observed that exercise programs of combined exercises (resistance training plus low impact) had the capacity for preserving BMD at the lumbar spine and femoral neck in postmenopausal women. Although the overall relative change in lumbar spine was small (0.011 g/cm^2), it was in accordance with previous reviews of the lumbar spine in this population and also in the femoral neck (Martyn-St James & Carroll 2006, 2008b; Wallace & Cumming, 2000).

A meta-analysis of the effects of high-intensity resistance exercise in postmenopausal women found a statistically significant benefit of 0.006 g/cm^2 in lumbar spine BMD and a nonsignificant benefit of 0.010 g/cm^2 in femoral neck BMD (Martyn-St James & Carroll, 2006). Moreover, other meta-analyses found that physical activity did not increase femur BMD significantly among postmenopausal women (Kelley & Kelley, 2006, 2009). The meta-analyses did find statistically significant benefits of high-intensity resistance exercise for femoral neck and lumbar spine aBMD in females 60 years of age and older. However, the amount of this new bone accretion was observed to differ between meta-analysis: 0.004 g/cm^2 for femoral neck BMD (Martyn-St James & Carroll, 2008b); 0.014 g/cm^2 and 0.012 g/cm^2 for femoral neck and lumbar spine aBMD, respectively, (Marques, Mota & Carvalho, 2011).

Current clinical guidelines for the prevention and management of bone loss recommend exercise training as an effective approach to improve, maintain, or slow bone loss in postmenopausal and older women (Beck et al., 2017). Nonetheless, as can be seen through the results of different reviews and meta-analysis mentioned above, not all quantities or types of exercise training are equally effective for eliciting a positive bone response. In addition, the application of the osteogenic exercises principles obtained from animal studies to human beings is not a trivial task, and sometimes the principles have not been correctly applied or many confounders' variables have affected the results. As a result, the optimal amount and modality of exercise required to strengthen bones for postmenopausal and older women are yet to be fully validated. The next sections summarize the basic osteogenic exercise principles and the current evidence of the effects of different exercise intensities and modalities on the bone health on the population studied in the present PhD dissertation.

i. Mechanism for exercise-induce bone mass

The current understanding of the most important loading characteristics necessary to stimulate an adaptive bone response has been informed mainly from several in vivo loading studies of animal bones. The studies included models of axial loading of the rat ulna (Torrance et al., 1994), four-point bending of the rat tibia (Turner et al., 1991), ground based vibrations (Rubin, Turner et al., 2001; Rubin, Xu & Judex 2001; Rubin et al., 2002), and functionally isolated avian ulna (Rubin & Lanyon, 1984). In addition, excellent reviews have been published on the mechanisms that mediate the bone adaptive responses to changes in loading (Lee & Lanyon, 2004; Rittweger, 2007; Rubin et al., 2006; Scott et al., 2008). All of this evidence has shown that skeletal response to loading is modulated and governed by the following fundamental components:

1. Type of strain: dynamic loading is associated with increased bone remodeling (Hert et al., 1971; Lanyon & Rubin, 1984; Robling, Duijvelaar et al., 2001), whereas static loading provides little adaptive stimulus to bone adaptation (Hert et al., 1969, 1971; Rubin & Lanyon, 1984; Turner et al., 1996).

2. Strain magnitude: bone is most responsive to physical activities that are moderate to high in load magnitude (O'Connor et al., 1982; Rubin & Lanyon, 1985; Turner & Robling, 2003). The strain magnitude is the most important component in triggering an osteogenic response to mechanical loading (Shi et al., 2017). Studies have found that higher loads are necessary to stimulate more new bone tissue, while lower loads were found not to be osteogenic due to their low magnitude loads (Duncan & Turner, 1995; Khan et al., 2000; Robling et al., 2002). The loads or strains applied to bone via gravitational (e.g., impact with the ground when jumping or tumbling) or muscle forces (e.g., muscle contractions in resistance training or racquet sports) must exceed a threshold determined by the habitual strain range from the daily activities, as Frost's mechanostat theory describes (Frost, 1987).

3. Strain rate: In animal studies, it has been thought that osteogenesis is evocated when mechanical loading is applied rapidly (Hert et al., 1971; Lanyon & Rubin, 1984; Robling, Duijvelaar et al., 2001; O'Connor et al., 1982; Rubin & Layon, 1985; Turner & Robling, 2003). According to this assumption, strain rate would play an important role in the adaptive remodeling bone response (Hsieh & Turner, 2001), as it would be one of the major contributors to the adaptive osteogenic response. In fact, it has been demonstrated that increasing strain rate (from -0.018 to -0.100 s-1) increases bone formation (Mosley & Lanyon, 1998; Turner et al., 1995). Moreover, the formation of new bone tissue is directly proportional to the rate of strain on bone tissue (Turner et al., 1995). The effect of applied high strain rates can stimulate the formation of both cortical and trabecular bone (Meakin et al., 2013, 2014; Rubin, Turner et al., 2001; Rubin, Xu & Judex 2001; Rubin et al., 2002; Saxon et al., 2011; Sugiyama et al., 2012). Consequently, exercises that involve high impact weight bearing activities, such as jumping or resistance training at high velocities (power training), are better at increasing the bone formation because these activities produce higher strain rates than isometric, normal velocity isotonic resistance exercise or walking. Unfortunately, high impact exercises in some clinical circumstances, such as osteoarthritis or in frail elderly subjects, are difficult to apply. Strength exercises performed at maximal velocity are a good alternative in the concentric phase.

4. Strain frequency/number of loading cycles/strain duration of bouts/rest periods: studies have shown that fewer loading cycles can elicit an adaptive skeletal response if an adequate load intensity is achieved (Forwood & Turner, 1994; Rubin & Layon, 1984, 1987; Umemura et al., 1997). For example, with adequate load intensity, only four loading cycles per day are needed to prevent the bone loss caused by immobilization (Rubin & Layon, 1984). The results of different animal studies have shown that the osteogenic response to mechanical loading is not increased when a loading regimen was lengthened from 36 to 1800

consecutive cycles per day in an isolated avian bone (Rubin & Layon, 1987). In addition, studies have found that dividing 360 loading cycles into four bouts of 90 cycles or six bouts of 60 cycles per day enhances the osteoblastic response (Robling et al., 2000, 2002). The osteoblastic response was observed to be enhanced by 80% when compared to one bout of 360 cycles per day (Robling et al., 2002). In fact, after 16 weeks the group in the study that received 4 bouts of 90 cycles per day had significantly greater bone strength when compared to those who received a single session of 360 cycles (Robling et al., 2002). Moreover, bone cells have been observed to need eight hours of recovery time to return their full responsiveness (Rubin, Xu & Judex et al., 2001). Nonetheless, some authors have found that inserting only a 10- to 15-second rest period between loading cycles optimizes the bone formation response when compared to no rest period (LaMothe & Zernicke, 1985; Robling, Burr & Turner, 2001; Srinivasan et al., 1985; Saxon et al., 1985). Thus, compared with an uninterrupted and long single bout of loading, intermittent short bouts of loading separated by periods of rest or several hours of rest have been found to trigger a greater osteogenic response (Robling et al., 2000, 2002; Rubin, Burr & Turner, 2001; Rubin & Lanyon, 1985; Rubin et al., 2002, 2011; Turner & Rubling, 2003). This situation occurs because bone cells are desensitized to repetitive mechanical loading, and they "accommodate" or adapt very quickly to loading stimuli, but sensibility returns after a period of rest (Burr, et al., 2002; Lanyon, 1996; Pivonka, 2018).

5. Strain distribution or direction: bones can be physiologically loaded in different directions as mentioned in the previous section. To create new bone tissue, loads that are applied in unusual or diverse loading directions or patterns (e.g., multidirectional movements) have more osteogenic potential compared with linear or customary patters of loading (e.g., running or cycling; Lanyon, 1996, Rubin & Lanyon, 1985). As with strain frequency, it is

necessary to have irregular strain distributions due to the diminished response of bone cells in response to continual loading.

6. Duration of bone-strain training period: it is necessary take into account that the typical bone remodeling cycle lasts around three to eight months. Therefore, the response of bone to loading is slow. Although it has been suggested that interventions last a minimum of 6 to 9 months, and preferably 12 to 24 months, to detect any measurable physiological skeletal changes beyond the normal bone remodeling transient, many short-term and long-term studies where measurements were made before 6 months of intervention have confirmed positive changes in bone tissue (Beverly et al., 1989; Dornemann et al., 1997; Lohman, Goinh et al., 2009; Pruitt et al., 1992). In addition, due to the principle of cellular accommodation of the bone cells, several exercise interventions that lasted over 12 to 18 months found the greatest changes occurring in aBMD during the initial 5 to 6 months of the intervention (Bassey & Ramsdale, 1994; Lohman, Goin et al., 2009). Other studies, however, have found a linear increase of aBMD with continued exercise training during a long training period (Heinonen et al., 1996; Winters & Snow, 2000). Overall, results of the studies may have been influenced by a range of factors, such as the frequency of training sessions, the intensity of loading, the specificity of skeletal loading, participants' hormonal status, the baseline values of aBMD of the subjects, the type of BMD scans performed, and whether the exercise program followed the progressive overload principle or not (Beck et al., 2017; Daly, Gianoudis et al., 2019; Harding et al., 2017; Hong & Kim, 2018; Shi et al., 2017; Turner et al., 2005; Weaver et al., 2016).

7. Site-specific adaptations: the response to mechanical loading of bone is not systemic but rather site-specific, meaning the response depends on where the load is applied (Daly, Dalla Via et al., 2019; Pivonka, 2018). This characteristic is based on the "use it or lose it" principle that governs human physiology. In the case of bone physiology, this means

that bone strength is reinforced by the loads applied through exercise or movement and is reduced by disuse. This phenomenon has been demonstrated by different retrospective studies that analyzed extreme physical conditions. For example, astronauts lose up to 2% of hip BMD each month that they are in microgravity (Lang et al., 2004). Conversely, professional tennis players can have up to 35% more BMD in their dominant arm than in their non-dominant arm (Jones et al., 1997). Without going to these extremes, a study found that postmenopausal women who had performed a 2-year back extension strengthening exercise program achieved greater spinal BMD and fewer vertebral fractures in the subsequent 8 years compared to the control group (Sinaki et al., 2002). Notably, Kerr et al. (1996) found that after 12 months, only the strength group who performed three sets of 8 RM in their study achieved significant increases in BMD on the side that the exercising intervention was applied (resistance exercise intervention was only applied to one side of the body) compared with the non-exercised side in postmenopausal women (trochanter [exercise 1.7%, non-exercise -0.6%]; Ward's area [exercise 2.3%, non-exercise 0.8%], intertrochanteric hip site [exercise 1.5%, non-exercise -0.1%], and the ultradistal radius site [exercise 2.4%, non-exercise -1.4%)]). Similarly, a high impact jumping exercise intervention performed in post-menopausal women was found to improve proximal femur, but not lumbar spine BMD after 12 months (Welsh & Rutherford, 1996).

Prescription of exercise must include targeted activities that load the most common skeletal fracture sites, the hips, spine, and wrist, to prevent fracture risk and increase bone accretion in these specific sites. The exercises can elicit bone accretion through direct (via gravitational force) or indirect (via muscle contraction) ways. Weight-bearing exercises will usually have greater effects on hip regions, while a combined, or multi-component, training program elicits higher benefits on lumbar spine (Bolam et al., 2013; Martyn-St James & Carroll, 2008a).

8. Age-specific adaptations: bone becomes less sensitive to mechanical loading after skeletal maturity (Hong & Kim, 2018). Consequently, the skeletal system is less responsive to mechanical exercise loads in adulthood and old age than in childhood (Kontulainen et al., 2003). Particularly, the ability of cells to respond to mechanical stimuli decreases with aging (Shi et al., 2017). In the elderly, osteoblast are less sensitive to mechanical loads, bone remodeling is less frequent, and the threshold for achieving bone formation in response to exercise strains are increased (Donahue et al., 2001; Lieberman et al., 2003; Turner et al., 1995; Vidal et al., 2003). However, considering the evidence to date, despite the lower sensibility of bone cells, physical exercise is still a significant activity in the production of new bone tissue.

Evidence indicates that to be osteogenic loading must be 1) dynamic not static, 2) induce moderate to high magnitude strains, 3) applied at high rates or quickly, 4) applied in relatively short bouts separated by periods of rest, 5) unusual and not customary, 6) applied during moderate to long training periods, 7) involve muscles that include the most common skeletal fracture sites – the hips, spine and wrist, 8) increase at advanced ages. Collectively, these characteristics, or principles, of mechanical bone adaptation must be considered when prescribing physical exercise for the prevention of bone loss (Beck et al., 2017).

However, we cannot forget that any given exercise program is characterized by selected parameters and must follow basic training principles to have an impact on designated aims. Most of the bone loading characteristics previously cited are regulated by an exercise's parameters. Thereby, the strain type of exercise will be regulated by the type of exercise selected (movement or static). The strain magnitude will be associated with the absolute and relative intensity (degree of voluntary failure or exercise perception) of training. The strain rate will be determined by the movement velocity. The number and frequency of loading will be regulated by the number of repetitions and sets, the time under tension, the rest periods,

the exercise frequency sessions, and the duration of the exercise session. The strain direction will be associated with the type of exercises selected (multi-directional or constant). Last, the site-specific adaptation will also be associated with the exercises chosen (e.g., weight bearing, resistance training, combined exercise).

The ACSM has recommended that general training principles also be considered when designing any exercise program to improve bone health (Kohrt et al., 2004). Daly and colleagues mentioned (Daly, Dalla Via et al., 2019) five key principles to take into account: 1) the principle of specificity (related with the site-specific and type of strain characteristic of bone loading); 2) the principle of progressive overload (related with the bone loading characteristics of magnitude, rate, frequency, duration, rest periods, and strain distribution); 3) the principle of reversibility (related with duration and strain rate) which indicates that bone adaptations will be progressively lost once the exercise program or the stimulus is over but with a minimal exercise dose can maintain initial exercise-induced skeletal gains. Exercise acts as a double-edged sword, it helps to model or remodel bone tissue, but once the exercise stimulus stops, the bone will suffer accelerated bone loss; 4) the principle of diminished returns (related with duration of strain and training program, and also with principles of progressive overload and initial values) which indicates that gains in bone mass, after the initial adaptations, are likely to be modest and slow if the loading regimen remains stable; 5) the principle of initial value which states that the greatest changes in BMD in response to exercise loading will usually occur in individuals with the lowest levels of BMD at the beginning of the training program. In addition, bone adaptive response also depends on other systemic and local factors, such as the levels of vitamin D or calcium and cytokines or paracrine changes, which should be considered (Frost, 2003; Rittweger, 2007; Rosen, 2008; Skerry, 2006).

Although physical activity contributes to increased bone strength in older adults, our understanding of how different exercise parameters can modulate the osteogenic response in human beings in general and, more particularly, in later postmenopausal women and older adults is still incomplete.

ii. Resistance training, variable resistance training, and bone health

- *Effects on areal bone mineral density*

Over the last 40 years strength training has been one of the most frequent types of exercise programs applied. Many studies have therefore focused on strength training's effects on bone status, and more than 50 studies analyzing a resistance training protocol in postmenopausal and older women have been published (Adami et al., 1999; Ayalon et al., 1987; Bassey & Ramsdale 1995; Beavers, Beavers et al., 2017; Bembem et al., 2000, 2010, 2011; Bilek et al., 2016; Bocalini et al., 2009; Borba-pinheiro et al., 2016; Bunout et al., 2001; Candow et al., 2019; Chilibeck et al., 2002, 2015; Cussler et al., 2004; De Oliveira et al., 2018; Duff et al., 2016; Daly et al., 2005; De matos et al., 2009; Fjeldstad et al., 2009; Hartard et al., 1996; Hawkins et al., 2002; Heikkinen et al., 1997; Holm et al., 2008; Humphries et al., 2000; Huovinen et al., 2016; Ilinca et al., 2010; Karaarslan et al., 2010; Kemmler et al., 2005; Kerr et al., 1996, 2001; Liu- Ambrose 2005; Maddalozzo & Snow, 2000; Maddalozzo et al., 2007; Nelson et al., 1994; Nichols et al., 1995; Nicholson et al., 2015; Orsatti et al., 2013;Pruitt et al., 1995; Revel et al., 1993; Rhodes et al., 2000; Ryan et al., 1998; Sinaki, 1998, 2002; Smidt et al., 1992; Stengel et al., 2005; Taaffe et al., 1996, 1999; Uusi-Rasi et al., 2015; Verschueren et al., 2004; Vincent & Braith et al., 2002; Watson et al., 2015; Woo et al., 2007; Zaki, 2014;). If we take into account the articles that include other modes of exercise along with resistance training in the same exercise session (combined exercise), it brings the number of studies to more than a hundred (Bebenek et al., 2010;

Bergstrom et al., 2008; Bolton et al., 2012; Bravo et al., 1996; Brentano et al., 2008; Chilibeck et al., 2013; Choquette et al., 2011; Chow et al., 1987; Chuback et al., 2006; De Jong et al., 2004; Engelke et al., 2006; García-Gomariza et al., 2018; Heinonen et al., 1998; Iwamoto et al., 1998; Iwamoto et al., 2001; Kerr et al., 2001; Kemmler et al., 2003, 2004, 2012, 2014; Kemmler, von Stengel, Bebenek et al., 2011; Kemmler, von Stengel, Engelke, Häberle , Mayhew & Kalender, 2010; Kohrt et al., 1995, 1997, 1998; Lau et al., 1992; Lynch & Judge, 1992 ; Marques, Mota, Machado et al., 2011; Miliken et al., 2003; Prince et al., 1995a, 1995b, 1995c; Shaw, 1998; Snow et al., 2000; Svendsen et al., 1993; Villareal et al., 2003; Villareal et al., 2004; Watson et al., 2018).

Due to the high amount of evidence around resistance training on this population, in the last 15 to 20 years many reviews, systematic reviews, and meta-analysis have been published about the effects of strength training on bone strength in postmenopausal women (Berard, 1997; Bonaiuti et al., 2002; Borer, 2005; Daly, Dalla Via et al., 2019; Hamilton et al., 2010; Howe, Shea et al., 2011; Kelley, 1998, 2002, 2006, 2012; Kim et al., 2016; Kistler-Fischbacher et al., 2021a; Kistler-Fischbacher et al., 2021b; Martyn-St James & Carroll, 2006, 2008a; Polidoulis et al., 2011; Rahimi et al., 2020; Rutherford, 1999; Sañudo et al., 2017; Schmitt et al., 2009; Segev et al., 2018; Shojaa et al., 2020; Wallace et al., 2000; Wolff et al., 1999; Xu et al., 2016; Zehnacker et al., 2007; Zhao et al., 2015, Zhao, Zhang & Zhang, 2017). Reviews, systematic reviews, and meta-analysis have also been published about the effects of strength training on bone strength in older adults (Benedetti et al., 2018; Cadore et al., 2005; Gómez-Cabello et al., 2012; Guadalupe-Grau et al., 2009; Hong & Kim, 2018; Kemmler et al., 2017; Nickander et al., 2010; Nordstrom & Hogstrom, 2011; Marques, Mota & Carvalho, 2011; Mcmillan et al., 2017; Souza et al., 2020).

Although progressive resistance training is perhaps the most widely researched exercise modality targeting the preservation of BMD in older adults and postmenopausal

women, there are inconclusive results at different skeletal sites. This heterogeneity can likely be attributed to the wide variance in exercise protocols, including methods of exercise progression, frequency, intensity, number of sets and repetitions, modes of delivery (e.g., group or individual; at home or a gym), supervision, devices, combined exercise or resistance training alone, and duration of training period. Other variance influences can be allotted to study populations, such as inadequate samples sizes, healthy postmenopausal women with normal BMD or at risk of osteoporosis development, older adults with functional deficits, and compliance of subjects. Finally, methods and sites of BMD assessment applied may also affect results (Daly, Dalla Via et al., 2019; Giangregorio, 2016; McMillan et al., 2017; Shojaa et al., 2020; Zhao et al., 2015).

In general, the findings from these reviews and meta-analyses of controlled trials indicate that the majority of resistance training studies show beneficial effects to bone density during aging. The reviews and meta-analyses conclude that resistance training has potentially modest beneficial effects for reducing postmenopausal bone loss at the femoral neck and lumbar spine regions (Benedetti et al., 2018; Bonaiuti et al., 2002; Gómez-Cabello et al., 2012; Guadalupe-Grau et al., 2009; Howe, Shea et al., 2011; Kelley, 1998; Kim et al., 2016; Marques, Mota & Carvalho, 2011; Martyn-St James & Carroll, 2006; Mcmillan et al., 2017; Nordstrom & Hogstrom 2011; Sañudo et al., 2017; Shojaa et al., 2020; Souza et al., 2020; Rutherford, 1999; Wallace et al., 2000; Xu et al., 2016; Zehnacker et al., 2007; Zhao et al., 2015, Zhao, Zhang & Zhang, 2017).

The studies of postmenopausal women indicate that progressive resistance training can produce modest gains in BMD (1% to 3% per year; Asikainen et al., 2004; Bonaiuti et al., 2002; Karikanta et al., 2007). Moreover, these studies show progressive resistance training can at least attenuate age-related losses in BMD at the hip and spine when the training programs are between 16 to 104 weeks (Guadalupe-Grau et al., 2009; Kelley et al.,

2012). However, as mentioned previously, there are mixed findings with regard to the effects of progressive resistance training on spine and hip BMD in postmenopausal women (Martyn-St James & Carroll, 2006; Zhao et al., 2015).

Regarding the lumbar spine, most of the studies conclude that in postmenopausal and older women, resistance training alone is an effective method to increase or maintain the BMD at this site (Benedetti et al., 2018; Bonaiuti et al., 2002, Howe, Shea et al., 2011; Martyn-St James & Carroll, 2006; Rutherford, 1999; Sañudo et al., 2017; Shojaa et al., 2020; Wallace et al., 2000; Zehnacker et al., 2007, Zhao et al., 2015). In particular, Bonaiuti and colleagues (2002) have found a statistically significant effect on BMD of the spine (WMD: 2.50; 95% CI = 0.44 to 4.57), and Martyn-St James & Carroll (2006) have shown that high intensity resistance training significantly increases (P = 0.006) the lumbar spine BMD (0.006 g/cm^2; fixed effect; 95% CI = 0.002 to 0.01, I^2=25.2%). Moreover, Zehnacker et al. (2007) have found that weighted exercises can help in maintaining BMD in postmenopausal women and can increase BMD in women with osteopenia and osteoporosis. In a more recent meta-analysis, Howe and colleagues (2011) have shown in a subgroup analysis that resistance exercises (high-force non-weight bearing exercises) produce a statistically significant effect on percentage change in BMD of the spine (MD: 0.86; 95% CI= 0.58 to 1.13). In addition, Zhao and colleagues (2015) have shown in their overall analysis that, again, resistance training significantly increases lumbar spine BMD (SMD: 0.311; 95% CI = 0.115 to 0.507; p = 0.002) in postmenopausal women. However, subgroup analysis has indicated that resistance-alone protocols only produce nonsignificant positive effects on lumbar spine BMD.

In a very recent meta-analysis focused only on dynamic resistance exercises, the authors found a significant low to moderate effect of resistance exercises on BMD changes in postmenopausal women. Though the study had a pooled estimate of random effect analysis of

SMD of 0.54 (95% CI = 0.22 to 0.87) in the lumbar spine, there was a substantial level of heterogeneity between trials (I^2 = 74.8%; Shojaa et al., 2020). In general, lumbar spine BMD can be increased by 1% to 2% by following resistance training (Nikander et al., 2010). Furthermore, only a few reviews have found no effect of resistance training on lumbar spine when performed alone (Marques, Mota & Carvalho, 2011; Rahimi et al., 2020; Rutherford, 1999; Zhao et al., 2015).

The reported effects of progressive resistance training in combination with other exercise protocols in the same session (combined exercise) are also heterogeneous. The other exercise protocols commonly included were weight-bearing activities, balance training, jogging, low-impact loading, high magnitude exercise, and simulated functional tasks. A recent meta-analysis of 24 studies (1,769 post-menopausal women) reported that progressive resistance training combined with high-impact or weight-bearing exercise significantly increased BMD at the lumbar spine (SMD: 0.431; 95% CI = 0.159 to 0.702; p = 0.002; Zhao et al., 2015). A systematic review and meta-analysis focused on the effect of impact exercise combined with resistance exercise on postmenopausal women demonstrated a reduction in postmenopausal bone loss in lumbar spine intervention groups (0.016 g/cm^2; 95% CI = 0.005 to 0.027; p = 0.02), when compared to the controls (Martyn-St James & Carroll, 2008a). In addition, in the review by Howe and colleagues (2011), combined exercise programs were found to significantly increase BMD at the lumbar spine (3.22%, 95% CI = 1.80 to 4.64). In a more recent systematic review and meta-analysis, combined loading was also shown to improve the lumbar spine segment (0.016 g/cm^2; 95% CI = 0.002 to 0.030; p = 0.028; Marques, Mota & Carvalho, 2011). In Xu and colleagues' (2016) overview of their systematic review and meta-analysis, they likewise advocated the use of odd and high impact exercise in combination with resistance exercise for the preservation of BMD levels in premenopausal and postmenopausal women. Furthermore, Bonaiuti et al. (2002), Kim et al.

(2016), Zhao, Zhang et al. (2017 ; SMD: 0.170; 95% CI = 0.027 to 0.313; p=0.019) and Benedetti et al. (2018) have also found positive effects of combined training on lumbar spine BMD in postmenopausal and older women. In contrast, some evidence has not supported these positive effects and, in some cases, has revealed negative outcomes after combined resistance training interventions (Chilibeck et al., 2013; Going et al., 2003; Miliken et al., 2003). For example, the meta-analysis by Rahimi et al. (2020) found no significant effects on lumbar spine BMD after applying combined training (MD: 0.03; 95% CI= − 0.01 to 0.08; p= 0.13).

As we can see, most of the reviews and meta-analysis confirm the positive effects of progressive resistance training, whether applied alone or in combination with other exercises, on lumbar spine BMD in postmenopausal and older women. The literature further suggests that combined training could produce even more benefits in this region than resistance training alone (Giangregorio et al., 2016; Howe, Shea et al., 2011; Zhao et al., 2015, Zhao, Zhang et al., 2017).

Focusing on the second most common site used for the evaluation of aBMD, the femoral neck, results from systematic reviews and meta-analyses suggest that resistance training alone could be more effective than combined-resistance training programs for this skeletal site (Benedetti et al., 2018; Howe, Shea et al., 2011). For example, Zhao et al. (2015) found that resistance training programs produced a significant increase in femoral neck BMD (SMD: 0.303; 95% CI = 0.127 to 0.479; p = 0.001) in postmenopausal women. Similarly, the meta-analysis by Howe et al. (2011) also showed resistance exercise to stimulate significant increases in BMD at the femoral neck (1.03%; 95% CI = 0.24 to 1.82). Most recently, Shojaa et al. (2020) found a low but statistically significant effect (SMD: 0.22) of dynamic resistance exercises on the femoral neck.

In a study by Martyn-St James & Carroll (2006), results showed a positive change, but after analyzing 11 RCTs that applied high intensity resistance training in postmenopausal women, the change was found to be statistically nonsignificant at the femoral neck BMD (0.010 g/cm^2; 95% CI= −0.002 to 0.021; p = 0.11; I^2=88.2%). Marques, Mota & Carvalho (2011) also found nonsignificant effects at the femoral neck BMD (0.023 g/cm^2; 95% CI = -0.009to 0.054; p = 0.157; Marques, Mota & Carvalho, 2011). Furthermore, Rutherford (1999), Wallace et al. (2000), and Rahimi et al. (2020) also found nonsignificant effects after analyses of RCTs that solely applied a resistance training program.

Concerning the effects of combined training on femoral neck BMD, Kim et al. (2016) found the combination of aerobic plus resistance training to be effective in improving the BMD at this site. Zhao, Zhang et al. (2017) further showed that integrating different physical activities in the same session significantly increased femoral neck BMD (SMD: 0.177; 95% CI = 0.030 to 0.324; p=0.018) in postmenopausal women. A systematic review and meta-analysis focused on the effect of impact exercise when combined with resistance exercise demonstrated a reduction in postmenopausal bone loss in the studies' intervention groups for femoral neck BMD (0.005 g/cm^2; 95% CI = 0.001 to 0.010; p = 0.03; Martyn-St James & Carroll, 2008a). However, Marques, Mota & Carvalho (2011) found nonsignificant BMD changes at the femoral neck in the studies that applied low-impact activities and resistance exercises in the same session. Recently, Rahimi et al. (2020) have shown similar results (MD: 0.02; 95% CI= -0.03 to 0.06; p =0.45).

Other studies have analyzed the effects of resistance training in other skeletal sites, such as the total hip, whole body, trochanter, and Ward's triangle. Shojaa et al. (2020), for example, have found a significant effect of resistance training alone on total hip (SMD: 0.48). Zehnacker et al. (2007) have also highlighted the benefits of weighted exercises in maintaining or increasing BMD at the hip in postmenopausal with osteopenia and

osteoporosis. Furthermore, in the meta-analyses of Zhao et al. (2015; Zhao, Zhang et al., 2017) combined resistance programs were found to significantly increase the total hip BMD (SMD: 0.411; 95% CI= 0.176 to 0.645; p = 0.001; SMD: 0.198; 95% CI = 0.037 to 0.359, p = 0.0 16, respectively). The effectiveness of progressive resistance training has also been confirmed in the review by Cheung & Giangregorio (2012) who considered this mode of intervention to be the best for postmenopausal women to improve hip BMD. However, Bonaiuti et al. (2002) have found no effect on the hip (WMD: 0.4; 95% CI= -8.5 to 1.67) nor the wrist (WMD: -0.28; 95% CI= -3.21 to 2.65) after resistance training, and the same results were shown by Howe et al. (2011; SM: 0.11%; 95% CI= -0.06 to 0.2).

Kim et al. (2016) and Zhao, Zhang et al. (2017) have shown that combined exercise improves total body and trochanter BMD. Howe et al. (2011), in contrast, have found that resistance exercise did not improve total body BMD (0.55%; 95% CI= -0.51 to 1.62), Ward's triangle BMD (-1.77%; 95% CI= -3.87 to 0.33), nor trochanter BMD (0.40%; 95% CI= -1.36 to 2.17). In addition, Martyn-St James &Carroll (2006) have also found no effect of resistance exercise on total hip BMD (0.002 g/cm^2; 95% CI = -0.001 to 0.005; p = 0.20).

As observed from the studies, strength exercise seems to be a powerful stimulus for improving and maintaining bone mass during the aging process, although it is difficult to generate exercise recommendations for bone strengthening based on the current meta-analytic results. In a very recent meta-analysis about the effects of dynamic resistance training on BMD in postmenopausal women, Shoja and colleagues (2020) analyzed the influence of different exercise variables (training program duration, type of exercise, training frequency, exercise intensity, and exercise volume/session) on the BMD results at the lumbar spine, femoral neck, and hip. The goal was to try to shed light on this difficulty of generating exercise recommendations. The authors found that at the femoral neck there was no difference between the five categories of exercise moderators. The categories are detailed in

the following list: 1) duration of training period, short (<8 months), moderate (9-18 months), and long (24 months); 2) type of exercise, resistance training devices, free weights, resistance band, or mix; 3) training frequency, low (< 2 sessions/week) or high (≥ 2 sessions/week); 4) exercise intensity, low (<65%), moderate (65% to 80%), and high (>80%); 5) exercise volume and session exercises (sets and reps), low (< 160rep/session), moderate (160 to 300 reps/session), and high (> 300 rep/session). At the lumbar spine and total hip, lower training frequency (< 2 sessions/week) resulted in significantly higher BMD changes compared to higher training frequency (≥ 2 sessions/week). Additionally, free weight training was found to be significantly superior to resistance training machines for improving total hip BMD (Shoja et al., 2020). For the rest of the parameters, no changes were found.

Results reported by Shoja et al. (2020) contrast with the previous evidence suggesting that higher training frequencies (≥ 2 or 3 session/week) are more osteogenic than lower frequencies (Kemler et al., 2017). It is important take into account that the authors analyzed the net training frequency, and it could be one of the reasons for their results. Usually in RCTs, authors have reported general frequency but lower rates of compliance from participants, which produces a decrease in the "real" or net exercise frequency. Another hypothesis for the contrast is that higher intensities might compensate for the effect of lower frequencies (and vice versa). Thus, high frequency combined with high intensity might result in incomplete bone adaptation to exercise (Weineck, 2019). In fact, different studies using rodents that have compared exercise frequencies found no differences between one, three, five, or seven exercise sessions a week (Hagihara et al., 2005; Raab-Cullen et al., 1994; Umemura et al., 2008). However, it is true that this scenario does not reflect conditions in the real human world where the adherence to an exercise protocol from the individuals in a study never reaches 100%. In this context, Bemben & Bemben (2010) did not observe frequency-induced differences (2 vs 3 session per week) in BMD in older adults after application of high

intensity resistance training for 9 months, although the intention-to-treat analysis may confound the results due to an underestimation of the participants that exercised less than required. Cussler et al. (2005) only found statistical differences between groups with the lowest and highest rates of attendance (0.15 vs 2.11 session/week) and not between the moderate- and high-rate groups (0.94 vs 2.11 session/week) in their 4-year resistance training program in postmenopausal women (three sessions/week, eight exercises for the main muscle groups, 2 sets, 6 to 8 reps at 70% to 80% 1 RM). In addition, another exercise trial that applied a resistance exercise protocol with a moderate to high exercise intensity found no significant difference between the high (≥ 2 to 3.5 session/week) and low frequency groups (1 to < 2 session/week) on lumbar spine and femoral neck BMD (Kemmler, Bebenek et al., 2011).

In the combined resistance training protocol of the TRACE study (periodized high-impact/high-intensity resistance exercise program) on early postmenopausal women, authors found significant differences between the high frequency group (≥ two session/week) compare to the low frequency group (< two session/week) at the lumbar spine but not at the femoral neck (Bebenek et al., 2010; Kemmler et al., 2013).

Finally, Kemmler and colleagues (2017) in their meta-analysis which analyzed seven RCTs of impact and resistance training protocols in older adults established the minimum effective dose of exercise frequency as being 2.1 and 2.5 sessions/week for the lumbar spine and femoral neck, respectively. Notwithstanding, these rates cannot be extrapolated to other cohorts.

In summary, most studies with positive results have used two to three training sessions per week, and it seems that at least two sessions per week could be the necessary

exercise frequency for improving BMD, but not for maintaining it (Guadalupe-Grau et al., 2009; Kemmler et al., 2017).

Greater skeletal benefits in response to progressive resistance training have been observed at the lumbar spine more than at the femoral neck or total hip. This finding could be attributed to the fact that resistance exercises may not produce enough strain across the proximal femur to elicit a positive skeletal response (Pellikaan et al., 2018) because this site suffers high levels of stress in everyday activities (e.g., weight-bearing loads in one legged standing situations, such as walking, which result in high tensions of the abductor muscles and high stresses especially at the femoral neck region; Shojaa et al., 2020). In addition, resistance training exercises, such as hip extension and flexion or hip abduction and adduction, performed at low to moderate intensities (40% to 80% 1 RM) only induce strains that are equivalent to those reported from walking at 4 km/h (Daly, Dalla Via et al., 2019), which could also be the reason for the mixed findings in this skeletal site.

The proximal femur mechanoresponse is variable and the varied distribution of strain across the proximal femur for different exercises leads to different bone adaptations, ranging from no response to a significant increase in bone mass (Bailey & Brooke-Wavell, 2010; Guadalupe-Grau et al., 2009; Kohrt et al., 1997; Lang et al., 2014). Thereby, some notable evidence has shown that exercise is more effective on the femoral neck if it involves the hip extensor muscles (gluteus maximus, semimembranosus, semitendinosus, and biceps femoris long head). Effective exercises then include deadlifts and squats. For the trochanteric area, exercise is more effective on the femoral neck if it involves hip abductor and adductor muscles (e.g., abduction and adduction exercises). On the lesser trochanter, exercise is more effective on the femoral neck if it involves hip flexor (iliopsoas; e.g., walking). Finally, on the Ward's triangle exercise is more effective on the femoral neck if it involves both hip adductor and hip extensor muscles (Daly, Gianoudis et al., 2019; Kelley et al., 2001; Kerr et

al. 1996; Lang et al., 2014; Martelli et al., 2017). However, it is difficult to quantify the exact bone response to different exercises because DXA examinations may not provide an accurate representation of highly localized femoral neck changes. It is also difficult because the different muscles that are normally active during an activity may induce different, spatially heterogeneous mechanical stimuli for bone tissue adaptation (Lang et al., 2014). In addition, is not easy to measure bone strain in vivo (Martelli et al., 2014).

As occurs with the hip muscle groups, it is necessary to increase the activity of the extensor muscles of the spine thought back extension exercises or exercise that involve these muscle groups to increase BMD in postmenopausal women and older adults (Beck et al., 2016; Sinaki et al., 2002). The erector spinae muscles are especially loaded in an excessively lengthened position in order to counteract the advancing kyphosis of the thoracic spine and trunk inclination in old ages, which reduces arm movement and force-generating capacity and requires greater activation to counterbalance the increased flexion moment. Hyperkyphotic curvature frequently develops following disk degeneration and vertebral wedge fracture and is associated with impaired balance in the elderly with osteoporosis (Greig et al., 2014), chronic pain and further fractures (De Smet et al., 1998; Mika et al., 1995). However, there is some evidence that back extension exercise training can reduce the risk of vertebral fracture in women with and without prior fracture (Sinkai et al., 2002). Moreover, these exercises may also reduce vertebral fractures in postmenopausal women in the long term, even in the absence of increased bone mass (Sinaki et al., 2002). Sinaki et al. (2002) found that the strength of the back muscles in osteoporotic women was significantly reduced compared to healthy subjects.

Exercises must be chosen to specifically act on clinically relevant sites: lumbar and thoracic spine, whole hip, greater trochanter, intertrochanteric and femoral neck regions. The easiest and safest activities that can be prescribed are weight-lifting exercises, such as

weighted squats, hack squats, leg press, hip extension, hip adduction, knee extension, hamstring curls, latissimus pull down, military press, seated rowing, rotary torso, back extension exercises with a weighted backpack, bench press, trunk extension, wrist curl, elbow flexion, tricep extension, reverse wrist curl, and forearm pronation and supination (Benedetti et al., 2018, Guadalupe-Grau et al., 2009). Although impact activities, such as jumping exercises, have an important osteogenic potential in premenopausal women and middle-aged adults, for postmenopausal women the response of this kind of exercises is diminished. Strength training or a combination of both modes (strength training and impact activities) is a better choice than impact exercise alone (Guadalupe-Grau et al., 2009).

The osteogenic effects of resistance training in postmenopausal and older women are site specific and can be achieved with moderate to high loading intensities (> 70% of 1 RM) of two or more sessions per week with two to three sets per session of exercises involving muscles of the upper limbs and lower limbs (preferable large muscles crossing the hip or spine) performed for at least four to six months. However, the efficacy of the training program is greater when extended to 12 months. The number of repetitions per exercise must be close to the maximum that can be performed. Further, 1- to 3-minute resting periods between exercises should be given, and the training session should last between 30 to 90 minutes (Beck et al., 2017; Gomez-Cabello et al., 2012, Guadalupe-Grau et al., 2009; Taaffe et al., 2013; Zehnacker et al., 2007).

Finally, regarding the use of devices in resistance training protocols, most strength training studies have used machines for their research. However, strength training needs to involve not only expensive equipment, but also safe, adaptable, and portable devices that can be used by older adults. Despite this necessity, only a few articles have used such devices (e.g., resistance bands) to apply variable resistance loads with the objective of improving the bone health of postmenopausal and older women, and they have found mixed results (Bravo

et al., 1996; Duckham et al., 2015; Going et al., 2003; Kemmler et al., 2004; Kemmler, von Stengel, Engelke, Häberle , & Kalender, 2010; Marques, Wanderley et al., 2011; Marques et al., 2013; Preisinger et al., 1995; Stengel et al., 2005; Tolomio et al., 2009; Woo, 2007).

- *Effects on bone turnover markers*

Some of the studies that applied resistance training programs alone or together with other types of exercise in older adults monitored changes in BTMs of bone formation and resorption along with the aBMD (Banitalebi et al., 2020; Beavers et al., 2018; Bemben et al., 2000, 2010; Gombos et al., 2016; Hawkins et al., 2002; Heikkinen et al., 1997; Holm et al., 2008; Humphries et al., 2000; Huovinen et al., 2016; Judge et al., 2005; Karaarslan et al., 2010; Kemmler et al., 2004; Klentrou et al., 2007; Lester et al., 2009; Marques et al., 2013; Pruit et al., 1992, 1996; Roghani et al., 2013; Ryan et al., 1998; Sen et al., 2020; Vincent & Brait, 2002). However, the number of studies that have done this is very small in proportion to the studies that have analyzed the effects of strength training on aBMD.

Results of these studies are inconsistent due to the training protocols and variance of samples between them. In addition, concerning the bone formation BTMs, only OC has been analyzed in a wide variety of studies (Bemben et al., 2000; Heikkinen et al., 1997; Holm et al., 2008; Humphries et al., 2000; Huovinen et al., 2016; Karaarslan et al., 2010; Kemmler et al., 2004; Klentrou et al., 2007; Lester et al., 2009; Marques et al., 2013; Pruit et al., 1992, 1996; Ryan et al., 1998; Sen et al., 2020; Vincent & Brait 2001). Furthermore, there are only a few studies that have analyzed the changes in bALP (Bemben et al., 2010; Gombos et al., 2016; Judge et al., 2005; Karaarslan et al., 2010; Lester et al., 2009; Roghani et al., 2013; Ryan et al., 1998; Vincent & Brait 2002) and PINP in postmenopausal and older adults (Beavers et al., 2018; Huovinen et al., 2016; Judge et al., 2005). The small number of studies that have measured the PINP was unexpected because PINP is the gold standard of BTMs for

the bone formation. The best BTM for measuring bone resorption is β-CTx, and some articles have analyzed β-CTx change after application of a resistance training program (Banitalebi et al., 2020; Beavers et al., 2018; Bemben et al., 2000, 2010; Gombos et al., 2016; Hawkins et al., 2002; Holm et al., 2008; Huovinen et al., 2016; Judge et al., 2005; Karaarslan et al., 2010; Kemmler et al., 2004; Marques et al., 2013; Ryan et al., 1998; Sen et al., 2020). As an example, Lester et al. (2009) found that 8 weeks of either combined resistance and aerobic training or resistance training alone stimulated increases in bALP and OC, and decreased bone resorption response. Fujimura et al. (1997) also reported significant increases in bALP and OC, but no significant changes in β-CTX of a training group that followed 4 months resistance training.

iii. Exercise intensity and bone health

- *Effects on areal bone mineral density*

Exercise intensity is one of the key parameters of an effective exercise prescription. For exercise to enhance bone mass, threshold intensity must be reached. However, this level has not been unequivocally established and may vary considerably across individuals.

There are relatively few investigations that have examined the dose-response effect of resistance training on bone in humans and specifically in postmenopausal women or older adults (Bembem et al., 2000, 2011; Bocalini et al., 2009; Humphries et al., 2000; Karaarslan et al., 2010; Kemmler et al., 2004; Kerr et al., 1996; Liu- Ambrose et al., 2004; Maddalozzo et al., 2000; Nichols et al., 1995; Pruitt et al., 1995; Taaffe et al., 1996; Vincent & Braith et al., 2001). Whereas some studies have reported the benefits of higher resistance training intensities (Kerr et al., 1996; Maddalozzo & Snow, 2000; Vincent & Braith, 2002), other studies have not found differences between the application of various intensities (Bemben et al., 2000; Bemben & Bemben, 2010; Pruitt et al., 1995). Thus, reported results are

inconclusive, and it is not clear if progressive resistance training at higher intensities is necessary to provide optimal increases in BMD of older adults.

In fact, in a recent meta-analysis by Souza and colleagues (2020), results have shown that both low-load (< 70 of 1 RM) and high-load (≥ 70 of 1 RM) resistance training protocols seem to be effective, and that they provide similar results in femoral neck (WMD: 0.00 g/cm²; 95% CI= -0.01 to 0.01; p = 0.63; I^2 = 47%) and lumbar spine (MD: 0.01 g/cm²; 95% CI, -0.00 to 0.02; p = 0.12; I^2 = 59%) BMD of older people with no significant differences between intensities. It seems that the intensity threshold to provide adaptations might be as low as 40% of 1 RM, as long as effort is adequate. Authors have indicated that a possible explanation for bone adaptations at low intensities might be the association between muscle and bone. As an endocrine organ, muscle releases muscle-derived factors during contractions (i.e., myokines, such as transforming growth factor-β, follistatin, insulin-like growth factor-I, fibroblast growth factor-2, osteoglycin, irisin, interleukin-6, leukemia inhibitory factor, IL-7, IL-15, monocyte chemoattractant protein-1, ciliary neurotrophic factor, osteonectin) that seem to have an influence on the bone resorption and formation process and, therefore, in bone health (Bettis et al., 2018; Kaji, 2016; Karsenty & Mera, 2018; Lombardi et al., 2016)

Additionally, in the meta-analysis by Shojaa and colleagues (2020) on the effects of dynamic resistance exercise on BMD in postmenopausal women, authors categorized the relative exercise intensity according to percentage of 1 RM in low (< 65%), moderate (65% to < 80%) and high (≥ 80%). In agreement with Souza et al. (2020), the sub-group analysis did not reveal significant differences between any of the skeletal sites analyzed: lumbar spine, femoral neck, and total hip.

The findings of the Cochrane meta-analysis by Howe and colleagues (2011) has suggested a positive response of the femoral neck (MD: 1.03; CI 95% = 0.24 to 1.82) and

spine BMD (MD: 0.86; 95% CI = 0.58 to 1.13) to high-intensity resistance training (> 60% 1 RM), but not at total hip BMD (MD: 0.11%; 95% CI = -0.06 to -0.29). While no effects at any site were reported for low intensity protocols (≤ 60% 1 RM), it appears that the sub-group analysis was limited because it only included eight clinical trials.

It is important to note that though Souza and colleagues (2020) reported no significant differences between low and high intensities, they realized that half of the included studies found superior results for high-intensity resistance training in at least one measure of BMD. However, the study found no superior results for low intensity resistance training. In addition, it seemed that the initial value of BMD and the duration of the exercise program were determinants of the training intensity's influence on bone response. Thereby, high-intensity resistance training appeared to provide higher results when done over shorter periods (< 6 months) for people with higher BMD at the initial values on femoral neck. Higher intensities seemed to produce more rapid results than lower intensities, possibly due to the discomfort caused by low-loads performed until, or close to, muscle failure (Fisher et al., 2017; Fisher & Steele, 2017). This method of exercise might prevent the participant from reaching high efforts, which can impair BMD adaptations, especially, in a short-term intervention. In fact, the performance of resistance training with lower loads and higher repetitions are associated with higher discomfort (Fisher et al., 2017; Fisher & Steele, 2017; Stuart et al., 2018).

Numerous studies have investigated the impact of high intensity resistance training (≥ 70% or 80% 1 RM, depending on the authors) on bone adaptation in older adults and postmenopausal women. Studies have looked at the results of this training either performed alone or in combination with other exercise modalities (Ayalon et al., 1987; Bembem et al., 2000, 2010, 2011; Bilek et al., 2016; Bocalini et al., 2009; Brentano et al., 2008; Chilibeck et al., 2002, 2013, 2015; Cussler et al., 2004; Daly et al., 2005; Hartard et al., 1996; Hawkins et al., 2002; Humphries et al., 2000; Karaarslan et al., 2010; Kemmler et al., 2003, 2004;

Kemmler, von Stengel, Engelke, Häberle, Mayhew & Kalender, 2010; Kerr et al., 1996, 2001; Kohrt et al., 1997; Liu- Ambrose., 2004; Maddalozzo et al., 2000; Marques, Mota, Machado et al., 2011; Miliken et al., 2003; Nelson et al., 1994; Nichols et al., 1995; Pruitt et al., 1995; Rhodes et al., 2000; Ryan et al., 1998; Smidt et al., 1992; Stengel et al., 2005; Taaffe et al., 1996, 1999; Verschueren et al., 2004; Villareal et al., 2003, 2004; Vincent & Braith et al., 2001; Watson et al., 2015, 2018). Results, in general, have demonstrated the positive effects of high-intensity resistance training on bone health in aging people, finding it to increase or preserve bone mass at lumbar, femoral neck, and hip sites. However, most of these studies only compare the high intensity exercise group with non-exercise and usual care controls, which makes it difficult to determine if the improvements on BMD are mainly influenced by the magnitude of mechanical stress or if higher intensities present greater effectiveness than lower intensities.

It is important to highlight the results of the only meta-analysis to date that has focused specifically on the effects of high-intensity resistance training in postmenopausal women. Martyn-St James & Carroll (2006) have found a statistically significant benefit of 0.006 g/cm^2 in lumbar spine BMD and a nonsignificant benefit of 0.010 g/cm^2 in femoral neck BMD. Thus, based on these results, high-intensity resistance exercise is only effective in preserving postmenopausal bone loss at the lumbar spine. However, this conclusion is based on an analysis that included studies which enrolled participants receiving antiresorptive agents, or HRT (14 and 11 RCTs). When a subgroup analysis excluded the studies with participants receiving HRT (11 and 17 RCTs), the results suggested that high-intensity resistance training did not significantly affect either the spine or hip BMD.

As we can see, although the superiority of high intensity resistance training is strongly supported by basic research (Hsieh & Turner, 2001; Rubin & Lanyon, 1985) and Frost's mechanostat theory, which indicates that higher strains can greatly improve the

mechanical properties of bone and therefore bone formation, the evidence concerning the effects of high-intensity resistance training on postmenopausal women and older adults BMD remains controversial. For this reason, comparing the effects of different intensities on bone health became one of the main objectives of this PhD dissertation.

In terms of the training devices used, none of the studies mentioned above analyzed the effects on bone health of the high–intensity with elastic resistnace. Neither did the studies compare the differences between high-, moderate-, or low-intensity resistance training with variable resistances, such as elastic bands, in postmenopausal women or older adults, which is one of the objectives of this thesis.

- *Effects on bone turnover markers*

In addition to the densitometry measures, some researchers have used the analysis of some BTMs to assess the effects of training intensity on the bone remodeling cycle. They have tried to find some relationship between changes in the aBMD and the variation in the concentrations of biomarkers in older adults (Bemben et al., 2000, 2010; Hawkins et al., 2002; Humphries et al., 2000; Huovinen et al., 2016; Karaarslan et al., 2010; Kemmler et al., 2004; Marques et al., 2013; Nelson et al., 1994; Pruitt et al., 1995; Ryan et al., 1998; Vincent & Brait 2002).

To date, there are few studies that have compared the effects of different training intensities on the BTMs of the same RCT in elderly populations (Bemben et al., 2000; Karaarslan et al., 2010; Pruitt et al., 1995; Vincent & Brait 2002). Vincent & Braith (2002) investigated the BMD, OC, BAP, and PYD responses to six months of resistance training at high intensity (80% 1 RM, 8 reps) and at low intensity (50% 1 RM, 13 reps) in men and women over 60 years of age. At the end of the study, only the high intensity group had significantly increased BMD at the femoral neck (1.96%). In addition, results showed

significant increases in OC in both groups (low intensity group: 25.1%; high intensity group: 39.0%), but only the high intensity group had significantly increased the BAP (7.1%) and the BAP to PYD ratio. Importantly, this measure indicated that the formation rate of bone was greater than the resorption rate and could result in increased BMD over time. Moreover, authors have found that there is a relationship between the changes in the concentration of BTMs and observed densitometric changes. Indeed, there is a relationship between the training intensity and the magnitude of the increase in the BTMs, as a major response from the BTMs has been observed at higher training intensities.

Benben et al. (2000) examined the BMD, OC, and CTX response from a six-month program involving high-intensity (80% 1 RM, 8 reps) and low-intensity (40% 1 RM, 16 reps) resistance training in early postmenopausal women. After six months of training, no changes in BMD at the spine and hip or CTX levels were seen in any group. However, there was a trend (p=0.008) in both intensity groups for increased OC levels. In addition, the percentage change in OC positively correlated to the percentage change in the total hip (r = 0.41) and trochanter BMD (r = 0.42). In this case, the fact that the women maintained bone mass may be of clinical significance, because early postmenopausal women are expected to lose as much as 3% to 4% of their BMD.

Some studies have analyzed only the effects of high-intensity resistance training in older adults and postmenopausal women (Bemben et al., 2010; Hawkins et al., 2002; Humphries et al., 2000; Huovinen et al., 2016; Kemmler et al., 2004; Marques et al., 2013; Nelson et al., 1994; Ryan et al., 1998). Nelson et al. (1994), for example, studied the effects of a 12-month high-intensity resistance training intervention (80% 1 RM, three sets, eight reps) with a frequency of two days a week and involving 39 postmenopausal women. Upon completion of the study, lumbar spine and femoral neck BMD was found to have increased 1.0% and 0.9%, respectively, while no changes were found in the control group. OC in the

resistance training group had also increased significantly by 14%, whereas the OC levels of the control group had decreased by 5%. In contrast, Hawkins et al. (2002) examined the effects of a four-month resistance training program performed at 70% to 90% 1 RM three days a week with postmenopausal women. Training was performed on alternating days with intensities equal to 90%, 80%, and 70% 1 RM. Subjects performed 3 sets of 9 resistance exercises. Results showed significant increases in BMD at the trochanter and total hip, however there were no changes in OC and urinary cross-laps.

It is important to note that, to date, there are no studies that have analyzed the effects of training intensity on the P1NP formation biomarker in older women after applying a resistance training program. Only OC, bALP, and β-CTx have been analyzed. In addition, the lack of conclusive results and the fact that no study used variable resistances in their strength training program with older adults make it necessary to highlight the relevance of this PhD dissertation to provide new information in this field of knowledge.

iv. Exercise modality and bone health

- *Effects on areal bone mineral density*

Exercise interventions incorporating multi-component programs that include three or more activity modes (programs that included just two modes were previously reviewed in the strength section as a combined or concurrent training), such as resistance, weight-bearing (e.g., running, skipping, stepping, jumping, hopping, dancing or moderate-to-high impact aerobics), balance, mobility and flexibility, and coordination exercises are currently recommended for the prevention of bone loss and fractures in elderly population. This combination is recommended because the exercises have been shown to positively influence multiple fall- and skeletal-related risk factors (Beck et al., 2017; Taafe et al., 2013). In addition, this kind of modality has been recently recommended by a Delphi consensus

guideline for individuals with osteoporosis, mainly vertebral, with or without vertebral fractures (Giangregorio et al., 2015).

Relatively few authors have carried out multi-component training programs in older adults and postmenopausal women to analyze the effects on aBMD (Chuin et al., 2009; Cusser et al., 2003; Daly, Gianoudis et al., 2019; Deng, 2013; Duckham et al., 2015; Englund et al., 2005; Gianoudis et al., 2014; Going et al., 2003; Jessup et al., 2003; Karinkanta et al., 2007; Kemmler et al., 2005, 2015; Korpelainen et al., 2006; Lord et al., 1996; Marín-Cascales et al., 2017; Marques, Mota, Machado et al., 2011, 2013; Metcalfe et al., 2001; Papaionnau., 2003; Park et al., 2008; Preisinger et al., 1995; Tolomio et al., 2009, 2010;Von Stengel et al., 2009, 2011).

In general, results have indicated that multi-component exercise programs may help to either increase bone mass or at least prevent bone mass decline with aging, especially in postmenopausal women, at the trochanter and femoral neck, but above all at the lumbar spine (Benedetti et al., 2018; De Kam et al., 2009; Giangregorio et al., 2016; Gomez-Cabello et al., 2012; Howe, Shea et al., 2011; Korpelainen et al., 2010; Martyn-St James & Carroll, 2008a; Nuti et al., 2019; Xu et al., 2016; Zhao et al., 2015). The benefit is due to the combined effects of resistance exercises, which provide muscular loading to bone, with weight-bearing aerobic exercises, which also provide an additional mechanical loading to the bone above gravity (Hong & Kim, 2018). Furthermore, it seems quite evident that multi-component exercise programs can also prevent functional decline due to their focus on improving not only aBMD, but also balance, muscle strength, and mobility (Binder et al., 2002; Gill et al., 2002; Liu-Ambrose, Khan, Eng, Heinonen et al., 2004).

However, it is necessary to note that participants of the studies have typically been frail with low bone mass, reduced physical function, and a history of previous falls and

fractures. Therefore, it is important to study whether multi-component training can prevent functional decline and bone loss in healthy, home-dwelling elderly people and postmenopausal women, which is perhaps the most profitable target population in terms of primary prevention.

Furthermore, dosage and effects on different outcomes for this group have not yet been well established by research. The large methodological differences between studies hinder a real comparison between them. Therefore, it is difficult to establish the 'dosage' of the treatment to obtain the best effect through this kind of modality training program.

To achieve bone mass gain or at least maintenance in older people, a correct exercise prescription of all the modalities that compose the multi-component training program is necessary. In this sense, along with resistance training, the weight-bearing activities are the most bone-osteogenic exercises, and it is especially important to prescribe them properly. In fact, in older women, the skeletal response to high impact activities is less consistent than in premenopausal women, and some, but not all, trials have reported positive effects (Bassey et al., 1998; Snow et al., 2000). It seems that mixed-impact loading programs including low- to moderate-impact exercises, such as walking, jogging, and stair-climbing, are the most effective for preserving BMD at the femoral neck and lumbar spine when combined with resistance training (Martyn-St James & Carroll, 2008a). For older women, the intensity of training is important, but the novel or diverse loading patterns performed in different directions (odd-impact exercises) may be particularly important for effective stimulation of bone, as older adults may not be able to tolerate high impact loads (Marques, Mota, Machado et al., 2011).

Although several meta-analyses have shown that walking appears to have little or no effect on either femoral neck or lumbar spine BMD (Kelley et al., 2013a, 2013b), it has

recently become well known that the effect of walking depends on its intensity, which is controlled via walking speed. In postmenopausal women, fast walking (5 to 6 km/h), hopping, and running (5 to 9 km/h) results in higher compressive and tensile strains at the femoral neck than walking at 4 km/h. The higher strains are considered to be the minimal level to induce an osteogenic response for bone preservation (Pellikaan et al., 2018). In addition, Hatori et al. (1993) also found that walking at high intensity improved the lumbar spine aBMD, while the study's low-intensity group showed a similar loss of bone as the study's control group. It is important to highlight that only three studies used elastic bands in their multi-component training programs for older adults (Preisinger et al., 1995; Tolomio et al., 2009; Duckham et al., 2015).

Much of the research on resistance exercise and bone health in postmenopausal and older adults has been performed using a traditional strength training strategy, which focuses primarily on strain magnitude. However, strain rate, defined as alteration in strain magnitude per second during the acceleration or deceleration of loading (μΣ/s) corresponding to movement velocity, has been rarely studied (Maddalozzo et al., 2007). Moreover, the time under load or velocity at different phases of movements (concentric–isometric–eccentric) has also been rarely mentioned in the studies (Hartard et al., 1996; Maddalozzo et al., 2007; Rhodes et al., 2000).

High-velocity resistance training has been reported to be more effective than conventional strength training in preventing osteoporosis in the only two studies that have compared both types of resistance training (Stengel et al., 2005; Von Stengel et al., 2007). Stengel et al. (2005) confirmed that 12 months of periodized power training performed twice weekly and designed such that 12 weeks of high-load training (70% to 90% 1 RM; concentric as fast as possible, 4-second eccentric sequence) is interleaved by 4 to 5 weeks of low-load training (50% 1 RM; 4-second concentric, 4-second eccentric phase) was more effective in

reducing bone loss in osteopenic postmenopausal women than traditional strength training at lumbar spine and hip. Those who followed traditional strength training in the study experienced a significant decrease at the total hip, -1.2% ($p<0.01$); femoral neck, -1.6% ($p<0.01$); trochanter, -0.9% ($p<0.05$); and intertrochanter, -1.4% ($p<0.01$). The power training group, however, maintained their aBMD in all the skeletal sites except at the total forearm, -1.0% ($p<0.01$). Notably, benefits in the spine persisted for 2 years (Von Stengel et al., 2007). Both groups in the study also performed one session per week of "gymnastics" (coordination, endurance, and flexibility training) and one session per week of home training, which consisted of 25 minutes of isometric exercises: stretching, rope skipping, and exercising with rubber bands.

Other authors who arrived at the same conclusion years later have found that a power training program based on high-load and low repetition (i.e., four sets of three to five repetitions at 85% to 90% of 1 RM) is effective in preserving BMD in postmenopausal women with osteoporosis or osteopenia (Mosti et al., 2013). However, in the Osteo-cise program, Gianoudis and colleagues (2014) have reported modest but statistically significant gains in BMD at the femoral neck and lumbar spine (1.0 to 1.1 %, $p < 0.05$). These results were found after application of a 12-month multi-component high-velocity progressive resistance training (power training with moderate loading; weight-bearing impact exercises with balance training) three times a week in older adults (men and women) without osteoporosis or low trauma fractures. This training program was also effective in improving functional muscle power (timed stair climb), muscle strength, and dynamic balance when compared to usual care controls (Gianoudis et al., 2014).

Nevertheless, these previous studies employed high-load power training (> 70% 1 RM), while the current evidence has indicated that maximal power output is achieved with light and moderate loads, specifically at 30% to 70% of 1 RM (Cuoco et al., 2004; Mohamad

et al., 2012; Sleivert et al., 2004). It seems that lighter loads allow subjects to move more quickly, resulting in greater power output even though the generated force output is smaller (Mohamad et al., 2012). In fact, a previous study found that peak power during low-load (35% of 1 RM) is comparable to, or even larger than, that of peak power during high-load (70% of 1 RM; Mohamad et al., 2012). Relevantly, Snow et al. (2000) demonstrated that for older postmenopausal women, light-load power training with a weighted vest was effective in increasing hip aBMD, and therefore, prevented significant bone loss in this population. It could be possible that light to moderate loads are a better choice than higher loads for preventing bone loss in older adults and postmenopausal women.

It is important to highlight that none of the studies that performed a high-speed resistance training program in older adults and postmenopausal women reported adverse events, like increase of injury risk or pain **(**Gianoudis et al., 2014; Hamaguchi et al., 2017; Kemmler et al., 2015; Mosti et al., 2013; Snow et al., 2000; Stengel et al., 2005; Von Stengel et al., 2007). Therefore, power training is a safe exercise modality to enhance bone health in this population. In addition, it is very important to promote this type of training because individuals with osteoporosis have been shown to have diffuse and preferential type II muscle fiber atrophy and this phenomenon has been related to the degree of bone loss in older women (Terracciano et al., 2013). Considering the importance of strain rate and fast movement velocity parameters in improving bone strength, and the safe and easy applicability of these exercises in older adults, more exercise studies should focus on this type of training. Moreover, the application of high-speed resistance training with variable resistance should be investigated because, to date, no study has used this type of load.

- *Effects on bone turnover markers*

Regarding the effects of multi-component and high-velocity resistance training on BTMs in postmenopausal and older adults, only data from four (Bilek et al., 2016, Marques et al., 2013; Miliken et al., 2003; Villareal et al., 2008) and one study (Mosti et al., 2013) have been reported. Most of the studies have not found any significant change in BTMs. For example, Marques et al. (2013) reported that after 32 weeks of exercise training on balance and lower-extremity muscle strength with healthy older adults, levels of OC and CTX remained unchanged.

Mosti and colleagues (2013) performed the only study to have investigated the effects of high-velocity resistance training on BTMs in postmenopausal women (with osteoporosis or osteopenia). After 12 weeks of performing squat exercises three days a week (four sets of three to five repetitions at 85% to 90% of 1 RM) no significant changes occurred in the serum levels of P1NP and CTX, even though the ratio of serum P1NP to CTX tended to increase ($p = 0.09$), indicating stimulation of bone formation.

In summary, much more research is needed in this field.

II.VII.II. Skeletal muscle tissue

A. Muscle physiology

Muscle is one of the primary tissues of the body, and it is probably one of the most studied tissues of all in the human body. There are three major muscle types: skeletal, cardiac, and smooth. The following sections deal briefly with the muscle structure, function, properties, and metabolism of human skeletal muscle

i. Skeletal muscle macrostructure

Human skeletal muscle constitutes approximately 40% of human body weight (Frontera & Ochala, 2015). Each skeletal muscle is composed of a common macro and microstructure. Regarding muscle macrostructure, each muscle is enclosed by three layers of connective tissue called "mysia" (epimysium, perimysium, and endomysium), which provide the general structure and form of the muscle. The connective tissue also compartmentalizes the central part of the muscle composition, namely, the muscle fibers (DeSaix et al., 2018). The outer layer of connective tissue, the epimysium, separates muscle from the rest of the tissues and organs in the area. The inside of each muscle is composed of muscle fibers that are bundled together into muscle spindles and fascicles, with the perimysium functioning as the layer of connective tissue that connects them together (DeSaix et al., 2018). This organization of the skeletal muscle allows the nervous system to trigger a specific subset of muscle fiber or fascicle and produce a specific movement. In each fascicle, the muscle fibers are covered by the inner most connective tissue layer, the endomysium, which provides the nutrients to the muscle fiber via the extracellular fluid and blood vessels (Figure 47; Noto & Edens, 2020).

ii. Skeletal muscle microstructure

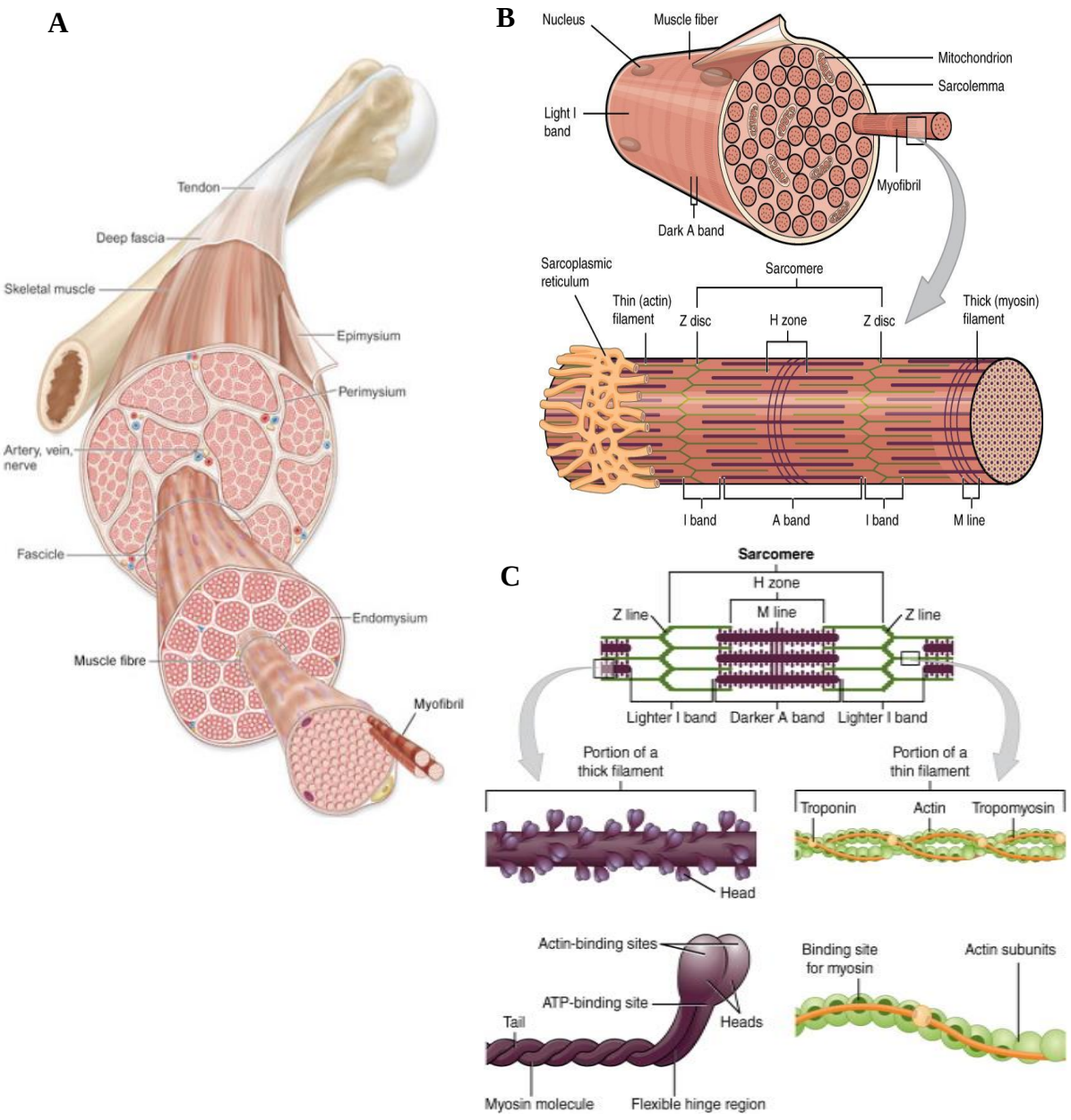
At microstructural level, a single muscle fiber is a multinucleated structure composed mostly of actin (thin filament) and myosin (thick filament) contractile proteins covered by a cell plasma membrane called sarcolemma. The cytoplasm and the endoplasmic reticulum that store and release calcium ions (Ca^{++}) are called sarcoplasm and sarcoplasmic reticulum, respectively (DeSaix et al., 2018; Noto & Edens, 2020). Each packet of the actin and myosin microfilaments, along with their main regulatory proteins (tropomyosin and troponin) and other proteins, are called sarcomere (Figure 47). Leading to contraction and relaxation, the sarcomere is the functional unit of the muscle fiber. The arrangement of sarcomeres in a

sequential order from one end of the muscle fiber to the other gives the muscle its striated appearance. The sarcomere itself is bundled within the skeletal muscle myofibril, which runs the entire length of the muscle fiber and attaches to the sarcolemma at its end. The size of each sarcomere is approximately 2 μm in length, and they have a three-dimensional cylinder-like arrangement (DeSaix et al., 2018; Noto & Edens, 2020). In addition, the sarcomere is bordered by structures called Z-lines which are the zones where the actin myofilaments are anchored.

Human muscle fibers can be broadly classified into two main categories, type I (slow oxidative) and type II (fast-twitch). The latter muscle fiber type is then subdivided into types IIa, IIx, and IIb (Brooke & Kaiser, 1970; Greig & Jones, 2016). According to research, it seems that humans do not have the fastest Type IIb, which is found in rodent muscle (Bottinelli et al., 1996; Li & Larsson, 1996; Bottinelli & Reggiani, 2000; Degens & Larsson, 2007; Greig & Jones, 2016). The broad classification of muscle fibers relates to the different characteristics of the muscle fibers, with muscle contraction being the most characteristic. In this sense, the type I fibers are the slowest in contraction and the type II are faster, in the order of IIa, IIx, to IIb (Greig & Jones, 2016). It is important to note that all the muscle fibers are innervated by the same motoneurons and that they have the same biochemical, histological, and contractile properties. Type I fibers are more fatigue resistant and are recruited preferentially in longer, lower intensity activities. Type II fibers are more powerful and are recruited for occasional high-intensity exercises. In fact, type II fibers are able to produce more force at any given shortened velocity than type I fibers and generate a higher power output than slower type I fibers (Figure 47). Consequently, the high and fast contractions provided by the type II fibers entail high levels of ATP that can only be met by glycolysis and the breakdown of phosphocreatine. In contrast, the energy requirements of type I fibers are lower and can be satisfied by the oxidative metabolism of carbohydrates and

fats, which are characterized by their high content of fat, mitochondria, and capillaries (Greig & Jones, 2016).

Figure 47. *An overview of skeletal muscle structure.*



Note. A. Macrostructure of whole skeletal muscle; B. Microstructure of muscle fiber; C. Microstructure of sarcomere. Reproduced and adapted from *Anatomy & Physiology* (p.95), by DeSaiz et al., 2018, OpenStax, and from *Skeletal muscle: from molecules to movement* (p. 134), by Jones et al., 2004, Edinburgh.

iii. Skeletal muscle contraction

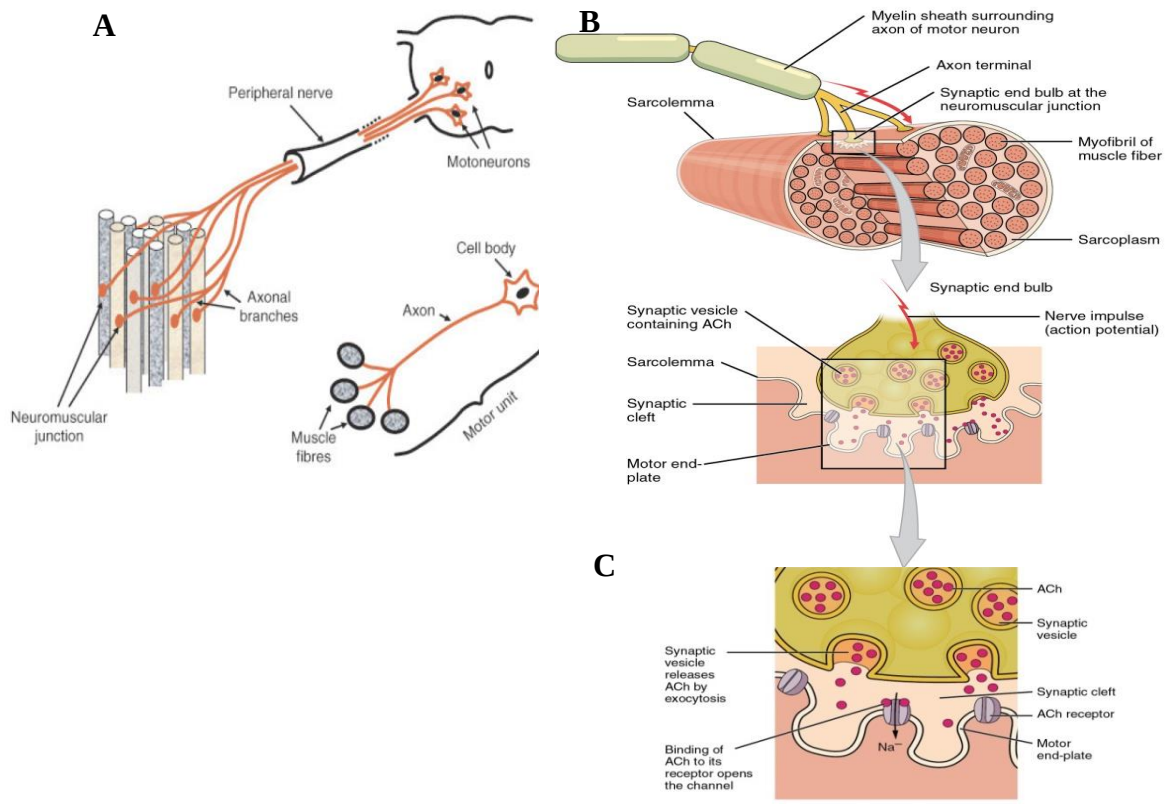
The most important characteristics of the skeletal muscle tissue are that it is an innervated and excitable tissue. Since Jan Swammerdam in 1667 who was the first to show that irritation of the nerve results in contraction of the muscle, and Luigi Galvani in 1791 who found that electrical impulses travelling along the nerves could cause muscle to contract (Cobb, 2002), the physiology of muscle contraction has been widely investigated to date.

Skeletal muscle fibers are innervated by a single branch of the axon arising from an α-motoneuron in the spinal cord. A smaller number of α-motoneurons are located in the brainstem for activation of skeletal muscles of the face, neck, and head. The α-motoneurons and all the muscle fibers that they innervate constitute a motor unit (Greig & Jones, 2016). The differences in α-motoneurons' excitability, size, and recruitment in the spinal cord determine which fibers are active during a movement. Small motor neurons innervate a relatively small numbers of muscle fibers and are more readily activated. Therefore, small moto neurons tend to be recruited for activities that involve low intensity and continuous contractions (type I fibers). Larger motor neurons are less excitable, and they have a greater number of axonal branches and control larger motor units. Thus, large motor neurons are involved when movements require rapid and short contractions (type II fibers; Greig & Jones 2016; Henneman et al., 1965).

At the neuromuscular junction, the site where the muscle fiber is innervated by the motor neuron's terminal, the axon flattens and swells along the muscle fiber membrane. When the action potential has passed down the axonal branches, the release of the neurotransmitter acetylcholine (ACh) from the synapse causes depolarization of the sarcolemma via interaction of acetylcholine with its receptors on the post-synaptic membrane (DeSaix et al., 2018; Greig & Jones, 2016; Noto & Edens, 2020; Figure 48). The action potential originated by the motor neuron is propagated along the membrane surface and into

the transverse T-tubules, which leads to the release of Ca^{2+} from the sarcoplasmic reticulum. This produces the union of Ca^{2+} to troponin C on the actin, causing a spatial change of the tropomyosin that exposes the myosin binding sites, and with the hydrolysis of ATP, the myosin heads attach to the actin filament and the cross-bridge power stroke occurs, drawing the Z-lines of the sarcomere closer together, and thus causing muscle contraction. This whole process is called excitation-contraction coupling because the excitation by neural stimulation is coupled to the resulting muscle contraction (the membrane must first be "excited" by the action potential of the motor neuron and then this action potential is "coupled" to the actual contraction through the release of calcium ions [Ca++] from the sarcoplasmic reticulum; DeSaix et al., 2018; Greig & Jones, 2016; Noto & Edens, 2020).

Figure 48. *Innervation of muscle fibers and biochemical process of skeletal muscle contraction.*



Note. A. Motor unit; B. Motor end-plate and neuromuscular junction; C. Axon terminal releasing ACh.

iv. Skeletal muscle function and properties

Skeletal muscle plays an important role in many functions, such as locomotion, posture maintenance, respiration, homeostasis maintenance by heat generation, communication (writing, speaking, and gesticulation), constriction of organs and blood vessels, pumping of blood, and the production of bone tissue by the contraction of muscle tissue. Skeletal muscles also protect internal organs, such as abdominal and pelvic organs, by acting as an external barrier and by supporting the weight of the organs. The best-known feature of skeletal muscle is probably its ability to contract and cause movement, which results from the ability of the muscle to shorten and produce force crucial for this function (Degens et al., 2009; Greig & Jones, 2016).

The functions performed by the skeletal muscle are possible because all muscle cells share four basic properties. These properties are contractibility, excitability, extensibility, and elasticity. Contractibility allows muscle tissue to forcefully shorten. As mentioned above, muscle cells exhibit excitability through their plasma membranes. Because they can respond to a stimulus by polarizing or depolarizing, muscle cells can send an action potential along the entire length of their membranes. Finally, extensibility and elasticity refer to the ability of a muscle to be stretched and the ability of the muscle to return to its original length after being contracted or stretched (DeSaix et al., 2018; Degens et al., 2009; Greig & Jones, 2016; Noto & Edens, 2020).

B. Sarcopenia

i. Definition

The term sarcopenia comes from the Greek word “sarx,” meaning “flesh,” and “penia,” meaning “loss or poverty”. Thus, sarcopenia means “poverty of flesh.” It was originally coined by Irwin Rosenberg in 1989 to describe the age-related decline of skeletal

muscle mass (Rosenberg, 1989). Rosenberg had observed that more than 25% of subjects over 65 years of age, and more than 50% of subjects over 80 years of age exhibited this characteristic.

The definition of sarcopenia has evolved over time. Since 2009, there have been six attempts to standardize the definition of sarcopenia internationally, resulting mainly from the efforts of several working groups. The most prominent statements regarding the definition have been from the European Working Group on Sarcopenia in Older People (EWGSOP), the Foundation for the National Institutes of Health, and the International Working Group on Sarcopenia. Each of these groups has its own sarcopenia definition, but no definition of sarcopenia has received universal acceptance.

Currently, all these groups recognize that sarcopenia is a multifactorial syndrome (Cruz-Jentoft et al., 2010) that refers not only to the loss of muscle mass but is also characterized by the age-related decreases in muscle strength and physical function (Cruz-Jentoft et al., 2019). In a landmark paper by the EWGSOP in 2010, which described the consensus guidelines on the definition and diagnosis of sarcopenia, sarcopenia was defined as "a syndrome characterized by the progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life, and death" (Cruz-Jentoft et al., 2010; Delmonico et al., 2007). However, in a 2019 review, the European consensus of 2010 by the EWGSOP was revised. Now sarcopenia is considered a muscle disease (muscle failure), and low muscle strength has overtaken the role of low muscle mass as the principal determinant that facilitates prompt identification of sarcopenia in practice (Cruz-Jentoft et al., 2019; Ibrahim et al., 2016; Schaap et al., 2018).

It is important to note that in 2001, Morley et al. (2001) added muscle strength to the original definition of sarcopenia, due to the discovery of a weak association between the loss

of muscle mass and muscle strength (age-associated changes in muscle mass explain less than 5% of the variance in muscle strength change; Hughes et al., 2001) and, furthermore, because DXA measurements of lean mass underestimated the prevalence of sarcopenia (Proctor et al., 1999). In addition, compared to muscle mass, muscle strength has a stronger relationship with disability and function (Newman, Kupelian et al., 2006; Schaap et al., 2012; Visser et al., 2002, 2005). Moreover, muscle strength is a better predictor than muscle mass of adverse outcomes (Ibrahim et al., 2016; Leong et al., 2015; Schaap et al., 2018). Therefore, muscle strength has become more clinically relevant. Nonetheless, other researchers believe that muscle mass, muscle strength, and physical function should be assessed separately.

However, in the last European Consensus on the definition and diagnosis of sarcopenia, performed by the EWGSOP in 2019, muscle strength came to the forefront as the main determinant of sarcopenia (Cruz-Jentoft et al., 2019), with the low muscle strength being the key characteristic of sarcopenia. Along with the detection of low muscle quantity and quality being used to confirm sarcopenia diagnosis, poor physical performance is also seen as indicative of severe sarcopenia (Cruz-Jentoft et al., 2019). Sarcopenia is not currently considered a geriatric syndrome because its development is now recognized to begin earlier in life (Sayer et al., 2008). Recently, sarcopenia was formally recognized as a muscle disease, receiving diagnosis code ICD-10-CM (M62.84) from the Centers for Disease Control and Prevention, which can be used to bill for care in some countries (Vellas et al., 2018).

The progressive decline in skeletal muscle mass, muscle strength, and physical function has been linked to an increased risk of falls and fractures, a decrease in functional capacity, and a loss of independence. These declines are also linked to frailty, inability to perform activities of daily living, osteoporosis, low quality of life, obesity, dementia, type 2 diabetes, respiratory diseases, and increased risk of death (Morley et al., 2014; Nascimento et al., 2020; Nilwik et al., 2013; Paddon-Jones et al., 2008; Saver et al., 2005, 2008; Thompson,

2007). Health care costs associated with sarcopenia-related disability in the year 2000 were estimated to be $29.5 billion for older women and $12.6 billion for older men (Janssen et al., 2004). Taking into account the rapid increase of the older adult population over the past two decades, these cost estimates are now likely to be far higher (Delmonico et al., 2017). How to combat sarcopenia is a major challenge, but exercise appears to be a potential solution.

ii. Pathophysiology

Sarcopenia has a complex multifactorial etiology with several mechanisms involved in its onset and progression (Cruz-Jentoff et al., 2010). The variety of mechanisms can be classified into four groups: aging, disease, inactivity, and malnutrition (Cruz-Jentoff et al., 2019). Overall, these mechanisms involve a decrease in physical activity, sedentary behavior, under-nutrition or malabsorption, over-nutrition or obesity, changes in neuromuscular integrity, changes in hormonal levels, a decrease in protein synthesis, proteolysis, nuclear apoptosis, a decrease in mitochondrial content and function, and an increase in oxidative stress and inflammation (Buford et al., 2010; Cruz-Jentoff et al., 2010; Degens et al., 2006; Johnston e tal., 2008; Rosenberg, 1997).

iii. Prevalence

Determining the prevalence of sarcopenia is complicated due to different diagnostic criteria, cutoff points, and methodologies that have been used to assess muscle mass, muscle strength, and physical function in older adults. A systematic review by the EWGSOP reported a prevalence of 1% to 29% in community-dwelling older people, with even higher estimated prevalence in long-term (14% to 33%) and acute care settings (~10%; Cruz-Jentoft et al., 2014). In terms of ages, it is estimated that sarcopenia affects approximately 5% to 13% of people aged 60 to 70 years, and the incidence increases to 11% to 50% for those aged 80 and above (Legrand et al., 2013; von Haehling et al., 2010). However, when a cut-off point of two SD for the appendicular skeletal muscle mass index has been used, researchers

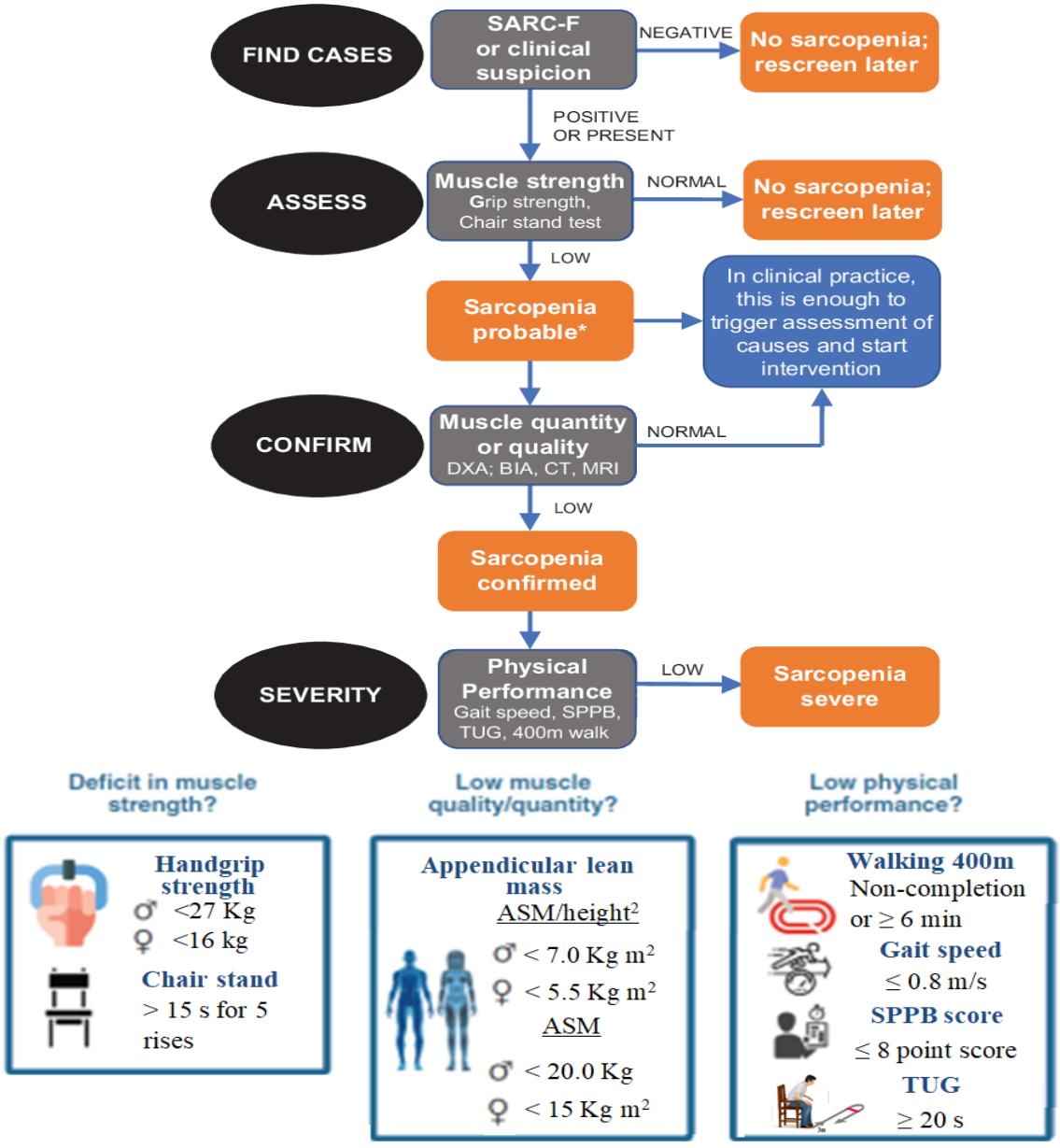
have reported a prevalence of 13% to 24% in those aged 65 to 70 years, and over 50% in those older than 80 years (Baumgartner et al., 1998). In any case**,** the WHO estimates that more than 50 million people worldwide are sarcopenic, with the prevalence expected to increase to 1.2 billion people by 2025 (Cruz-Jentoft et al., 2010) and to increase 10-fold in the year 2050 (Hida et al., 2013).

iv. Diagnosis

Currently there is no gold standard method or algorithm to diagnose sarcopenia because there is no consensus on the definition of this syndrome, but several algorithms have been proposed by different working groups. The algorithm proposed by the EWGSOP in 2019 is the most recent and the most widely supported by scientific societies because it provides recommendations for cut-off points for different parameters, thus allowing higher harmonization (Cruz-Jentoft et al., 2019). Specifically, EWGSOP's algorithm is recommended for sarcopenia case-finding, diagnosis, and severity determination. It follows a pathway called Find-Assess-Confirm-Severity (F-A-C-S) and evaluates muscle strength, muscle mass quality and quantity, and physical performance (Figure 49).

To identify individuals who may have sarcopenia, a self-reported five-item questionnaire, SARC-F, can be used by individuals to express their limitations in muscle strength, their abilities (rise from a chair, walk, climb stairs), as well as any experiences they have had with falls (Malmstrom et al., 2016). In order to confirm the presence of sarcopenia, muscle strength of upper and lower limbs has to be assessed with the handgrip strength test and the repeated chair stand test. If the individual presents a deficit in muscle strength (cutoff values: < 27 kg for men and < 16 kg for women in handgrip strength; > 15 s for 5 rises in the repeated chair stand test) the condition of sarcopenia is probable.

Figure 49. Algorithm for the diagnosis of sarcopenia and for quantification of its severity proposed by the EWGSOP and the cut-off points of the tests for its assessment.



Note. ASM: appendicular skeletal mass, SPPB: short physical performance battery, TUG: up and go test. Reproduced and adapted from "Sarcopenia: revised European consensus on definition and diagnosis" (p.24), by Cruz-Jentoft et al., 2019, *Age and Ageing, 48*(1), and from "Physical Exercise in the Oldest Old" (p. 1289), by Valenzuela et al., 2019, *Comprehensive Physiology, 9*.

However, a low muscle quality and quantity (< 20 kg for men and < 15 kg for women of appendicular skeletal mass [ASM]; < 7.0 kg/m^2 for men and < 6.0 kg/m^2 for women of appendicular lean mass to height) assessed by DXA, BIA, MRI, or CT is necessary to confirm the sarcopenic condition. In addition, multiple physical performance tests, such as SPPB ≤8 points), walking (400 m in ≥ 6 m), or the TUG (performed in ≥ 20 s), can be used for the assessment of low physical performance and the diagnosis of severe sarcopenia (Cruz-Jentoft et al., 2019).

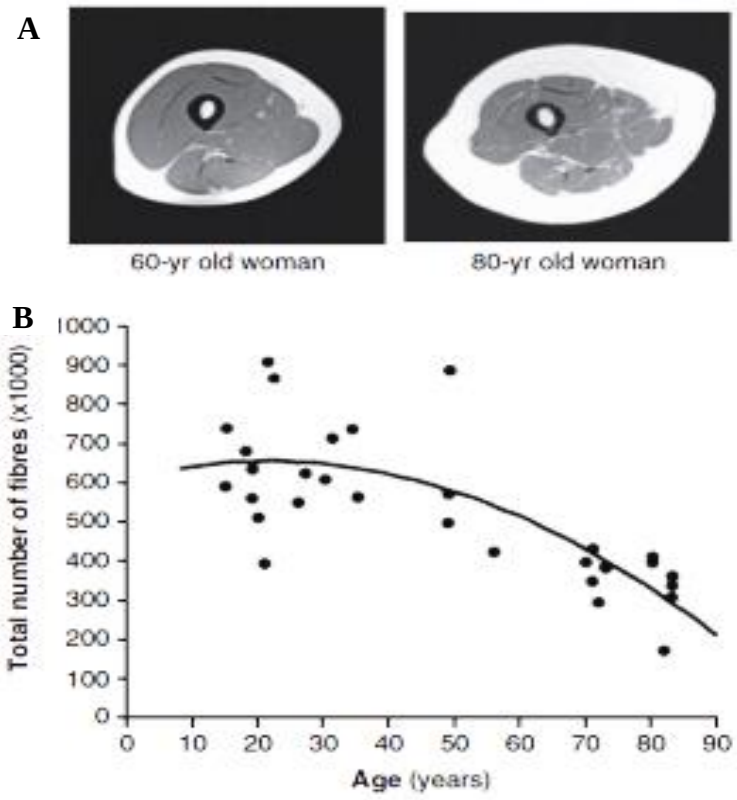
These cut-off points have been extracted from normative references of healthy young adults (Dodds et al., 2014). The cut-off points are usually set at -2 standard deviations from the mean reference value (Baumgartner et al., 1998; Morley et al. 2001) or at -2.5 standard deviations in more conservative diagnoses (Dodds et al., 2014). Some other researchers have defined the cut-off points for ASM (the appendicular skeletal mass) by the sum of arm and leg muscle mass, adjusted by squared height. For example, Baumgartner et al. (1999) defined the cut-offs at < 7.26 kg/m² for men and < 5.45 kg/m² for women. Janssen et al. (2004) defined them at < 8.5 kg/m^2 for men and < 5.75 kg/m^2 for women . Finally, according to the International Working Group on Sarcopenia, the cut-offs were set at < 7.23 kg/m2 for men and < 5.67 kg/m2 for women (Marty et al., 2017). Other indexes have also been used to assess muscle mass, such as ASM adjusting for fat mass and BMI, whole body fat-free mass to height (Yu et al., 2014).

C. Age-related changes in skeletal muscle tissue

Age-related muscle loss is a well-accepted and widely reported phenomenon by both cross-sectional and longitudinal studies that compare the structural changes of muscle tissue between young adults and older adults (Borkan et al., 1983; Frontera et al., 1991, 2000; Goodpaster et al., 2006; Janssen et al., 2000; Kyle et al., 2001; Lexel et al., 1983, 1988; Young et al., 1985).

There is a strong consensus in the literature that the loss of muscle mass or atrophy with age is mainly the result of either a reduction in muscle fiber size (CSA) or the number of muscle fibers (Faulkner et al., 2007; Lexell et al., 1988; Figure 50). In humans, both processes contribute to the decrease in muscle mass, but the significance of each process on age-related muscle loss depends on heredity and several other factors – some of which are unknown (Faulkner et al., 2007). However, it seems that the loss in muscle mass is explained more by the reduced number of myofibers than the decrease of myofiber area (Fontera et al., 2000; Lexell et al., 1988)

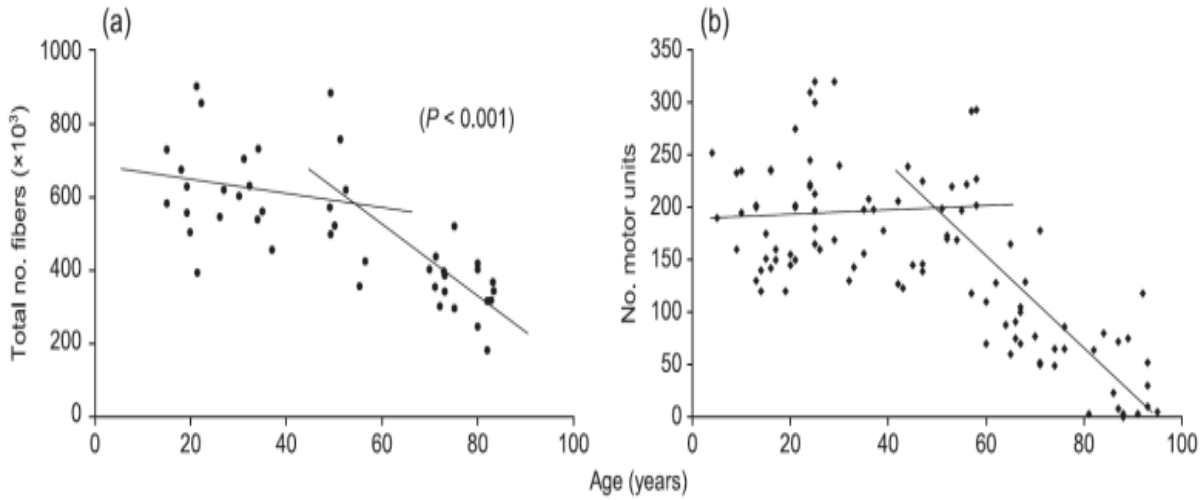
Figure 50. *Age-related skeletal muscle changes.*



Note. A. Decrease in CSA and increase of non-contractile tissue; B. decrease in the total number of muscle fibers. Reproduced from "Role of the nervous system in sarcopenia and muscle atrophy with aging: strength training as a countermeasure" (p. 53), Aagaard et al., 2010, *Scandinavian Journal of Medicine & Science in Sports, 20*(1).

A decline in skeletal muscle mass begins generally and gradually during the third decade of age in both men and women (Distefano & Goodpaster, 2018; Maltais et al., 2009). An acceleration in decline appears when individuals reach the fifth decade (Aloia et al., 1991; Lexell et al., 1988; Melton et al., 2000). Until the age of 50 years, approximately 10% of muscle can be lost (Lexell et al., 1988). This is mostly attributed to a loss in the CSA of muscle fibers caused by a sedentary lifestyle because no difference in the number of fibers has been observed between 20 and 50 years of age (Figure 51; Faulkner et al., 2007; Lexell et al., 1988).

Figure 51. *Age-related changes before and after 50 years of age.*



Note. A. Total number of fibers in the vastus lateralis of men between 18 and 82 years of age. B. Number of motor units in the extensor digitorum brevis of men between 5 and 88 years of age. Reproduced from "Age-related changes in the structure and function of skeletal muscles" (p. 1093), by Faulkner et al., 2007, *Clinical and Experimental Pharmacology and Physiology, 34*(11).

According to previous studies, skeletal muscle mass is reported to decline at a rate of 1% to 2% per year when an individual is above the age of 50 (Hughes et al., 2002; Rolland et al., 2008; Thomas, 2007; Valenzuela et al., 2019). However, Francis et al. (2017) have claimed that these rates may be overestimated. They consider a rate of 0.3% to 0.5% as more realistic than the widely reported rate of 1% to 2% (Francis et al., 2017). Concerning women, a cross-sectional study by Rolland et al. (2007) reported a muscle mass decline of 0.6% per year after the menopause period. Overall, some studies have established a 30% to 50% decrease in skeletal muscle mass in both men and women between the ages of 40 and 80 years (Akima et al., 2001; Allen et al., 1960; Young et al., 1985; Lexell et al., 1988). Nonetheless, others have reported a decrease of 20% to 28% between the second and eighth decades of life (3.3% to 4.6%, or 0.4 to 0.8 kg per decade; Gallagher et al., 1997; Mitchell, Williams et al. 2012; Narici & Maffulli, 2010).

The decline of muscle mass is not uniform and linear across populations. Moreover, it does not occur at the same rate and age in sexes, and decline is not even the same for an individual's whole body or specific regions of the body (whole body or appendicular muscle mass). For example, in women, an accelerated loss of muscle mass occurs at an earlier age than in men, around menopause (Calmels et al., 1995; Lindle et al., 1997; Phillips et al., 1993). This difference is due to the decrease of estrogen that occurs at a mean age of 50 years in women (Dionne et al., 2000). In addition, due to life expectancy being higher for women than it is for men, women will experience a higher loss of muscle mass.

Focusing on the regions that are more prone to muscle loss, reductions have been reported in muscle groups of both the upper and lower extremities (Gallagher et al., 1997; Janssen et al., 2000; Lynch et al., 1999; Overend et al., 1992; Rice et al., 1989). Nevertheless, muscle CSA tends to decrease more in the lower body muscles than in the upper body muscles (Janssen et al., 2000) because the muscle fibers are generally smaller in older adults,

as compared to younger persons, especially in the lower limbs (Gonzalez et al., 2014; Granacher et al., 2009, 2013). In fact, previous longitudinal studies have suggested that muscle mass in the lower limbs decreases by 0.7% to 0.8% and up to 1.0% to 1.4% per year in both men and women (Goodpaster et al., 2006; Frontera et al., 2000; Koster et al. 2011). This decrease is more than the rate of loss reported in upper-limb muscles (Gallagher et al., 1997; Janssen et al., 2000). In particular, it is estimated that at least one-third of the knee extensor muscle mass is lost between the ages of 20 and 80 years old (Porter et al., 1995; Young et al., 1985), and by 80 years of age, a decrease in fiber numbers of 50% in the large limb muscles also occurs (Daw et al., 1988).

It is important to note that in terms of functional capacity, the loss of the appendicular skeletal muscle mass, especially in the lower limbs, is more relevant than in any other part of the body. This is because the muscles involved in locomotion (e.g., walking, rising from a chair, and stair-climbing) are located in this region. Results of several studies has revealed that the muscle mass of lower limbs is a more sensitive index of age-related change in skeletal muscle between the fourth and seventh decade than the whole-body muscle mass index (Francis, McCrmack et al. 2016; Francis, Toomey et al., 2016; Janssen et al., 2000; Lynch et al., 1999). In addition, findings suggest that women have a greater rate of decline in lower limbs than men between the fourth and seventh decade (4.9% to 5.75% vs 2.6% to 3.5% per decade; Francis, McCrmack et al. 2016; Francis, Toomey et al., 2016; Janssen et al., 2000; Lynch et al., 1999). The knee extensor muscles of the thigh decrease in a greater proportion than the knee flexor (Frontera et al., 2008; Maden-Wilkinson et al., 2013; Ogawa et al., 2012).

Cross-sectional research using both direct measurement in cadavers and in vivo biopsy techniques has shown that muscle catabolism is different in different types of muscle fibers. In general, type II fibers (fast fibers) are more susceptible to the age-related changes

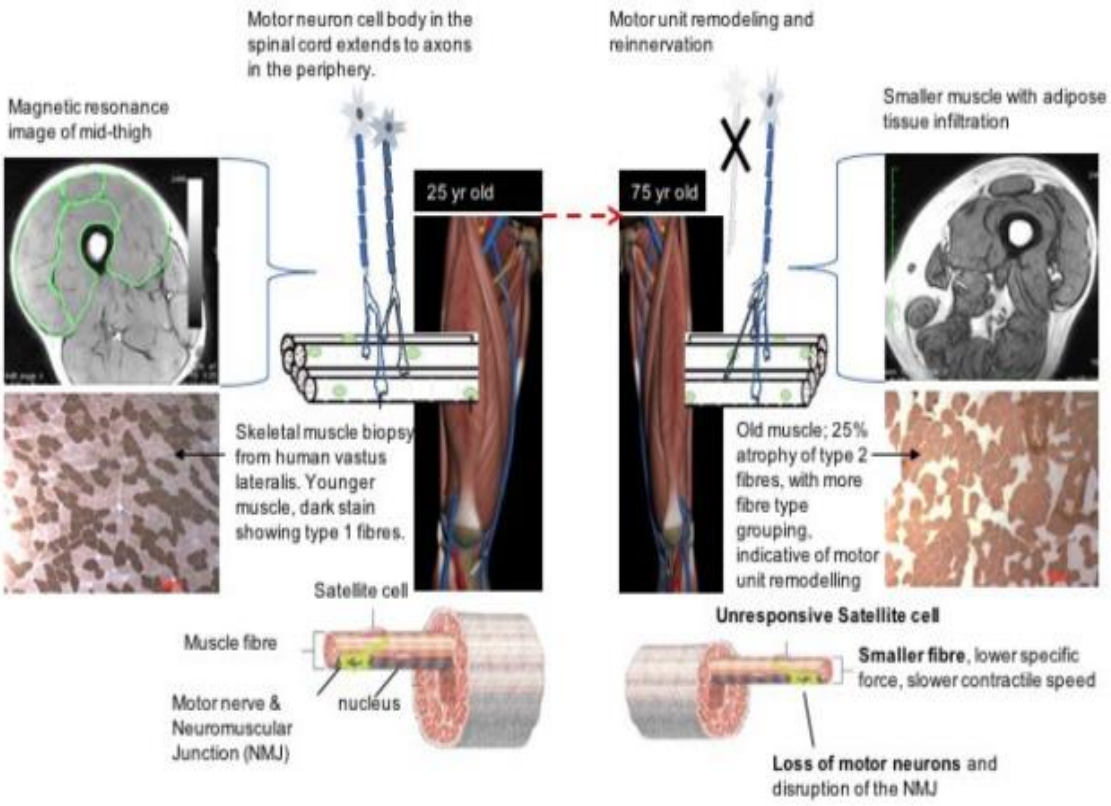
than type I fibers (slow fibers; Clarkson et al., 1981; Klitgaard et al., 1990; Lexell et al., 1988). In fact, muscle atrophy occurs to a greater extent in type II fibers with age, showing a fiber size measured via CSA to be 10% to 40% smaller in older adults as compared to young individuals (Frontera et al., 2000; Idland, Syllias et al., 2013; Pamuk et al., 2014). Type I fibers, however, do not change significantly with age (Martel et al., 2006; Snikders et al., 2009). Thus, even in elderly subjects, type I fibers tend to maintain their CSA and their size, (Lexell et al., 1988, 1995; Nilwik et al., 2013; Verdijk et al., 2007). In contrast, some studies have found no reduction in type II fiber size (Frontera et al., 2000; Lexell et al., 1983). However, aging leads to a general reduction in the number of muscle fibers, causing reductions in both types of muscle fibers (Lexell et al., 1983, 1988), but it especially reduces type II fibers (Bougea et al., 2016). Despite the observed changes in muscle fiber size, there is not yet a clear understanding of how age is associated with the loss in the number of muscle fibers (Nilwik et al., 2013). It seems that the major underlying cause for muscle fiber loss is the loss of motor units (Faulkner et al., 2007).

As we can see, skeletal muscle mass undergoes numerous changes during adult aging. The two most relevant changes are the loss of muscle size and the loss of muscle fibers. However, age-related changes in skeletal muscle mass may be attributable to a variety of mechanisms and process that are also contributors of muscle atrophy.

Although many of them remain of unknown origin, scientific progress has been elucidating others (Bonaldo & Sandri 2013; Rudrappa et al., 2016; Sandri et al., 2013). These include changes in the nervous system (clustering of type I fibers, decline of motor units, muscle fiber denervation, remodeling of motor units, loss of α-motoneurons, incomplete reinnervation of previously denervated muscle fibers, decreased rate of axonal transport, degeneration of neuromuscular junctions; Aagaard et al., 2010; Alchin, 2014; Doherty & Brown, 1993; Doherty et al., 1993; Gonzalez-Freire et al., 2014; Kanda &

Hashizume, 1989; Kostek & Delmonico, 2011; McComas et al., 1971), changes in muscle satellite cells (decreases in the number of muscle satellite cells or stem cells and changes in their capacity to regenerate; Kadi et al., 2004), changes in muscle structure (decreases in muscle thickness, pennation angle, the length and obliquely of the fascicle; Kubo et al., 2003a; Narici et al., 2003), changes in vascular system (decreases in muscle capillary density, changes in the endothelial wall function and the central arterial compliance; Gonzalez-Freire et al., 2014), changes in muscle metabolism (decreases in mitochondrial number and function and changes in protein synthesis; Bougea et al., 2016; Dardevet et al., 2000; Hasten et al., 2000; Marzetti et al., 2013; Rooyackers et al., 1996) , increases of oxidative stress (Marzetti et al., 2013; Semba et al., 2007), low grade chronic inflammation in aging, or "inflammaging," (increases in chronic concentration of IL-6; Baylis et al., 2014; Kalinkovich & Livshits, 2017; Schaap et al., 2009), changes in anabolic hormones (decreases in the levels and sensibility of anabolic hormones, such as testosterone, estrogen, growth hormones, dehydroepiandrosterone, insulin-like growth factor, the expression of gene transcription co-activator protein; Kang, 2013; Louard et al., 1992; Maltais et al., 2009; Phillips et al., 1993), decreased levels of physical activity and protein intake (Lexell et al., 1988; Sandri, 2008; Signorelli et al., 2006; Valenzuela et al., 2019), apoptosis (Degens & Always, 2006), and changes in adiposity **(**increases in the accumulation of non-contractile components, including intramuscular, intramyocellular fat and connective tissues, and decreases in the activity of lipoprotein lipase enzyme; Alchin, 2014; Alnaqeeb et al., 1984; Hamilton, Areiqat et al., 2001; Kent-Braun & Ng, 2000; Kostek & Delmonico, 2011; Yoshiko et al., 2017; Figure 52). Women aged 65 to 80 years old have twice the amount of non-contractile muscle tissue per unit of CSA as compared to younger women aged 23 to 57 years old (Jubrias et al., 2997).

Figure 52. *Comparison between young and old skeletal muscle*.



Note. Reproduced and adapted from from "Age-dependent motor unit remodelling in human limb muscles" (p. 494), by Piasecki et al., 2015, *Biogerontology, 17*(3).

For most elderly people, these structural changes in muscles contribute to the loss of muscle function. Causing equal or even greater declines than muscle mass, these structural changes also effect muscle strength (Frontera et al., 1991; Goodpaster et al., 2006; Young et al., 1985) and rate of force development (da Rosa Orssatto, Wiest, Diefenthaeler, 2018). The effect is mainly due to the preferential loss in number and size of type II fibers and α-motoneurons.

Despite the significant advances in the field of muscle aging, many questions remain, especially concerning the roles of training intensity and modality on both muscle mass and function in elderly subjects, and particularly in older women.

D. Methods to assess skeletal muscle mass

A wide range of techniques and tools are available for valid and reliable measurements of muscle mass in the elderly. Availability, cost, and ease of use can determine which techniques are better for clinical contexts or research contexts. Body imaging techniques have been widely used for estimating muscle mass or lean body mass, and some of the available options are CT, MRI, DXA, and muscle ultrasonography (Cawthon et al., 2015; Cruz-Jentoff et al., 2010, 2019; Francis et al., 2017; Mijnaredns et al., 2013; Tosato et al., 2017; Yu et al., 2014).

CTs and MRIs are considered to be gold standards for non-invasive assessment of muscle mass, especially in research (Beaudart et al., 2016). These body imaging techniques are able to provide additional information through the detection of smaller changes in the muscle mass and the ability to distinguish fat from other soft tissues in the body, like skeletal muscle, or other non-muscle fat-free components, such as connective tissue (Delmonico et al., 2008; Levine et al., 2000; Mitsiopoulos et al., 1998; Wang et al., 1996). However, the high cost, high radiation, limited accessibility, lack of portability, requirement for highly trained personnel to use the equipment, and the lack of consensus for the cut-off points to determine low muscle mass in the diagnosis of sarcopenic individuals make CTs and MRIs less useful tools in clinical settings (Beaudart et al., 2016; Cooper et al., 2013; Cruz-Jentoff et al., 2019; Mclsaac et al., 1998; Sierra et al., 2008).

DXA has been found to be a valid, reliable, non-invasive, cost effective instrument for quantifying whole body and appendicular (regional) skeletal muscle mass with a minimal to low radiation dose (Cruz-Jentoff et al., 2019; Haarbo et al., 1991; Levine et al. 2000; Mijnarends et al., 2013; Tothill, 1995; Wang et al. 1996). Moreover, DXA is the most widely used instrument in both research and clinical approaches (Cruz-Jentoff et al., 2019; Yu et al., 2014). It also has a strong correlation with CTs and MRIs ($r = 0.88$; Francis et al., 2017;

Mijnarends et al., 2013). Nonetheless, it is necessary to be cautious using DXA because it can sometimes overestimate the whole body and regional values of skeletal muscle mass (Francis et al., 2017). DXA estimates the total amount of lean tissue, but it does not directly measure muscle mass (Cawthon et al., 2015). It is also unable to provide information on visceral or intramuscular fat, which account for approximately 15% of the measured muscle mass (Plank, 2005).

Regarding the sarcopenic approach, the most common indexes for measuring the muscle mass represented in the DXA scans are total body skeletal lean mass (SLM; also called skeletal muscle mass, SMM), appendicular lean mass (ALM, also called ASM) derived from DXA scans, which is the sum of the lean tissue in the arms and legs excluding fat and bone tissue, or the ALM scaled to height squared (ALM/height^2), body mass index (ALM/body mass index), or weight (ALM/weight)(Cawthon et al., 2014, 2015; Cooper et al., 2013; Heymsfield et al., 1990; Kim et al., 2016; Maden-Wilkinson eta al., 2013). Currently, there is an ongoing debate about which index is the preferred adjustment and whether the same method can be applied for different populations.

An advantage of DXA is that it can provide a reproducible estimate of ALM in only a few minutes when using the same instrument. Furthermore, there is a relative consensus on the cut-off points for estimating low muscle mass in older adults (Cruz-Jentoff et al., 2019). However, the main disadvantages to DXA are that is not portable and the measurements can be influenced by the hydration status of the subject (Cruz-Jentoff et al., 2019).

According to a recent systematic review, ultrasonography appears to be a valid, non-invasive, and practical tool for the assessment of muscle mass in elderly individuals (Nijholt et al., 2017; Ticinesi et al., 2017). This approach assesses the thigh muscles due to the quantity and quality of the muscle mass of this region and because this region has been

proven to predict the risk of rehospitalization, functional decline, and death in older adults (Guerreiro et al., 2017).

Other techniques, such as bioelectric impedance analysis (BIA) in single or multifrequency modality, anthropometric measurements (calf circumference, skin-fold thickness, mid-upper arm circumference), and the assessment of muscle mass via the air displacement plethysmography throught the BOD POD have also been widely used (Cawthon et al., 2015; Cruz-Jentoff et al., 2010, 2019; Francis et al., 2017; Mijnaredns et al., 2013; Tosato et al., 2017; Yu et al., 2014). Despite the fact that these methods are very easy to use, portable, and continue to be widely used (especially BIA and anthropometric measurements in the clinical settings) the prediction equations are not always as accurate as DXA, especially in overweight older adults (Ramsey et al., 2012).

Finally, other techniques based on biochemical markers for muscle mass estimation include total or partial body potassium per fat-free soft tissue, serum and urinary creatinine, deuterated creatine dilution method, isotope dilution. Further additional techniques are neutron activation and electrical impedance myography. These methods are rarely used today, especially in clinical practice, because they are expensive, invasive, and involve radiation (Cooper et al., 2013). To consult the reliability and validity of the mentioned methods, and to deepen understanding of their usefulness see the reviews of Mijnarends et al. (2013) and Tosato et al. (2017).

E. Exercise-related effects on skeletal muscle tissue

i. Effects of resistance training and variable resistance on skeletal muscle tissue[6]

Over the last 30 years, numerous studies have examined the effects of resistance training on measures of muscle hypertrophy and morphology in older adults. Resistance training is probably the most widely recognized training strategy to combat age-related muscle atrophy and improve muscle health in this population (Borde et al., 2015; Csapo & Alegre, 2016; Lavin et al., 2019; Peterson et al., 2011; Sueta et al., 2008).

The growing literature has confirmed with high-quality evidence (Beckwée et al., 2019) the effectiveness of resistance training in improving muscle mass among the elderly and, specifically, older women (Beckwée et al., 2019; Borde et al., 2015; Buch et al., 2017; Csapo & Alegre, 2015; Johnston et al., 2008; Morley, 2007: Peterson et al., 2011; Theodorakopoulos et al., 2017; Yoshimura et al., 2017). Many studies have examined the effect of resistance training on measures of total and appendicular lean mass (Balagopal et al., 1997; Binder et al., 2005; Frontera et al., 2003; Häkkinen et al., 1996; Roth et al., 2001; Sipilä & Suominen 1995; Welle et al., 1993, 1994; Yarasheski, 2003, 1993). Studies have also investigated the effect of resistance training on CSA in older adults (Bemben et al., 2000; Kryger & Andersen, 2007; Roth et al., 2001), as well as changes in muscle fibers

[6] Related publications:

1. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

2. Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High- and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press).*

3. Fritz, N. B., Juesas, Á., Gargallo, P., Calatayud, J., Fernández-Garrido, J., Rogers, M. E., & Colado, J. C. (2018). Positive effects of a short-term intense elastic resistance training program on body composition and physical functioning in overweight older women. *Biological Research for Nursing, 20*(3), 321-334. https://doi.org/10.1177/1099800418757676

(Frontera et al., 1988; Häkkinen et al., 1998, 2001; ; Kryger & Andersen, 2007). Most of the research has found significant or nonsignificant improvements in these parameters. The heterogeneity of the results may be due to the effectiveness of resistance training on muscle size in the elderly population. The inconsistency across the results could also be due to the muscles analyzed (Häkkinen et al., 2001), muscle length (Häkkinen et al., 2001; Reeves et al., 2004), the type of technique used, (Reeves et al., 2004), and the sex and age of the participants (Peterson et al., 2011).

In attempts to collect all of this information, several reviews and meta-analyses have been performed (Beckwée et al., 2019; Buch et al., 2017; Csapo & Alegre, 2016; Peterson et al., 2011; Theodorakopoulos et al., 2017; Yoshimura et al., 2017). The meta-analysis by Peterson et al. (2011) has revealed that resistance training with a mean training period of 20.5 weeks, three training sessions per week, an intensity of 75% of the 1 RM, two to three sets of ten repetitions with a 110-second rest between sets was effective enough to significantly increase muscle whole body mass in older adults (both in men and women) an approximate 1 kg (weighted pooled estimate 1.1 kg; 95 % CI = 0.9 to 1.2; data derived from 49 studies, 81 cohorts, 1328 participants, men and women aged 65.5 ± 6.5 years). Regarding lean body mass, results from the meta-regression did not identify any significant relationships between program duration, intensity or frequency, and subsequent changes in lean body mass.

In addition, authors have suggested that a higher volume created by a higher number of sets per session were associated with significantly greater increases in lean body mass (Peterson et al., 2011). As older individuals experienced less increase, researchers concluded that resistance training results in superior effectiveness when it is introduced as early as possible. These gains in muscle mass can compensate for the nearly 0.2 kg annual decline that may occur from sedentary lifestyles beyond 50 years of age (Delmonico et al., 2009).

Thus, resistance training may allow for greater preservation of muscle function and independence.

A recent systematic umbrella review by Beckwée et al. (2019) included 14 systematic reviews and a meta-analysis in their investigation of the effects of different exercise interventions in the prevention and treatment of sarcopenia. The authors arrived at the conclusion that resistance training has a positive and significant effect on muscle mass in older adults, while nutritional supplementation in addition to resistance training was not recommended. Data from the meta-analysis by Vlietstra and Hendrickx (2018) are in accordance with the meta-analysis by Peterson et al. (2011) and Beckwée et al. (2019), as they suggest that resistance training significantly improves the appendicular muscle mass and leg muscle mass in older adults with sarcopenia.

The meta-analysis by Borde et al. (2015) has suggested that resistance training has small effects on measures of muscle morphology (mean SMD = 0.42; nine studies). However, the meta-analysis established the most effective dose-response characteristics of the resistance training program for improving muscle morphology in healthy older adults. According to the study, the resistance training program has to be composed of a training period of 50 to 53 weeks with a training frequency of three sessions per week, a training volume of two to three sets per exercise, seven to nine repetitions per set, a training intensity from 51% to 69% of the 1 RM, a total time under tension of 6.0 s, a rest of 120 s between sets, and a rest of 2.5 s between repetitions. Moreover, the meta-regression revealed that none of the examined training variables of volume (e.g., period, frequency, number of sets, and number of repetitions) predicted the effects of resistance training on measures of muscle morphology. The narrative reviews by Mayer et al. (2011) and Petrella & Chudyk (2008) recommended the following dosage of resistance training variables to prevent the loss of muscle mass in the elderly: a training period of 8 to 12 weeks with three training sessions per

week, training intensities of 60% to 80% of 1 RM, and three to four sets with 8 to 12 repetitions per exercise. Finally, to improve muscular mass and strength and avoid sarcopenia in the elderly, the ACSM recommends resistance training two to three times a week composed of eight to ten exercises, with one to three sets of 8 to 15 repetitions at 60% to 80% of one 1 RM (Chodzko-Zajko, 2009; Garber et al. 2011).

In their network meta-analysis, Lai et al. (2018) found no significant differences between the effects of exercise (resistance training, whole-body vibration, endurance training) or usual care on lean body mass in older people. However, resistance training was associated with the largest increase of lean mass.

Regarding sex, while some studies have reported similar gains among sexes (Häkkinen et al., 1995, 1996; Leenders et al., 2013; Tracy et al., 1999), others have shown that men have greater improvements in muscle mass from resistance training than women (Bamman et al., 2003; Da Boit et al., 2016; Ivey, Roth et al., 2000; Joseph et al., 1999). These findings are particularly noteworthy for later postmenopausal and older women who tend to have lower amounts of lean body mass than older men (Jankowski et al., 2008; Valentine et al., 2009).

It should be noted that resistance training has also been found to increase CSA of type II muscle fibers in older women (Häkkinen et al., 2001; Leenders et al., 2013). In some cases increases were greater than 20% (Charette et al., 1991; Leenders et al., 2013). However, some studies have found that the training-induced increase in muscle mass of older women may be attenuated relative to the change in younger women (after 6 months of resistance training, 0.7kg vs 1.2 kg, respectively; Dionne et al., 2004; Lemmer et al., 2001). Although in older women the magnitude of change is lower, these kinds of interventions are necessary to at least preserve or decrease the age-related decline of muscle mass in this population.

Moreover, maintaining skeletal muscle mass, especially in the lower body, may be critical, as evidence from a study found that the leg lean mass and total body weight ratio have a significant association with physical function only in older women and not in men (Valentine et al., 2009). Thus, women with greater leg lean mass to total body weight have a significantly better physical function.

Notably, little is known about the effects of elastic band training on muscle hypertrophy in older adults. Nonetheless, several studies have demonstrated that resistance exercises involving elastic bands are effective in increasing lean mass in older people (Aniansson et al., 1984; Colado & Triplett, 2008; Colado et al., 2009; Egaña et al., 2010; Flandez et al., 2020; Fritz et al., 2018, 2021; Kraemer et al., 2001; Liao et al., 2018; McNee et al., 2009; Morse et al., 2005; So et al., 2013; Thiebaud et al., 2013; Yasuda et al., 2015; Yasuda et al., 2016; Park et al., 2016). It is true that mixed results have been reported by several studies, and some have shown no significant differences in the fat-free mass parameter (Coelho-Júnior et al., 2019; Kraemer et al., 2001; Lubans et al., 2013; Martins, Safons et al., 2015; Oh et al., 2016; Skelton et al., 1995). This fact has been highlighted very recently in the review of Colado and colleagues (Colado, Mena et al., 2020).

Among the studies that found positive results, the study by Fritz et al. (2018) reported that after eight weeks of elastic resistance training (twice a week, six overall body exercises, and three to four sets of 10 repetitions at an RPE of 7 to 9 on the OMNI-RES scale) performed with traditional elastic bands or with elastic handle devices (for the group of overweight older women), both training groups significantly increased fat-free mass in the upper limbs, and the traditional elastic band group also improved in trunk lean mass. In addition, 72.72% of the participants in the traditional group and 66.66% of the participants in the handle elastic band group showed clinically significant increases in fat-free mass (Fritz et al., 2018), whose cut-off point is located at an increase of 1.6% of lean mass (Donnelly et al.,

2009; Romero-Arenas et al., 2011; Santos et al., 2017). In contrast to the findings by Fritz et al., other authors who also applied an elastic resistance training program in postmenopausal and older women found no significant results (Coelho-Júnior et al., 2019; Liao et al., 2018; Thiebaud et al., 2013).

Based on the current evidence of prevention and treatment of muscle mass loss related to age, more attention needs to be given to resistance training programs that use variable resistance in older adults. More research in this area will help to find the training parameters that produce the minimum and significant benefits for muscle mass in untrained older adults and older women.

ii. Effects of exercise intensity on skeletal muscle tissue[7]

It is well known that performing regular resistance training can counteract the age-muscle loss and improve body composition of older adults (Raymond et al., 2013; Steib et al., 2010). To produce these desirable training adaptations, world-leading organizations in exercise-related research such as ACSM and American Heart Association (AHA) (Chodzko-Zajko et al., 2009; Peterson & Gordon, 2011) have recommended that older adults have to engage at least twice a week progressively in muscle strengthening activities at moderate to vigorous intensity (Chodzko-Zajko et al., 2009; Peterson & Gordon, 2011) to prevent loss of muscle mass. Such intensities coincide with subjective intensity at a scale or perceived exertion of 5 to 6 to 7 to 9 on a scale of 0 to 10 or with objective loads equivalents to approximately 60 to 80% to > 80% of the individual 1 RM with a wide range of repetitions per set in base of the load selected (Chodzko-Zajko et al., 2009).

[7] Related publication: Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High-and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press)*

Several studies and meta-analyses support these recommendations and confirmed that training at moderate to high intensities is associated with relatively greater gains in muscle mass (Bemben et al., 2000; Campbell, 1994; Cassilhas et al., 2007; Csapo & Alegre, 2016; Fatouros et al., 2005; Fiatarone et al., 1990; Frontera et al., 1988; Kalapotharakos et al., 2004; Kemmler, von Stengel, Engelke, Häberle, Mayhew & Kalender, 2010; Nickols et al., 1993; Onambélé-Pearson et al., 2010; Peterson et al., 2010; Steib et al., 2010; Silva et al., 2014; Treuth et al., 1994; Van Roie et al., 2013; Vincent et al., 2002) **,** muscle CSA (Fiatarone et al., 1994; Hurley et al., 1995; Roth et al., 2001), and muscle fiber area (Charette et al., 1991; Frontera et al., 1991; Fry, 2004; Roth et al., 2001) in older adults.

However, although there is a consistent evidence about that higher intensities lead to greater improvements in muscle mass in the elderly (Csapo & Alegre, 2016), in recent years some authors have questioned whether strength and muscle mass gains would also be achievable with lighter load resistance training programs (Burd et al., 2013; Schoenfeld, 2013a; Schuenke, Herman, Gliders et al., 2012, Schuenke, Herman & Staron, 2012) and it seems is possible at least in previous untrained individuals (Bemben et al., 2000; Burd et al., 2010; Mitchell, Churchward-Venne et al., 2012; Pruitt et al., 1995; Schoenfeld, 2013b; Taaffe et al., 1996). The key might be to equalize the total mechanical work in terms of volume and the training-induce fatigue, being no relevant the training intensity if the total work is the same. As Schoenfeld et al. (2017) has postulated in their recent meta-analysis, muscle hypertrophy can be equally achieved across a spectrum of loading ranges which it called "hypertrophy continuum".

In addition, in a recent study of Stec et al. (2017) authors found that the group which trained three days a week at high intensities achieved lower gains in total body lean mass and thigh muscle mass than the group which introduce a lower intensity session instead a high

intensity in the midweek. This finding highlight that recovery must be consider as carefully as intensity when design exercise programs for older adults.

Finally, it is necessary to mention the results showed by Csapo & Alegre (2016) in the only meta-analysis that compares the efficacy of heavy (~80% 1 RM) vs light-moderate load (~45-60% 1 RM) resistance training programs in inducing skeletal muscle hypertrophy in elderly people (15 studies included, 448 subjects, mean age of 67 years of age). They found that both high and lower intensities provoke only minor increases in total muscle size, with increases of 11% and 9%, respectively, which indicates that the hypertrophic potential of skeletal muscles is blunted at older ages, but that muscle hypertrophy can be achieve with both low and moderate to high intensities (Csapo & Alegre, 2016). Moreover, in the position statement from the NCSA (Fragala et al., 2019), authors mentioned that moderate intensities of 51% to 69% of 1 RM yield larger effects than either lower or higher intensities on muscle morphology in base of the results found in the meta-analysis of Borde et al. (2015).

In base of the current evidence, it seems muscle mass can be improve in older adults by a high spectrum of loads when a resistance training program is applied, being moderate intensities who maybe achieve greater adaptations

iii. Effects of exercise modality on skeletal muscle tissue[8]

While there is a very large number of studies that highlight the benefits of resistance training, the most beneficial modality to reduce the prevalence of low muscle mass and the onset of sarcopenia in the elderly population still has to be defined. In fact, only a few studies have assessed the effect of different training modalities on muscle mass in older adults, and

[8] Related publication: Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

even fewer in postmenopausal and older women, where decrements of muscle mass are mainly apparent due to the hormonal deficits associated with menopause (Calmes et al., 1995) and not all exercise interventions can have positive findings.

Focusing on multi-component training, several authors have studied its influence on muscle mass in postmenopausal (Chien et al., 2000; Marín-Cascales et al., 2015, 2017; Park et al., 2015; Rossi et al., 2016) and older women (Bernabei et al., 2014; Calvani et al., 2013; de Resende-Neto et al., 2019; Grassi et al., 2014; Kemmler, von Stengel, Engelke, Häberle, Mayhew & Kalender, 2010; Landi et al., 2015). The results indicate conflicting findings in postmenopausal women but especially at older ages, as some studies found increments in muscle mass (de Resende-Neto et al., 2019; Grassi et al., 2014; Kemmler, von Stengel, Engelke, Häberle, Mayhew & Kalender, 2010; Marín-Cascales et al., 2015; Rossi et al., 2016), whereas others reported no significant changes (Bernabei et al., 2014; Calvani et al., 2013; Chien et al., 2000; Landi et al., 2015; Marín-Cascales et al., 2017; Park et al., 2015). This conflicting evidence is likely due to the heterogeneity in the training parameters, the length of the training period, the characteristics of the participants (age, basal conditions, and comorbidities) and the regions assessed between studies. The small number of studies available makes these differences more noticeable.

Despite it not being fully clear whether multi-component training is able to improve muscle mass in postmenopausal and older women, it seems, based on the results from the review by Marín-Cascales et al. (2017), that those multi-component training programs that combine resistance training using high-intensity loads and impact aerobic activities may be the most optimal to enhance muscle mass in this population. In addition, in the very recent systematic umbrella review by Beckwée and colleagues (2019), the authors recommended multimodal exercise therapy to improve muscle mass in older adults, with a moderate quality of evidence, due to various systematic reviews, reporting significant effects of multimodal

exercise programs on sarcopenia in healthy older adults (Bibas et al., 2014; Dublicate et al., 2017; Liberman et al., 2017).

By comparison, progressive traditional or low-velocity (at least 2s for each movement phase) resistance training, especially at high intensities, has been recommended for older adults to improve lean mass in the last decades (Binder et al., 2005; Fiatarone et al., 1990; Kalapotharakos et al., 2004; Chalé et al., 2012). However, despite the great effects on muscle mass that can be achieved with this type of training modality, some evidence suggests that high-velocity resistance training results in greater benefits than traditional low-velocity resistance training for increasing lean mass (Henwood et al., 2008; Reid et al., 2008). However, to date, the results remain inconsistent (Binns et al., 2017; Coelho-Júnior et al., 2019; de Resende-Neto et al., 2019; Gray et al., 2018; Henwood et al., 2008; Reid et al., 2008; Stec et al., 2017), with the main problem being the lack of data directly comparing both training modalities in the same study. Very recently, a meta-analysis by da Rosa Orssatto and colleagues (da Rosa Orssatto et al., 2020) found that power training is effective to induce muscle hypertrophy in older adults to a similar extent to moderate-velocity resistance training (da Rosa Orssatto et al., 2020).

Despite the lack of evidence to date, it is believed, from a physiological point of view, that power training can act to improve muscle mass by reducing the high threshold activation of large motor units, in response to the high velocity of concentric contraction, regardless of exercise intensity (Kraemer et al., 1996), while high-intensity resistance training would act to induce the recruitment of large motor units, and, consequently, type II muscle fibers, base on the size principle (Mendell, 2005), where the size of the recruited motor unit increases according to the muscle tension generated during contraction.

In conclusion, further investigations are necessary to determine the optimal training modality to improve the age-related loss of muscle mass in the elderly population, especially in older women.

II.VII.III. Adipose tissue

A. Adipose tissue physiology

Along with bone and muscle, adipose tissue is the third main component of the human body composition and plays a key role in numerous biological pathways, especially in the aging process. This section details the characteristics of the adipose tissue and the main findings of the effects of exercise on this tissue in the elderly population.

i. Adipose tissue structure and characteristics

Traditionally, adipose tissue, also named body fat or fat mass, has been defined as loose connective tissue that constitutes an organ for storing excess calories and for releasing free fatty acids to fuel the energy demands of the human organism (Birbrair et al., 2013; Scherer, 2006; Rosen & Spiegelman, 2014). However, in recent years, scientists have discovered that adipose tissue is also an endocrine organ, one of the largest of the body, being present in a wide range of biological pathways of many human processes (Fain et al., 2004; Ibrahim, 2010).

Adipose tissue contains different cell types that can be categorized as adipocytes and non-adipocyte cells (van Meijel et al., 2019). The latter comprise, collectively, the stromal vascular fraction of adipose tissue which is composed of preadipocytes, fibroblast, vascular endothelial cells, nerve cells, and a diverse number of immune cells such as macrophages, leukocytes, lymphocytes, mast cells, eosinophils, neutrophils, and foam cells (Unamuno et al., 2018; Rodríguez et al., 2015; Tsiloulis & Watt, 2015; van Meijel et al., 2019), with

various interplays among them and contributing to the main functions of the adipose tissue (Lynes & Tseng, 2017).

However, adipocytes, which are differentiated fibroblasts, comprise the largest proportion of cells present within adipose tissue (Garrow, 1982). Adipocytes originate from mesenchymal stem cells and differentiate into preadipocytes, that is, adipose tissue derived from these preadipocytes when large amounts of them cluster together (van Meijel et al., 2019). The majority of lipids are stored in adipocytes. It is important to note that in mammals three types of adipocytes or adipose tissues have been distinguished: these differ in their origin, morphology, function and location: white, brown and beige or "brite" (brown in white) (Frühbeck et al., 2009).

White adipocytes are by far the most abundant fat cells and are characterized by containing a single unilocular lipid droplet surrounded by a layer of cytoplasm, with a small number of mitochondria with a low oxidative rate and a well-vascularized system (Jeanson et al., 2015; Luo & Liu, 2016). Their metabolic functions are determined by their different human anatomical locations (Kusminski et al., 2016; Lee et al., 2013), with the central intra-abdominal and peripheral areas (visceral and subcutaneous adipose tissue depots, respectively) being the most common (Unamuno et al., 2018).

Brown adipocytes, by comparison, are cells that contain many mitochondria with high oxidative capacity which is responsible for its brownish color (Unamuno et al., 2018). In addition, they have small lipid droplets in a multilocular pattern and are highly vascularized and innervated by the sympathetic nervous system, promoting their function (Lynes & Tseng, 2017; Park, 2014). Brown adipose tissue is mainly located in the supraclavicular area, the ventral neck, the mediastinum, and paravertebral and suprarenal fat (Schulz, Huang et al., 2010; Virtanen et al., 2009). Finally, very recently, beige adipose tissue has been proposed

(Wu et al., 2013), but little is still known about it, only that there is a "browning" process of the white adipocytes due to sustained thermogenic activation induced by prolonged cold exposure, exercise or environmental enrichment (Siersbæk et al., 2012 Schulz, Huang et al., 2010; Wu et al., 2012). In fact, it is still unknown in which human adipose tissue depots are located (Elabd et al., 2009; Harms & Seale, 2013).

Regarding the location of adipose tissue, in humans it is located in several anatomical locations. These include subcutaneous adipose tissue (beneath the skin), which stores 80% of total body fat, mainly in the lower (gluteal-femoral depot) and upper body (subscapular and abdominal fat depots) (Tsiloulis & Watt, 2015; van Meijel et al., 2019); and visceral adipose tissue (also called intra-abdominal), which is dispersed between the abdominal organs and composed of several adipose depots, including the omental, mesenteric, epididymal and retroperitoneal fat depots (kidney) (Tsiloulis & Watt, 2015; van Meijel et al., 2019), and together account for 20% of total body fat (Abate et al., 1995; Neamat et al., 2014). In addition, along with these two main storages of fat (subcutaneous and visceral), it is possible to find small amounts of fat in tissues other than adipose, such as bone, liver, the skeletal muscle, heart and pancreas. This is what is known as ectopic fat. Based on the distribution of the adipose tissue between the areas mentioned above, its molecular, morphological and metabolic responses will be different, for example increasing the risk of cardiovascular diseases when it is located in certain areas (visceral) (Tsiloulis & Watt 2015). In addition, the distribution of the fat mass is also different between men and women (Tsiloulis & Watt 2015) and it is necessary to take this into account to implement effective strategies.

ii. Adipose tissue function

Adipose tissue has important physiological functions. Its main and classical role is to store the excess of energy, derived from the diet and from liver metabolism, in the form of lipids (triglycerides) and also to release free fatty acids and glycerol (necessary to produce

ATP) via the process of lipolysis when other tissues are in need of energy, such as during exercise or states of fasting (Ahmadian et al., 2007). In addition to maintaining triglyceride and free fatty acid levels, adipose tissue also has thermal insulation properties, providing protection from heat and cold (Bohler et al., 2010; Fruhbeck, 2008). Moreover, it also provides protective padding to delicate organs and certain areas of the body exposed to high levels of mechanical stress (Yuan et al., 2015).

Regarding the specific functions of the three types of adipocytes, the major role of white adipose tissue is maintaining energy homeostasis through storing triglycerides and releasing free fatty acids for energy synthesis (Unamuno et al., 2018). By comparison, brown adipose tissue is highly specialized in adaptive thermogenesis and energy expenditure in mammals. It is a key regulator of thermogenesis by dissipating the stored energy in the form of heat, due to the presence of uncoupling protein 1 within the many mitochondria in these cells (Fedorenko et al., 2012; Wu et al., 2012). Lastly, beige adipose tissue possesses the functions of both white and brown adipocytes due to the fact that it normally stores energy but also has the ability to increase the expression of uncoupling protein 1 and become energy-releasing adipocytes (Harms & Seale, 2013). In addition, these adipocytes have a remarkable plasticity and can transform into white or brown adipocytes under specific conditions (Cinti, 2011).

iii. Adipose tissue metabolism

In addition to the functions of adipose tissue in lipid metabolism, in the past two decades it has been revealed that adipose tissue is a metabolically active endocrine organ with a key role in a wide range of biological processes, such as the regulation of food intake, blood pressure, immune and inflammatory response, bone health, angiogenesis and glucose and whole-body energy homeostasis (Catalán et al., 2009; Ilich et al., 2014; Sethi & Vidal-Puig, 2007), by secreting active molecules known as adipokines (Fain et al., 2004; Ibrahim, 2010).

To date a great number of adipokine- derived hormones have been described, but the most relevant ones include leptin, adiponectic, estrogen, resistin, and stradiol cytokine (especially TNFα) (Hoehn & Marieb, 2008; Unamuno et al., 2018). Leptin was the first to be discovered and is the most studied; it principally acts both centrally (hypothalamus) and in peripheral organs to regulate food intake and energy homeostasis (Klok et al., 2007).

B. Overweight and obesity

i. Definition and classification

The WHO defines overweight and obesity as the abnormal accumulation or excess of fat mass that can negatively affect health (WHO, 2000). Both conditions are chronic metabolic diseases characterized by an increase of body fat stores. This expansion of the adipose tissue is produced by the processes of adipocyte hyperplasia (increase in the number of fat cells) and adipocyte hypertrophy (increase in the size of fat cells) (Sun et al., 2011), although it has been postulated that during adulthood there are only small variations in the numbers of adipocytes, because this process is maximally achieved during childhood and early adulthood, when the hypertrophy of the fat cells is the main process (Arner et al., 2011; Spalding et al., 2008; Tchoukalova et al., 2010).

In clinical practice, the most commonly accepted categorization of body composition in relation to fat mass is the BMI-referenced classification provided by the WHO (WHO, 2000). According to this definition, in Caucasian adults (aged over 18 years), independent of age, the WHO defines the normal BMI range as 18.5 to 24.9 kg/m^2, whereas overweight (also termed "pre-obesity") is associated with a BMI between 25.0 and 29.9 kg/m^2 and adults with a BMI $\geq$ 30.0 kg/m^2 are considered obese (WHO, 2000). In addition, there are three grades of obesity based on its severity: grade I or moderate (BMI = 30.0–34.9 kg/m^2), grade II or severe (BMI = 35.0–39.9 kg/m^2) and grade III or very severe (BMI $\geq$ 40 kg/m^2) (WHO,

2000). Lower cut-off points apply to some ethnic groups, such as African Americans, Hispanics, Chinese Americans, and South-East Asian populations (James et al., 2008; WHO, 2000).

Nonetheless, even though BMI is a widely applied measure for categorizing weight status in both the clinical and research fields, its use is still controversial for several reasons and has been questioned, especially for older individuals (Seidell & Flegal, 1997; Stenholm et al., 2008). This index, also called Quetelet's index, is calculated by dividing a person's body mass in kilograms by their squared height in meters. Because it is very easy to calculate, it is widely used as an indicator of obesity. In younger adults, it correlates reasonably well with body fat; however, the accuracy of BMI as an obesity indicator has been addressed in older adults, mainly for two reasons (Coutinho et al., 2011; Rothman, 2008). On the one hand, it does not take body composition into account, as it is not an assessment of fat mass due to not differentiating between lean and fat tissues (Han et al., 2011; Ormsbee et al., 2014). Thus, in individuals with large muscle mass or in older adults who have lost large amounts of fat-free mass and increased the subcutaneous and intra-abdominal fat mass, its use may be inappropriate (DeCaria et al., 2012; Rothman, 2008). On the other hand, the prevalence of spinal shortening as a consequence of kyphoscoliosis or degenerative bone disease is high in older individuals, which induces a reduction in height and contributes to producing errors in the BMI accuracy (Han et al., 2011). In addition, age and gender cut-offs are not defined, so that the same limits are applied to all individuals.

It is currently being discussed whether the use of other available measures to assess fat mass, such as percentage body fat mass or waist circumference, would be more appropriate to defining and categorizing obesity (Cetin & Nasr, 2014; Han et al., 2011; Poggiogalle et al., 2014; Villareal et al., 2005). It seems that a more appropriate assessment, especially in older individuals, would be to assess the percentage body fat using the DXA.

However, although deemed necessary, there is still no consensus about the cut-off point for the classification of overweight and obesity for older adults. Considering the cut-off points by sex, age, and ethnicity published by Gallagher et al. (2000), values of 25% and 38% in white men and women, respectively, at 60–79 years of age were considered indicative of overweight, and values of 31% and 43%, respectively, were considered indicative of obesity in the same elderly population. The WHO has suggested setting obesity in older adults at values > 28% for men and > 40% for women (Baumgartner et al., 2004) while in other studies the cut-off point has been established as between 32% and 35% in older women (American Society of Bariatric Physicians, 2015; Ilich et al., 2015, 2016; Inglis et al., 2017; JafariNasabian, Inglis, Reilly et al., 2017; Liu, Ilich et al., 2014; Wanner et al., 2016).

to-hip ratio, have been used as an index of obesity risk and adiposity in older adults (Gallagher et al., 1996), due to the accumulation of intra-abdominal fat being associated with higher cardiovascular and metabolic disease risk (WHO, 2000; Zhu et al., 2002). The advantage of waist circumference is that it correlates highly with both total and intra-abdominal fat, being a direct indicator of abdominal obesity rather than BMI (Han et al., 2011). In addition, it is not influenced by height (Han et al., 1996). According to the WHO (WHO, 2000), central obesity is characterized by a waist circumference greater than 102 cm in men and greater than 88 cm in women (Lean et al., 1995; Pi-Sunyer, 2000), or a waist-to-hip ratio > 0.90 in men and > 0.80 in women (Center for Disease Control and Prevention, 2011). As a result, other body composition measurements rather than BMI which estimate fat mass would be more favorable as indicators of obesity. However, more research is necessary to designate an appropriate indicator of obesity in an aging population.

ii. Health consequences of overweight and obesity in the elderly

The excess of adipose tissue, particularly when obesity is reached, produces a chronic state of low-grade inflammation that adversely affects nearly all physiological functions of

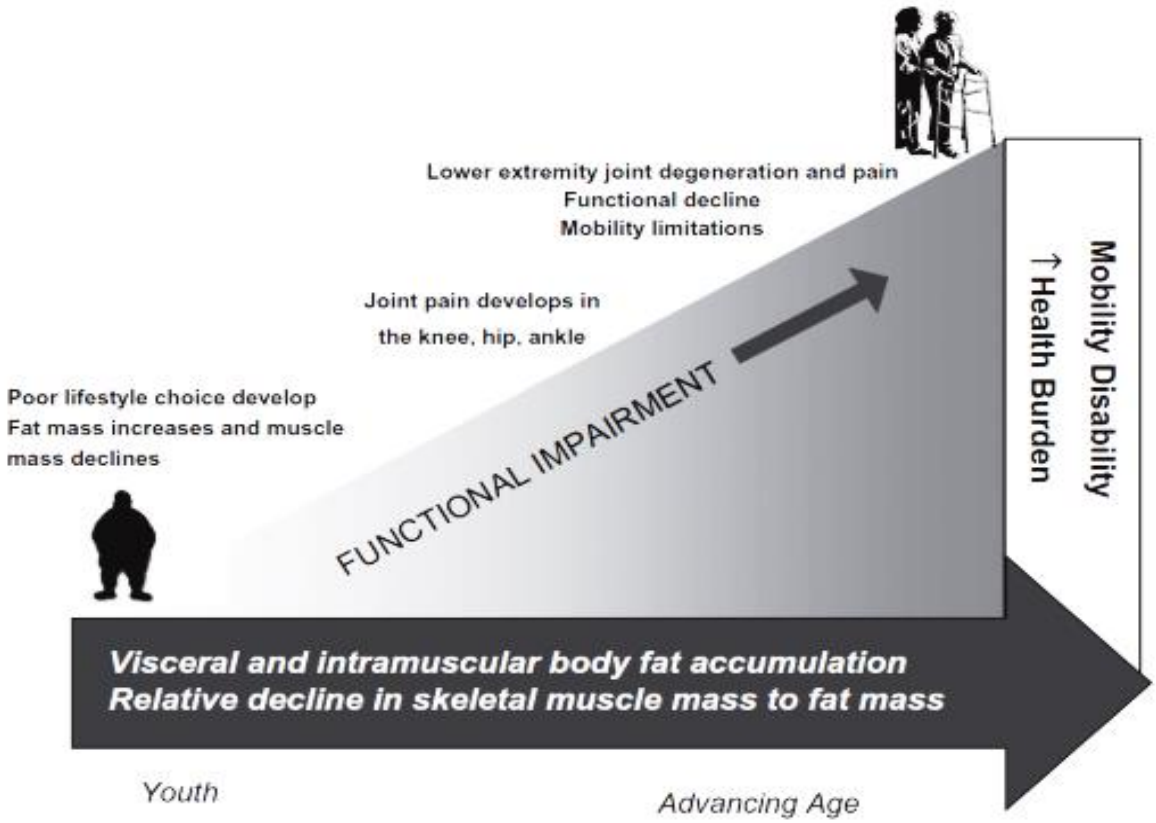
the human body (Wellen & Hotamisligil, 2003). Being overweight or obese increases the risk of developing multiple obesity-associated disease conditions, such as type 2 diabetes mellitus (Mokdad et al., 2003); dyslipidemia (Poirier et al., 2006); metabolic syndrome (Kopelman, 2000); insulin resistance (Kopelman, 2000); chronic liver diseases, such as nonalcoholic fatty liver and cirrhosis (Moore, 2010); obstructive sleep apnoea (Trayhurn, 2013); asthma (Schwartz et al., 2008); skin problems (Yosipovitch et al., 2007); urinary incontinence (Han et al., 2011); cardiovascular diseases (Czernichow et al., 2011; Singh et al., 2013), such as coronary heart disease, heart failure, ventricular dysfunction, cardiac arrhythmias (Klein et al., 2004), hypertension (Mokdad et al., 2003; Must et al., 1999), and cerebrovascular disorders (Landsberg et al., 2013; Van Gaal et al., 2006); several types of cancers (Calle & Kaaks, 2004; Lauby-Secretan et al., 2016; Picon-Ruiz et al., 2017); an array of musculoskeletal disorders (osteoarthritis, foot and ankle tendinitis, plantar fasciitis, low back pain and chronic lower extremity pain, arthritis) (Anandacoomarasamy et al., 2008); depression (Luppino et al., 2010); and cognitive decline (Anstey et al., 2011; Nguyen et al., 2014), all of which have negative effects on the quality of life and work productivity. All of these conditions have been confirmed in the elderly population (Han et al., 2011). In addition, obesity increases the risk of all-causes mortality (Flegal et al., 2013): it has been demonstrated that a BMI of 30–35 km/m^2 shortens life expectancy by 2–4 years, while an 8–10 year loss was associated with a BMI of 40–45 kg/m^2 (Berrington de Gonzalez et al., 2010). It is estimated that in 2010, overweight and obesity caused 3.4 million deaths in the entire world (Ng et al, 2014).

However, not only the total amount of fat, but also the distribution of body fat is one of the most important risk factors for the development of obesity-associated comorbidities (Rodríguez et al., 2007; Ibrahim, 2010), especially metabolic and cardiovascular disorders (Goossens, 2017). In fact, it is well established that intra-abdominal adipose tissue (central or

android distribution) is related to an increased risk of metabolic and cardiovascular diseases, such as diabetes, metabolic syndrome, dyslipidemia, insulin resistance and coronary heart disease, as well as an increased risk of morbidity and mortality (Moore, 2010; Trayhurn, 2013; Calle & Kaaks, 2004; Picon-Ruiz et al., 2017), whereas fat distributed around the hips, thighs, and buttocks (gynoid distribution) appears to pose less of a health risk compared to visceral fat (Hunter et al., 2000). The typical pattern of body fat distribution in females is the gynoid pattern, although in older ages the fat is also redistributed in the abdominal area, increasing the metabolic and cardiovascular risk of this population.

Along with the health consequences mentioned above, overweight and obesity are recognized as major risk factors for impairments of physical function, muscle strength, cardiovascular fitness and the capacity to perform activities of daily living in older adults (Han et al., 2011; Miller et al., 2013; Rejeski et al., 2010). Several studies have reported a relationship between declining mobility and adiposity, finding that chair rise, walking and stair-climbing activities were compromised with obesity, especially when BMI exceeded 35kg/m^2 (Stenholm et al., 2009; Vincent et al., 2010). Furthermore, ongoing research has demonstrated that obesity synergistically exacerbates the age-related decline in muscle mass and also the muscle quality, with the localized adipose tissue within and surrounding the muscle being responsible for this fact (Figure 53) (Delmonico et al., 2009; Goodpaster et al., 2000; Goodpaster et al., 2001). Therefore, overweight, and especially obesity, can lead to musculoskeletal fragility, increasing the risk of developing old age frailty by five times compared to healthy weight individuals (Stenholm et al., 2013).

Figure 53. *Graphic description of the hypothetical model of the development of mobility disability condition throughout life due to the excess of total and regional body fat mass.*



Note. Reproduced from "Obesity and mobility disability in the older adult" (p. 576), by Vincent et al., 2010, *Obesity Reviews, 11*(8).

iii. Pathophysiology

It is known that overweight and obesity are complex multifactorial disorders (Haslam & James, 2005; Yanovski & Yanovski, 2002) and, thus, much research has been conducted in order to identify the mechanisms and factors that give rise to these health problems (Bakr et al., 2002; Chaput et al., 2010; Greenfield & Campbell, 2008). However, they are still not fully understood (Unamuno et al., 2018). At a simple level, overweight and obesity are physical states resulting from a chronic period of energy imbalance in favor of dietary energy intake (meals) over energy expenditure (physical activity). This process is accentuated in the

elderly, due to the loss of muscle mass and aging per se which results in a lower basal metabolic rate (Han et al., 2011), and also because the decreased energy expenditure and decreased physical activity that accompany aging predispose a person to fat accumulation (Stehr & Lengerke, 2012).

However, this simple rule is involved with complex interactions, including both external and internal factors, such as environmental, behavioral, physiological, social, metabolic and inherited (genetic and epigenetic) factors (Haslam & James, 2005; Farooqi & O'Rahill, 2006; Guyenet & Schwartz, 2012; Kaila & Raman, 2008; van Meijel et al., 2019). In addition, changes in endogenous hormones and neurohumoral modulators of appetite, such as oestrogens, testosterone, insulinlike growth and leptine, are also involved (Han et al., 2011). In fact, at least 137 factors have been identified that are involved in overweight and obesity metabolic disorders (Vandenbroeck et al., 2007).

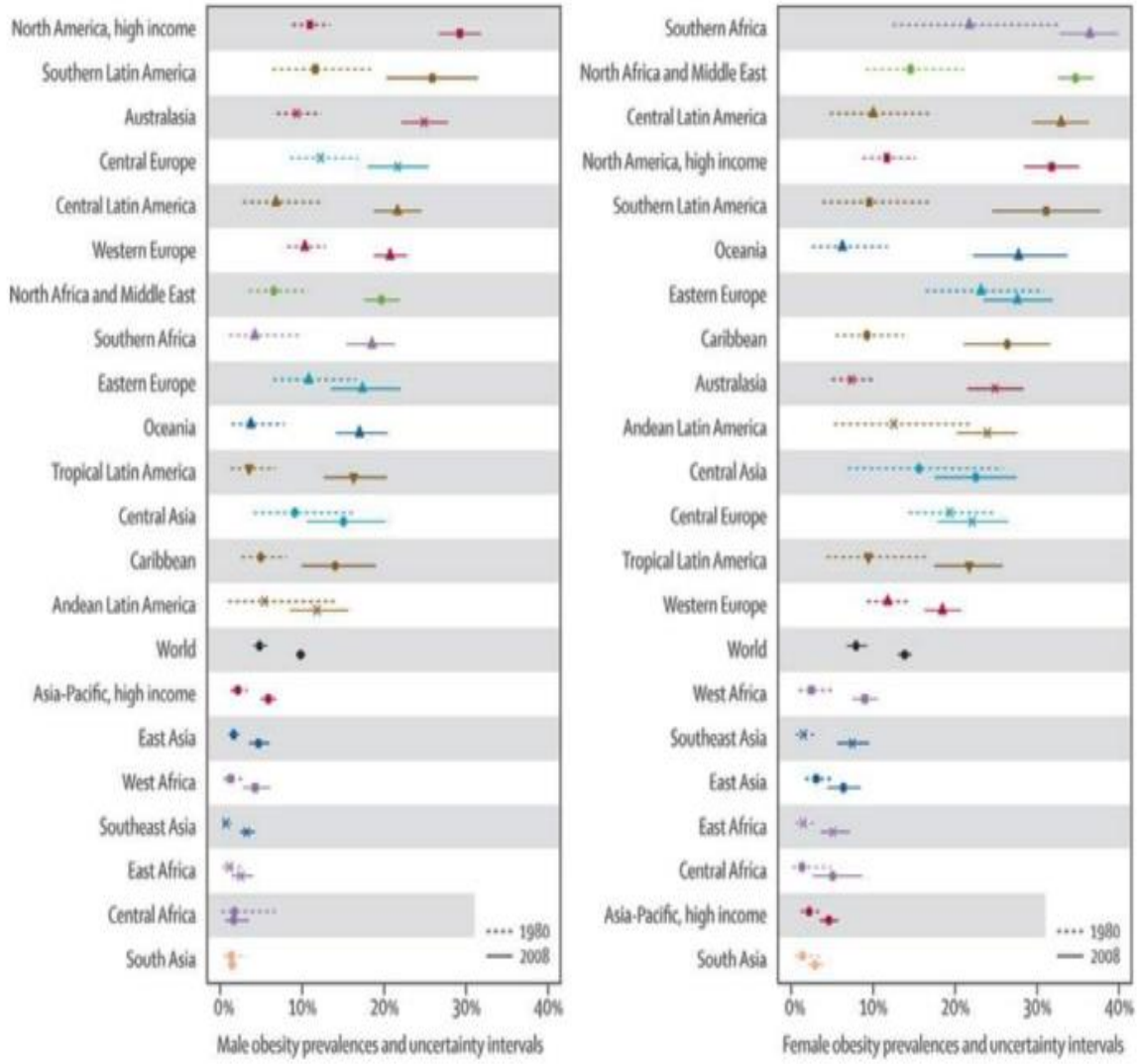
Of all these, an unhealthy lifestyle (physical activity patterns, food intake) is thought to be one of the most important factors (Branca et al., 2007; Frühbeck, 2012), both in the younger (Ara et al., 2006; Vicente-Rodriguez et al., 2008) and elderly population (Garcia-Alvarez et al., 2007; Vernay et al., 2009).

The rapid economic development of the past 30 years has increased access to high-energy-dense foods with high concentrations of fat and sodium, with these foods replacing traditional diets rich in protein and fiber (Eaton & Eaton, 2000). At the same time, technological advances have increased the adoption of a sedentary lifestyle, reducing the demands for physical activity. In combination, these factors have contributed to the creation of an obesogenic environment with individual and global health consequences.

iv. Prevalence

Currently, approximately a third of the world's population (2.1 billion) is overweight (> 1.9 billion) or obese (> 650 million) (Ng et al., 2013). Recent evidence provided by the WHO illustrates that the global prevalence of overweight and obesity has increased significantly over the past four decades, and cases have more than doubled since 1980 (from 26.5% to 39% for overweight, and from 7% to 12.5% for obesity) (Chooi et al., 2018; Finucane et al., 2011; GBD 2015 Obesity Collaborators, 2017; NCD Risk Factor Collaboration, 2017; WHO, 2016), mainly as a result of rapid changes in socioeconomic and demographic status, with the global incidence classified as an epidemic situation (Figure 54). These are probably the major public health problems facing us at the start of the twenty-first century (Yumuk et al., 2015), turning into an even more serious problem than malnutrition. Although there is some variability between countries, regions, ages, sexes, ethnicities and socioeconomic statuses, this trend of an increasing prevalence is relatively uniform worldwide. For example, the American and European regions represent the highest rates of prevalence. Together, overweight and obesity are exhibited by approximately 66.3% of adults in the US (Ogden et al., 2006)**,** with 64.2% of US adults being overweight (in contrast with 45.3% in 1980) and 28.3% suffering from obesity (in contrast with 12.9% in 1980) (Chooi et al., 2018). By comparison, 59.6% of the European population is overweight (in contrast with 48% in 1980) and 22.9% is obese (in contrast with 14.5% in 1980) (Chooi et al., 2018).

Figure 54. *Prevalence of obesity in 1980 and 2008 in men (left) and women (right).*



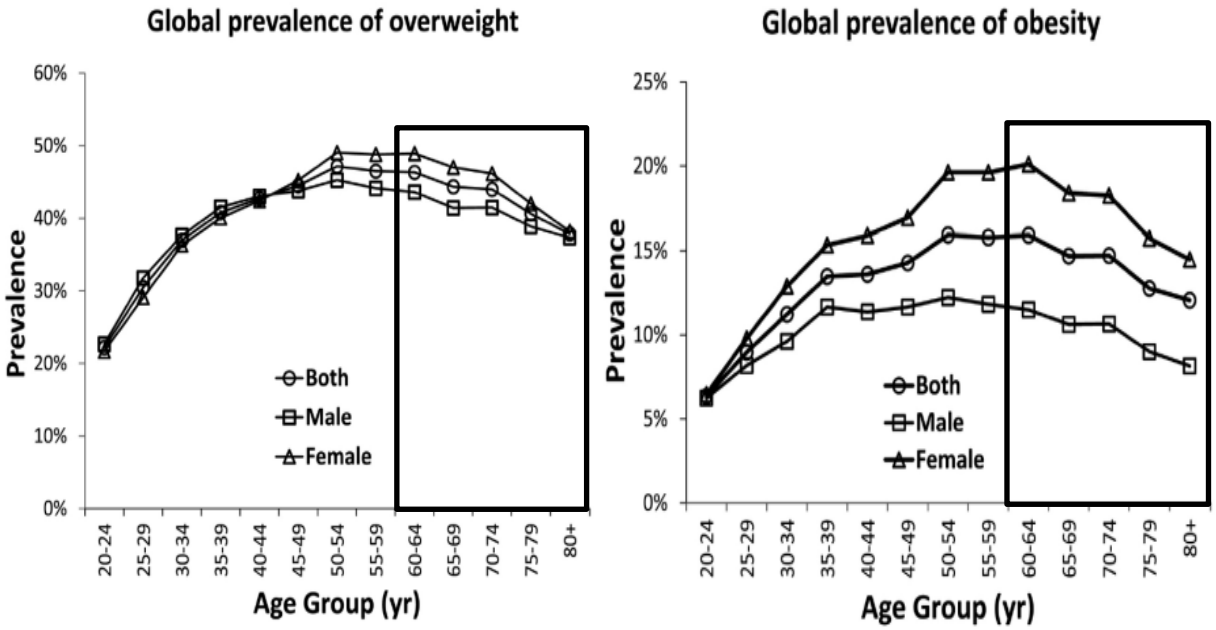
Note. Reproduced from "National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9· 1 million participants" (p. 253), by Finucane et al., 2011, *The Lancet, 377*(9765).

Although most of the existing data in relation to adiposity prevalence refer to adults, it is known that the prevalence of overweight and obesity is increasing as more people reach old age, as the prevalence is generally greater in older persons (Chooi et al., 2018; Mathus-Vliegen et al., 2012). The increasingly aging population and the prevalence of both metabolic conditions signify a double disease burden for the future, with obesity in the elderly an issue of serious concern (Rossner, 2001). In fact, recent data suggest that, worldwide, 35% of adults aged 60 years and over are obese (Fakhouri et al., 2012; Fregal et al., 2012), with the prevalence of obesity in older adults doubling over the past decade (Hendley et al., 2004). For example in the U.S, which has the highest population of obese individuals today, approximately 71% of Americans 60 years or older and 60% of those 65 years or older are overweight (Li et al., 2005; Ogden et al., 2006), while 39% of older adults are obese (Flegal et al., 2016)**,** manifesting wide variability across ethnicities/races (non-Hispanic black: 48%; non-Hispanic white: 39%; Asian: 8%; and Hispanic: 39%). In Europe, rates are even higher due to a higher proportion of aging population and lifestyle, especially in the Mediterranean regions (Greece, Italy and Spain) (Gómez-Cabello et al., 2011).

With regard to Spain, Gomez-Cabello et al. (2001) have found that 84% of the Spanish population of 65 years of age or older are overweight or obese, according to their BMI values (85.3% of men and 84% of women). When the percentage of body fat was used, the prevalence diminished to 67% (81.1% of men and 62.5% of women). Moreover, according to waist circumference, central obesity is present in 56% of the elderly Spanish population. The authors also found that the prevalence of overweight and obesity among elderly people in Spain is still increasing (from 81% in 2004 to 84.3% in 2010) (Gutierrez-Fisac et al., 2012). Previous research has also found that, in addition to age, the prevalence rates for overweight and obesity were usually greater in women than in men throughout this

period of life (Ogden et al., 2013), with sex differences being maximal between 50 and 65 years of age (Figure 55) (Chooi et al., 2018).

Figure 55. *Global prevalence of overweight and obesity in adults >20 years old by age group and sex in 2015.*



Note. Marked with the black box the prevalence of older adults (>60 years of age). Reproduced from "The epidemiology of obesity" (p. 7), by Chooi et al, 2019, *Metabolism, 92.*

In the US, among women 65–74 years of age, 38.9% of non-Hispanic white, 46.6% of Hispanic and 53.9% of non-Hispanic black women are obese, while among women 75 years of age and older, 27.5%, 30.2% and 49.2% are obese, respectively (Fakhouri et al., 2012; Fregal et al., 2012). In Spain, men are more frequently overweight than women (58.7% vs 43.1%), but the prevalence of obesity is much higher for women than for men (40.9% vs 26.6%) (Gómez-Cabello et al., 2011). In summary, the prevalence of overweight and obesity is greater in women than men and increases with age.

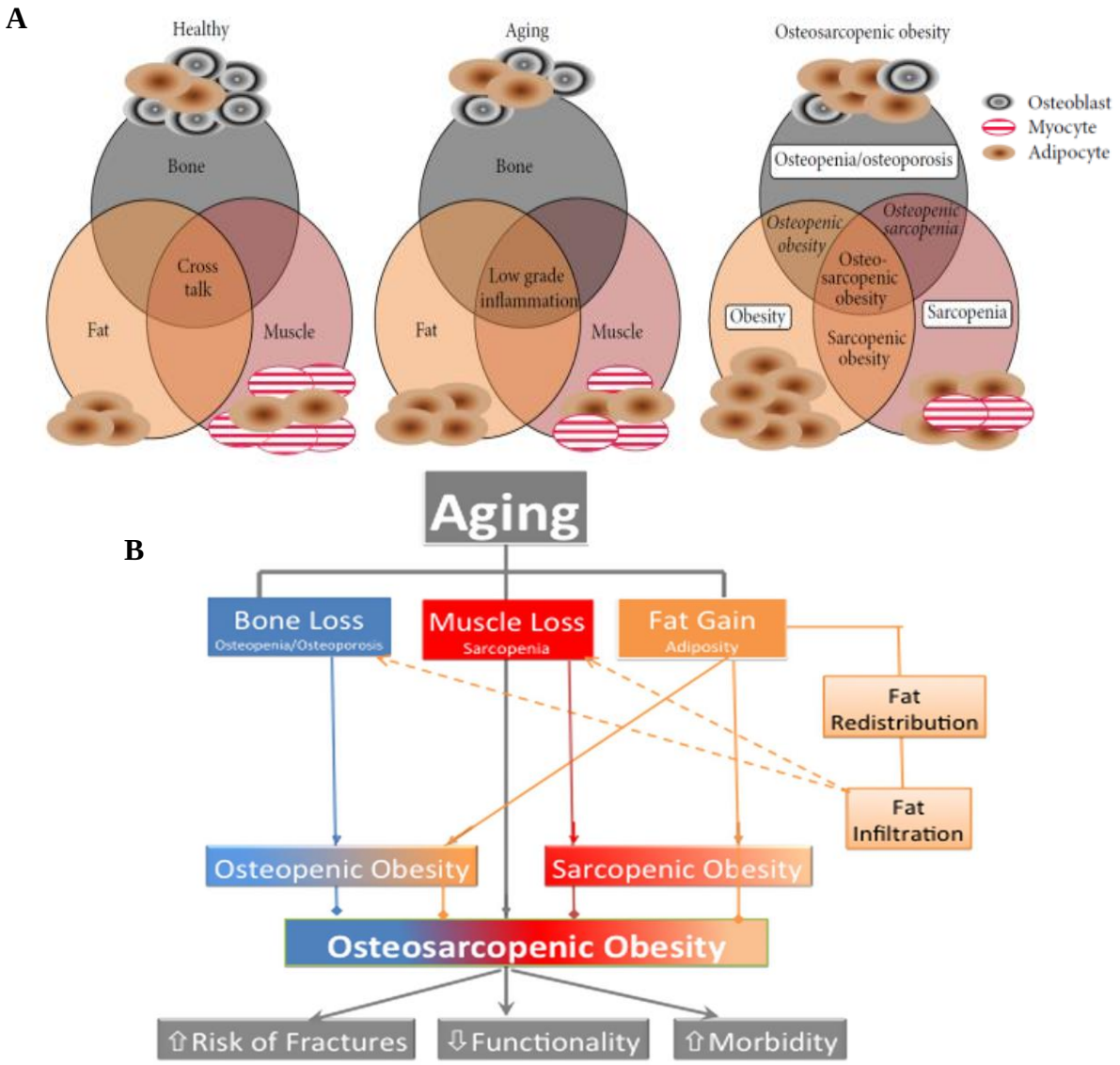
v. Health care costs

The impact of overweight and obesity is especially manifested in economic costs associated with the loss of productivity and the health care burden, due to the acute and long-term complications and comorbidities related to both metabolic diseases. In the US it has been estimated that the economic cost of health care for a single obese person was US$1,901 per annum in 2014 (in comparison US$1,429 higher than that for a person of normal weight) (Kim & Basu, 2016). Extrapolating this figure nationally, the cost amounts to US$149.4 billion (Kim & Basu, 2016), which represents 9.1% of annual medical costs (Finkelstein et al., 2009). In Europe, the total indirect and direct cost attributable to overweight and obesity was equivalent to 0.47–0.61% of the gross domestic product (von Lengerke & Krauth, 2011).

vi. Sarcopenic obesity and osteosarcopenic obesity

With aging, the coexistence of obesity with the musculoskeletal diseases of sarcopenia and osteopenia/osteoporosis has been described in the elderly population (Ormsbee et al., 2014). In fact, sarcopenic obesity is the term used to describe the health condition involving both sarcopenia and obesity (Stenholm et al., 2008), first defined by Baumgartner (2000), while recently a new syndrome has been identified termed "osteosarcopenic obesity," characterized by age-related changes in body composition, including bone impairment, along with skeletal muscle and adipose tissue, the triad of osteoporosis, sarcopenia and obesity (Ilich et al., 2014, 2016; Kalinkovich & Livshits, 2017; Ormsbee et al., 2014). In addition, there are two other conditions that were not fully recognized until recently: osteopenic/osteoporotic obesity and osteosarcopenia (also called sarco-osteopenia or sarco-osteoporosis) (Figure 56) (Binkley & Buehring, 2009; Ilich et al., 2014, 2016).

Figure 56. *Osteosarcopenic obesity consequences.*



Note. A. Conceptual model of proportion changes in bone, muscle and fat mass through healthy state, aging and the different disease states that compromise impairment in bone, muscle, and adipose tissue. B. Consequences of osteosarcopenic obesity. Reproduced and adapted from " Osteosarcopenic obesity syndrome: what is it and how can it be identified and diagnosed?" (p. 3), by Ilich et al., 2016, *Current Gerontology and Geriatrics Research, 2016,* and from "Aging human body: changes in bone, muscle and body fat with consequent changes in nutrient intake" (p. R39), by Jafarinasabian, Inglis, Reilly et al., 2017, *Journal of Endocrinology, 234*(1).

The presence of any of these conditions may lead to the highest rates of disabilities (Davison et al., 2002; Fielding et al., 2011), increased risk of fractures (JafariNasabian, Inglis, Ave et al., 2017), falls (JafariNasabian, Inglis, Reilly et al., 2017), metabolic disorders (Hsu et al., 2019), morbidity (JafariNasabian, Inglis, Ave et al., 2017), mortality (Prado et al., 2012; Zamboni et al., 2008) and declined functionality, such as walking speed or stair-climbing (Baumgartner, 2000; Hirani et al., 2017; Levine & Crimins, 2012; Vincent et al., 2012), to a greater extent than in older adults with only the presence of one of these diseases (osteoporosis, sarcopenia or obesity). Depending on the definition and the diagnostic criteria used, the prevalence of sarcopenic obesity has been estimated in the general older population at between 4% and 20% (Bouchonville et al., 2013; Prado et al., 2012). Data from the National Health and Nutrition Examination Survey (NHANES) III study indicated a prevalence of 9% in the US (Davison et al., 2002), while in Spain the prevalence rose to 15% (17.7% in men and 14.0% in women), curiously reaching the peak of prevalence in women later than in men (> 75 years) (Gómez-Cabello et al., 2011).

As we can see, it is apparent that all three tissues (adipose, muscle and bone) are closely interrelated and that osteopenia/osteoporosis, sarcopenia and increased adiposity with aging need to be evaluated, prevented and treated concomitantly.

C. Age-related changes in adipose tissue

With normal aging there is a progressive increase in fat mass, increasing gradually from 20 to 30 years of age until the beginning of the seventh decade of life (Droyvold et al., 2006; Hunter, Gower & Kane, 2010; Schutz et al., 2002; Wilson & Kannel, 2002). During this period, generally adult individuals gain 9 to 10 kg of body weight (mostly fat) (Going et al., 1995), with a consequent increase in BMI (approximately 0.4% per decade) (Meeuwsen et al., 2010), with women being the most affected (Meeuwsen et al., 2010). At any given weight, older adults on average have more body fat than young adults, about twice, as has

been reported previously (the mean body fat of 20-year-old men weighing 80 kg was 15%, compared to 29% for 75-year-old men of the same weight) (Prentice & Jebb, 2001). After the age of 70 years, fat mass tends to plateau and eventually decreases, in parallel with muscle mass (Flegal et al., 2009; Heo et al., 2012; Visser & Harris, 2012).

Moreover, with aging not only the body fat increases, but even and more importantly, with a marked decrease in people over the age of 80 (Ding et al., 2007), the adipose tissue is redistributed. In older adults, fat mass tends to decline at the peripheral and subcutaneous levels and at the same time tends to increase at the abdominal, visceral (intra-abdominal), bone, cardiac, intramuscular and intrahepatic levels (Beaufrere & Morio, 2000, 2000; Enzi et al., 1986; Horber et al., 1997; Zamboni et al., 1997). One of the main problems of this redistribution of fat mass is that the age-related increases in visceral adiposity are strongly associated with several risk factors and diseases, such as cardiovascular diseases (Prineas et al., 1993), insulin resistance (O'Leary et al., 2006), dyslipidemia (Hunter, Chandler-Laney et al., 2010), type 2 diabetes (Tiikkainen et al., 2002), metabolic syndrome (Lau et al., 2005), long-term morbidity (Ilich et al., 2014), and mortality (Tiikkainen et al., 2002). In addition, visceral fat has also been linked to a negative impact on muscle tissue, favoring the catabolism process, reducing muscle strength and contributing to the development and progression of sarcopenia (Cesari, Kritchevsky, Baumgartner et al., 2005; Zhang et al., 2015).

This redistribution of the adipose tissue at the visceral area is more marked in women than in men (Perissinotto et al., 2002). In fact, focusing on women, several studies have found that premenopausal women frequently develop a gyneoid phenotype, with subcutaneous fat accumulation in the buttocks, thighs, and hips, but during menopausal transition fat mass migrates to the waist, predominantly at the intra-abdominal area, thus acquiring an android phenotype (Cervellati et al., 2009; Hamer & Stamatakis, 2012; Ho et al., 2010) and increasing the risk of developing cancers, and metabolic and cardiovascular diseases (Hartz et

al., 2012; Krishnan et al., 2013). It is important to note that, in older adults, increased overall body fat appears to promote visceral fat accumulation. It has been established that the cut-off value of 38.3% of total body fat is an inflection point where the relation between visceral fat and percentage body fat increases significantly in older women (Bosch et al., 2015).

At the neuromuscular level, intramuscular fat increases in two depots: fat that is located between the muscle fibers (intermuscular fat) and fat that lies within the myocytes (intramuscular fat). Both increases are associated with lower muscle strength in the lower limbs (Goodpaster et al., 2001; Visser et al., 2002) and contribute to impaired insulin action through locally released free fatty acids and adipokines (Mathus-Vliegen et al., 2012), which can produce the development of peripheral insulin resistance and metabolic syndrome (Ryan & Nicklas, 1999).

Multiple factors are responsible for these changes of the adipose tissue with aging, with decreased levels of physical activity (in intensity and duration) being one of the major causes (Wilson & Morley, 2003). In fact, it has been estimated that decreased physical activity accounts for around half of the reduced total energy expenditure that occurs with aging (Elia et al., 2000). Other contributors are a reduced resting metabolic rate (decreases by up to 30% between young adulthood and old age, decreasing by 2–3% per decade after the age of 20 years and by 4% per decade after the age of 50 years, which is equivalent to approximately 150 kcal / 630 kJ per day) (Chau et al., 2008; Kennedy et al., 2004; St-Onge & Gallagher, 2010) and the thermic effect of food (Cannon & Nedergaard, 2011; Dulloo et al., 2004), reduced mitochondrial volume and oxidative capacity (Conley, Mccaulley & McBride, 2000; Conley, Mccaulley, Triplett & McBride, 2000), and also reduced hormone secretions (oestrogen, testosterone, dihydroepiandrosterone, growth hormone, insulin-like growth factor-1, leptin and insulin) (Batsis & Villareal, 2018; Mathus-Vliegen et al., 2012).

D. Methods to assess fat mass

A wide variety of methods for evaluating body composition, and specifically fat mass, are currently available to assess from the largest to the smallest level: whole-body, tissue-organ, cellular, molecular, and atomic (five-level model) (Lohman et al., 2005; Wang et al., 1992). Each level has different compartments (two, three or four). The effectiveness and accuracy of the measuring device will depend on how many compartments it is able to measure. In this sense, the four-compartmental models, such as MRI and CT, represent the gold standard for estimating total and segmental adipose tissue (especially visceral fat) (Woodrow, 2009), because they have the greatest degree of sensitivity to inter-individual variability (Aragon et al., 2017). However, their use is usually limited to primary research, due to their logistical challenges (Aragon et al., 2017).

At the next level, DXA is based on a three-compartmental model, because it measures bone, lean mass and fat mass and is recommended for assessing fat mass due to its affordability, availability and diagnostic accuracy (Kendler et al., 2013). In addition, DXA has a high correlation with the gold-standard devices and also provides estimates of fat mass from the whole body or from specific segmental regions (Bridge et al., 2011; Fakhrawi et al., 2009; Xu et al., 2011). However, the assessment of visceral fat by DXA is not as accurate as in other regions (Kaul et al., 2012; Micklesfield et al., 2012; Park et al., 2002; Woodrow, 2009).

At the last level, the two-compartmental model estimates fat mass and fatfree mass and operates under the assumption that the water, mineral and protein contents of lean mass are constant (Aragon et al., 2017). This method assesses adipose tissue content; however, it fails to distinguish the components of fatfree mass. Methods based on the two-compartmental model are the most used in clinical and sport practice, due to their relative low cost, easy operation and non-invasiveness (Aragon et al., 2017), although they are less sensitive to

changes compared with the three- and four-compartmental models. Methods based on the two-compartmental model include BIA, air-displacement plethysmography (BodPod), hydrodensitometry, near-infrared and skin folds (Fields et al., 2005; Marks & Rippe, 1996).

Of all of these, BIA and skin folds are the methods most frequently implemented. BIA is a simple, inexpensive, non-invasive, rapid and portable diagnostic tool, but has notable limitations, as hydration must be constant not to overestimate the results (Houtkooper et al., 1996; Kyle et al., 2004), there are no valid equations for different ethnic groups (Chumlea et al., 2002), lack of specificity with large standard errors (Roubenoff, 1996), and lack of validation in individuals aged ≥ 80 years (Batsis et al., 2013, 2015). By comparison, anthropometric measurements comprise the evaluation of circumferences (waist, abdomen, hips, arm, calf, forearm, thigh, and mid-thigh), segment length, height, and subcutaneous adipose tissue skinfold (abdomen, triceps, chest, mid-axillary, subscapular, suprailiac, and thigh) (Tran & Weltman, 1988; Weltman et al., 1988). Given the broad range of fat mass measurement techniques, the researcher or clinician must weigh the practical considerations of their assessment needs against the limitations of the methods and choose the one most suited to their objectives.

Along with the different devices to assess the adipose tissue, there are also different methods to calculate body fat using body composition indexes such as the BMI, body fat percentage, waist circumference, waist-to-hip ratio, and the fat mass index (fat mass (kg) / height $(m)^2$). Despite the fact that the BMI is the most widely used method, it does not provide an accurate measurement of fat mass (Kelly et al., 2019), especially in older adults, because it can either underestimate the degree of fatness because of changes in body composition (loss of muscle mass and intra-abdominal fat) or overestimate it due to loss of height from vertebral compression and kyphosis in this population. In addition, it also indicates large inter-individual variability in the percentage body fat for any given BMI

value, partly attributed to sex, age and ethnicity (Chooi et al., 2018). Moreover, there are no data to define optimal BMIs in the elderly of different ethnicities. The percentages of fat mass in terms of DXA and waist circumference seem more appropriate assessments (Shea et al., 2012; Stenholm et al., 2008), and the combination of these will increase accuracy in order to better identify older people with health risks due to overweight, obesity or an excess of visceral fat.

F. Exercise-related effects on adipose tissue

Given the high prevalence of overweight and obesity in the elderly population, there is an ongoing need to find effective treatments and prevention methods for this population. However, although both metabolic disorders are an important cause of disability in older adults (Jensen & Hsiao, 2010; Rejeski et al., 2010), there remains a concerning dearth of knowledge regarding the best therapeutic approaches for managing the excess of adipose tissue in older persons (Batsis et al., 2017), and currently, evidence-based data to guide the treatment of older adults with overweight or obesity are limited (van Baak & Visscher, 2006; Witham & Avenell, 2010). In fact, the most recent guidelines of three of the most important organizations in weight management (the American College of Cardiology, the AHA, and the Obesity Society guidelines for the management of obesity) state that there is a need for further research to understand the most appropriate strategies and prescriptions for weight loss in the elderly population, because *"the overall safety of weight loss interventions for patients aged 65 and older remains controversial"* (Jensen et al., 2014).

To date, most of the evidence is based on weight loss interventions, evaluating the effect of different therapies on overall weight loss (most of them), or on the body composition components (fatfree mass, fat mass, bone tissue), although little is known regarding the benefits and risks of these interventions (Bales & Buhr, 2008; Witham & Avenell, 2010). There are multiple types of treatments, such as pharmacotherapy, bariatric

surgery, diet and exercise, but the latter two are established cornerstones in primary prevention as well as in the management of excess body fat mass in older adults (Galani & Schneider, 2007).

Nevertheless, the clinical approach to overweight and obesity in older adults is controversial (Houston et al., 2009; Miller & Wolfe, 2008), because weight loss could accelerate the usual age-related loss of muscle mass (Baumgartner, 2000; Blaum et al., 2005), adversely affecting physical function and producing frailty (Roubenoff, 2004). In multiple RCTs, changes and interventions in lifestyle based on caloric restriction of 500 to 1000 kcal/day (Mathus-Vliegen et al., 2012), a very-low-calorie diet (intake of as little as 800 to 1000 kcal/day) (Haywood et al., 2017), and adequate intake of high-biological-quality protein (0.8 to 1.6 g/kg/day) (Churchward-Venne et al., 2014; Jiang et al., 2018), calcium (1,000 mg/day) (Mathus-Vliegen et al., 2012), and vitamin D (10–20 g/day) (Mathus-Vliegen et al., 2012) are effective at inducing weight loss in older adults, at least in the short term (Batsis et al., 2017; Mathus-Vliegen et al., 2012).

However, although dieting, or more specifically, caloric restriction, is the first therapeutic option and the most common approach for the treatment of overweight and obesity in the general population, this approach can impact negatively on older adults due to the associated loss of bone and muscle mass that can further exacerbate the increase of fracture risk and age-related sarcopenia (Locher et al., 2016). In addition, caloric restriction alone has a relatively poor long-term success rate for weight reduction in older adults (Tsai & Wadden, 2005; Weiss et al., 2007), with only 18% of individuals who attempted to lose weight being able to maintain the weight loss over a period of one year (Kraschnewski et al., 2010). Thus, treating overweight and obesity in older adults requires interventions to simultaneously reduce excess adiposity but at the same time stimulate muscle mass, to

preserve the lean body mass and bone mass. In this sense, physical activity and exercise training are the only therapies that can achieve these goals.

Currently, physical activity is recommended as an important part of weight management (for weight loss, prevention of weight gain and prevention of weight regain after weight loss) (Donnelly et al., 2009) by medical societies (the American Medical Association, the AHA, the American Academy of Family Physicians) (Lyznicki et al., 2001), scientific organizations (the ACSM) (Donnelly et al., 2009), and public health agencies (the National Heart, Lung, and Blood Institute (NHLBI), Centers for Disease Control) (Expert Panel on the Identification, Evaluation, and Treatment of Overweight in Adults, 1998; Haskell et al., 2007), being the exercise training used by 90% of individuals who attempt weight loss (Klem et al., 1997).

It is likely that any increase in physical activity has the potential for weight loss; however, in recent decades researchers have speculated on the amount of physical activity necessary to achieve weight loss and to prevent weight gain. Current recommendations of physical activity for long-term weight loss (fat mass) suggest that < 150 $min \cdot wk^{-1}$ results in minimal weight loss compared to controls, but ~ 250 $min \cdot wk^{-1}$ results in modest weight loss of ~ 2–3 kg in overweight and obese individuals, and the achievement of weight loss of ~ 5–7.5 kg with exercise levels of up to 420 $min \cdot wk^{-1}$ (Donelly et al., 2009; Haskell et al., 2007). This means that physical activity seems capable of providing a 3% or greater weight loss from the initial weight (Donnelly et al., 2009). Although the NHLBI guidelines recommend a minimum of 10% reduction of weight from the initial weight over six months to achieve beneficial improvements in cardiovascular factors (NHLBI, 1998), it is necessary to take into account that there is also considerable evidence indicating that a reduction in health risks could be achieved with a reduction of 3% to 5% of the initial weight (Ditschuneit et al., 1999; Flechtner-Mors et al., 2000). Moreover, the ACSM position for weight loss and prevention of

weight regain for adults recommends 150 to 250 min·wk^{-1} of moderate to vigorous physical activity, with an energy equivalent of 1,200 to 2,000 kcal per week, to prevent weight regain greater than 3% in most adults (Donnelly et al., 2009).

The benefits of physical activity for weight control, reducing total and central adiposity and managing obesity are well documented in adults (Chin et al., 2016; Jakicic et al., 2019; Ohkawara et al., 2007; Shaw et al., 2006; Verheggen et al., 2016), indicating a modest effect for reducing total body weight (approximately ≤ 3 kg) when it is applied without caloric restriction but with larger effect in reducing visceral adiposity (Verheggen et al., 2016). As in adults, physical activity has also proven to be an effective strategy to reduce increases in body fat mass in older adults (Geffken et al., 2001; Villareal, Chode et al., 2011). A review by Stehr and Lengerke (2012) of preventing weight gain through exercise and physical activity in the elderly concluded that exercise is effective to prevent weight gain in the elderly, either in terms of weight loss or weight maintenance. For both groups analyzed, aged adults and postmenopausal women with overweight, exercise or physical activity was associated with weight loss in all the interventions (1.1–6 kg), independent of the intensity and the indicators of obesity applied (Stehr & Lengerke, 2012). Thus, physical activity and exercise can effectively prevent weight gain in postmenopausal women and older adults, either in terms of weight loss or weight maintenance.

It is important to note that, in adults, physical exercise achieves greater loss of weight and fat mass when combined with dietary intervention (hypocaloric diet) (Verheggen et al., 2016; Shaw et al., 2006; Clak, 2015; Miller et al., 2013; Schwingshackl et al., 2014; Witham & Avenell, 2010). This phenomenon also applies to older adults and postmenopausal women, as Stehr and Lengerke (2012) found in their review. The opposite is also true: programs based on nutritional modifications alone are less effective than those also including physical activity (Johns et al., 2014).

Despite consistent evidence from studies indicating physical activity and exercise training can prevent weight gain and produce modest weight loss in older adults, the changes in weight and fat mass in response to exercise training without caloric restriction are highly heterogeneous (Barwell et al., 2009; Boutcher & Dunn, 2009; Church et al., 2009; King et al., 2008). The variability among individuals following an exercise training intervention regarding adipose tissue can be explained by: 1) high variability and low adherence to training programs (Fedewa et al., 2017); 2) increased dietary intake (Donnelly & Smith, 2005); 3) decreased resting energy expenditure (Byrne et al., 2012; Pontzer, 2015); 4) decreased non-exercise physical activity (reflected as changes in ambulatory physical activity) (Herrmann et al., 2015; Melanson et al., 2013); 5) decreased non-exercise activity thermogenesis (reflected as changes in activity-related energy expenditure such as postural changes) (Herrmann et al., 2015; Melanson et al., 2013); and 6) different training protocols applied. As a result, weight or fat mass reductions can be substantially less than predicted (usually the weight loss achieved is 30% of the initial predicted value) (Drenowatz, 2015; Manthou et al., 2010; Ross & Janssen, 2001).

Nonetheless, even though exercise training may not report the expected weight loss, it should still be integrated as part of the treatment plan for overweight and obese older adults, regardless of weight loss goals, because it is associated with numerous cardiovascular and metabolic benefits, such as reductions of blood pressure, anxiety, depression, and chronic inflammation and the improvement of the lipid profile, physical fitness, glucose tolerance, insulin sensibility, and quality of life, as well as the reduction of the risk of cardiovascular diseases, type II diabetes and all-cause mortality (Kay et al., 2006; Lee et al., 2005; Ross et al., 2004; Swift et al., 2013).

Against this background, effective fat-loss strategies, including dietary and physical activity interventions, or both, are required. However, physical exercise can be performed in

numerous ways and designed to target cardiovascular fitness (aerobic or anaerobic training), muscle strength (resistance training focusing on hypertrophy, power or resistance), balance (static, dynamic, proactive), flexibility (static, dynamic), coordination, or a combination of these aims. In the following sections the main findings on training intensity and training modalities conducted in this PhD dissertation regarding changes in adipose tissue and body weight are discussed in detail.

i. Effects of resistance training and variable resistance on adipose tissue[9]

During weight loss in the general population, but more specifically in older adults, a large proportion of lean mass can be lost, increasing the risk of physical disability in later life (Beavers et al., 2011; Byrne et al., 2003; Rantanen, Guralnik, Foley et al., 1999; Rantanen, Guralnik, Sakari-Rantala et al., 1999). Resistance training has been determined as the best training modality to increase the lean mass in young and older adults, with the repercussions that this entails in terms of maintenance of metabolic rate, muscle strength, physical function, skeletal integrity and the prevention of sarcopenia and sarcopenic obesity in the elderly population (Miller et al., 2008).

[9] Related publications:

1. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

2. Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High- and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press).*

3. Fritz, N. B., Juesas, Á., Gargallo, P., Calatayud, J., Fernández-Garrido, J., Rogers, M. E., & Colado, J. C. (2018). Positive effects of a short-term intense elastic resistance training program on body composition and physical functioning in overweight older women. *Biological Research for Nursing, 20*(3), 321-334. https://doi.org/10.1177/1099800418757676

However, to date, strength training has not been assigned a major role by clinicians, exercise professionals and public health services in overweight and obesity prevention or treatment, because it is generally believed to be ineffective for weight loss and post-weight-loss maintenance, particularly in postmenopausal women and older adults (Donnelly et al., 2009; Fragala et al., 2019). In fact, the exercise guidelines of professional organizations have historically focused on endurance or aerobic training (Jakicic et al., 2001), and currently no guidelines for progressive resistance training in the management of overweight and obesity exist. In a 2009 position statement of the ACSM, the authors concluded that there is no evidence supporting that resistance training induces weight loss but there is some evidence that strength training improves body composition (increased lean body mass and reduced body fat) (Donnelly et al., 2009).

In the last decade a long-standing volume of literature has demonstrated that although the energy expenditure associated with resistance training is not large, strength training could prove useful for weight loss and weight maintenance, since it can contribute to increasing muscle mass, which may in turn increase resting energy expenditure (or resting metabolic rate), physical activity energy expenditure, insulin sensibility and fat oxidation (Dionne et al., 2004; Giles et al., 2016; Hunter, Chandler-Laney et al., 2000; Hunter et al., 2015; Kirk et al., 2009; Lemmer et al., 2001). Also, an increase in muscle mass is an important driver of appetite and energy intake after weight loss (Dulloo et al., 1997). In addition, resistance training can also produce positive adaptations in cardiorespiratory, neuromuscular, endocrine, metabolic and morphological pathways and systems, independent of modifications in body composition and weight loss (Fragala et al., 2019).

The results obtained from strength training will largely depend on whether it has been performed alone or in combination with aerobic exercise or caloric restriction. Less research has been conducted on resistance training alone. In this case, investigations have

demonstrated inconsistent results, some with positive alterations in fat mass or weight loss (Banz et al., 2003; Donnelly et al., 2009; Fielding, 1995; Hersey et al., 1994; Hunter et al., 2002; Ibanez et al., 2005; Lemmer et al., 2001; Marx et al., 2001; Nichols et al., 1993; Pollock et al., 2000; Schmitz et al., 2003; Treuth et al., 1994; Williams et al., 2007; Winett & Carpinelli, 2001) and some with no changes at all (Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al., 2007; Schmithz et al., 2007; Polak et al., 2005). In general, when resistance training is applied alone, it contributes to a modest reduction of body fat (Hunter et al., 2002; Ibanez et al., 2005; Lemmer et al., 2001; Schmitz et al., 2003); however, the effect on overall weight loss is minimal, possibly due to the increase in lean mass (Bateman et al., 2011; Church et al., 2010; Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Schmitz et al., 2003; Schmitz et al., 2007; Sigal et al., 2007).

Specifically, several studies have found that resistance training applied at moderate to high intensities decreases total adipose tissue, usually in studies of more than 12 weeks in duration, with losses ranging from 1.6% to 3.4% of fat mass (Bond et al., 2002; Campbell et al., 1994; Cavalcante et al., 2018; Donnelly et al., 2000; Ferley et al., 2013; Hunter et al., 2002; Ibañez et al., 2005; Irwin et al., 2003; Lemmer et al., 2001; Marcos-Pardo, Orquin-Castrillón et al., 2019; Neter et al., 2003; Nickols et al., 1993; Norman et al., 2003; Norris et al., 1990; Olson et al., 2007; Pi-Sunyer et al., 2007; Treuth et al., 1994; Treuth et al., 1995).

However, others found no effects on body fat (Ferrara et al., 2006; Hintze et al., 2018; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Willis et al., 2012). Some researchers have attempted to determine the effects of resistance training on regional fat mass (intra-abdominal and subcutaneous adipose tissue), reporting no changes in both areas (Binder et al., 2005), only significant effects in older women but not in men in both regions

(Hunter et al., 2002), or found only improvements for both men and women in the intra-abdominal fat mass (Ibanez et al., 2005; Treuth et al., 1995).

Interestingly, a few randomized trials have directly compared the effects of aerobic training, resistance training or a combination of both on fat mass in overweight and obese adults and older adults, with or without caloric restriction. It seems that combining resistance training with aerobic training has been demonstrated to be superior in the reduction of whole and central adiposity and body weight (Arciero et al., 2006; Davidson et al., 2009; Ismail et al., 2011; Laird et al., 2014; Park et al., 2003; Schwingshackl et al., 2013; Visser et al., 2013; Willis et al., 2012), and to result in greater muscle mass (Park et al., 2003) when compared to aerobic exercise alone, resistance training alone or caloric restriction alone (Delecluse et al., 2004; Kraemer et al., 1999; Janssen et al., 1999; Joseph et al., 2001; Miller et al., 1997; Rice et al., 1999; Schwingshackl et al., 2013). If the implementation of both training modalities in the same session is combined with caloric restriction, the results are more favorable (Beavers, Ambrosious et al., 2017; Daly et al., 2005; Silverman et al., 2009; Villareal et al., 2017). Thus, current evidence suggests that overweight and obese older adults should participate in both aerobic endurance training and resistance training, whether they are undertaking caloric restriction or not.

There is also an interesting interaction between resistance training and dietary protein intake in overweight and obese older adults, with data indicating positive results when moderate to high protein intake is complemented by resistance training over at least 12 weeks (Arciero et al., 2006, 2008; Beavers, Ambrosious et al., 2017; Doi et al., 2001; Donnelly et al., 2009; Layman et al., 2005).

Most resistance training protocols to improve body composition in the elderly have been carried out with machines and free-weight resistance exercises, whether performed in

combination with aerobic exercise or alone. However, several studies have reported significant improvements in percentage body fat, body weight or BMI after resistance training using variable resistance, such as elastic bands, in postmenopausal women (Colado & Triplett, 2008; Colado et al., 2009, 2012; Flandez et al., 2020; Fritz et al., 2021; Neves et al., 2017; Sillanpää et al., 2009) and older adults (Lee & Kim, 2012; Lee et al., 2010; Park et al., 2016; Sillanpää et al., 2009; So et al., 2013), while others have reported no changes (Coelho-Júnior et al., 2019; de Alencar Silva et al., 2020; Lubans et al., 2013; Oh et al., 2016; Skelton et al., 1995; Souza et al., 2019). Of all of these, only six studies specifically analyzed the effects of resistance training in healthy older women (Coelho-Júnior et al., 2019; Lee & Kim, 2012; Lee et al., 2010; Oh et al., 2016; Sillanpää et al., 2009; Souza et al., 2019), with the studies of Oh et al. (2016) and Souza et al. (2019) being the only ones that did not combine resistance training with other training modalities. It is notable that the improvements in body composition induced by elastic-band resistance training programs were similar to previously reported traditional weight training effects in the elderly.

Based on all reported evidence above, the mixed findings might be related to the different training methodologies and parameters employed (intensities, duration, exercises, repetitions, number of sets, rest interval between sets and exercises, time under tension, intervention length), as well as the differences in the subjects' characteristics, dietary intake control or methods employed to evaluate body composition. Miller and colleagues (2013), in their systematic review of the effects of aerobic training or resistance training on body composition in obese adults during weight loss, in order to shed light on the dose-response exercise prescription, found that the resistance training protocols typically used were composed of two to three sets of 8–12 repetitions, at approximately 65% to 85% 1RM, for eight to nine different exercises on alternate days of the week (two or three sessions a week). These parameters are quite similar to those proposed by Fragala and co-authors (2019) in the

position statement of the NSCA on resistance training for older adults. By comparison, Miller and colleagues (2013) found that aerobic training was predominately performed at moderate to vigorous intensities (65–85% maximum or peak heart rate), between 90 to 225 minutes per week, distributed over three to five sessions a week.

Despite the inconclusive results reported above, such evidence of the general benefits of the implementation of resistance training in the prevention and treatment of overweight and obesity in older adults, through the increase in lean mass and the decrease in fat mass, has initiated a debate on the need to develop an optimal training program for these objectives. Given that there is no consensus on the optimal way to train older adults, especially postmenopausal and older women, different training variables and modalities should be assessed to determine their potential in the reduction of fat mass. In fact, the analysis of exercise-based changes in body composition in older adults is of vital clinical importance (Després et al., 2008; Haskell et al., 2007), even more so when it is implemented in a real-world public health context where the evidence is weak, since most studies are carried out in laboratory settings. These motives promoted the implementation of the projects reflected in this PhD dissertation.

ii. Effects of exercise intensity on adipose tissue[10]

The amount of physical activity necessary to improve body composition in terms of reducing fat mass and preventing weight gain may depend on the intensity of the exercise prescribed. However, in the elderly population, and specifically in postmenopausal and older women, a limited number of studies have examined the effects of different training intensities when a resistance training program is carried out (Avila et al., 2010; Campbell et al., 2002;

[10] Related publication: Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High-and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press)*

Delecluse et al., 2004; Olson et al., 2007; Pereira et al., 2007; Shioutsu et al., 2018; Wallerstein et al., 2012). In fact, to date, there are no studies that directly compare the effect of different training intensities (low, moderate and high) on adipose tissue (whole body and regional) or applying resistance training programs alone in older adults, neither with continuous or variable resistance. Based on the evidence available to date, it seems that moderate, high and moderate-to high intensities decrease body weight, BMI and total body fat mass in populations older than 65 years of age (Avila et al., 2010; Pereira et al., 2007; Vincent et al., 2006; Wallestein et al., 2012). Nevertheless, to be sure of these effects, the different resistance training programs have to be matched to caloric expenditure and exercise training dose (session time, volume, series).

Most authors analyzing the effect of training intensity on weight loss and fat mass in older adults have performed different aerobic training programs, such as HIIT or moderate-intensity continuous training (Ismail et al., 2012; Jakicic et al., 2019; Swift et al., 2014; Visser et al., 2013). The evidence suggests that only aerobic training at moderate (60–70% maximal heart rate (MHR) or 45–55% of maximal oxygen consumption (VO_2max) or 3.0 to 5.9 METs) (Donnelly et al., 2009; Visser et al., 2013), or high intensity (> 70% HRmax or > 55% of VO_2max or > 6 METs) (Donnelly et al., 2009; Visser et al., 2013) leads to reducing total and visceral adipose tissue in overweight males and females (Donnelly et al., 2009; Visser et al., 2013). In addition, high-intensity training can contribute to greater body and visceral fat mass and weight loss, compared to moderate-intensity training, when the time of the session is matched, due to the fact that the total energy expenditure is greater at higher intensities (Swift et al., 2014). For example, at least one hour a week of moderate-intensity physical activity was demonstrated to reduce the risk of developing obesity in both overweight and normal-weight women (incidence rate ratio of 0.88 and 0.81, respectively) (Rosenberg et al., 2013), but to produce high metabolic stress by engaging in high-intensity

aerobic exercise it will be necessary to lower the time to achieve the same effects (Clark et al., 2015; Jakicic et al., 2019).

Thus, based on the current evidence, the impact of resistance training intensity on adipose tissue has not been thoroughly examined in healthy, overweight or obese older adults. The optimal "dose–response" to achieve weight loss or improve fat mass still has to be determined, specifically in relation to regional and whole body changes (Wewege et al., 2017).

iii. Effects of exercise modality on adipose tissue[11]

Although there is growing evidence that regular physical activity is associated with improvements in body composition and cardio-metabolic risk in older adults, there is still no consensus in the literature regarding the best training modality for reducing total and regional body fat mass and, at the same time, for increasing muscle mass in postmenopausal women and older adults. However, more recently, relatively "new" training modalities, such as multi-component training (also called multi-modal or functional) and high-velocity resistance training (also called power training) have been applied to improve physical function in older adults, but little is known about their effects on adipose tissue.

Some studies have analyzed the effect of multi-component training alone (Blasco-Lafarga et al., 2020; Cadore et al., 2014; Cancela et al., 2020; Carvarhlo et al., 2010; Godoy-Izquierdo et al., 2017; Grant et al., 2004; Kang et al., 2015; Manini et al., 2010; Neves et al., 2017; Schlenk et al., 2011), or plus diet intervention (Anton et al., 2011; Arciero et al., 2014; Focht et al., 2005; Frimel et al., 2008; Messier et al., 2000; Messier et al., 2004; Miller et al.,

[11] Related publication: Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

2008; van Gool et al., 2005; Villareal et al., 2006; Villareal, Smith et al., 2011; Vincent, Raiser & Vincent, 2012), or in comparison with other training modalities such as resistance training (de Resende-Neto et al., 2019; Grossman et al., 2016; Marques et al., 2009; Leite et al., 2015; Sousa et al., 2013), combined aerobic plus resistance training (Rossi et al., 2017) and whole body vibration (Marín-Cascales et al., 2015, 2017).

Most of these studies focused specifically on postmenopausal (Godoy-Izquierdo et al., 2017; Grossman et al., 2016; Marín-Cascales et al., 2015, 2017; Neves et al., 2017; Rossi et al., 2017) and older women (Carvarhlo et al., 2010; de Resende-Neto et al., 2019; Grant et al., 2004; Kang et al., 2015; Marques et al., 2009; Souza et al., 2013; Villareal et al., 2006), with machines and free weights the exercise devices more frequently used.

Some of the studies reported the beneficial effects of multi-component training on the different body fat mass assessments (BMI, total and regional body fat in absolute (kg) or relative terms (%) when it was applied alone (Blasco-Lafarga et al., 2020; Carvahlho et al., 2010; Godoy-Izquierdo et al., 2010; Grant et al., 2004; Neves et al., 2017), or in combination with an energy restriction diet (Arciero et al., 2014; Villareal et al., 2006; Villareal, Chode et al., 2011). Moreover, multi-component training demonstrated similar results to combined strength plus aerobic training in fat mass percentage after eight weeks in postmenopausal women (Rossi et al., 2017), and also to whole body vibration in total fat mass after 12 and 24 weeks in the same population. However, other authors found no changes in body weight, body fat mass or BMI (Cancela et al., 2019; Carvarlho et al., 2010; Grant et al., 2004; Grossman et al., 2016; Kang et al., 2015; Leite et al., 2015; Marques, Mota, Machado et al., 2011; Sousa et al., 2013).

These controversial outcomes in the adipose tissue variables following different multi-component protocols may be explained by differences in the training programs (length

of the training program, sessions per week, number and types of exercises, number of repetitions and series, rest between exercises and sets) and in the participants (different ages, sex and health conditions). Thus, because the results of the effects of multi-component training in postmenopausal and older women on fat mass remain conflicting, further studies to examine specific multi-component protocols and their effects on body composition compared with other training modalities are needed in this population.

However, for decades, progressive resistance training, performed at low velocities (rate of 2s per each lifting phase (concentric and eccentric)) and especially at moderate and high intensities, has been recommended for older adults to improve body composition as well as physical function (Joseph et al., 1999; Latham et al., 2004). Yet among older adults the effect of this type of training on the adipose tissue remains controversial, as mentioned in previous sections. Recent evidence suggests that high-velocity resistance training results in greater benefits than traditional low-velocity resistance training for improving physical performance (Henwood et al., 2008; Reid et al., 2008), but little is known about its effects on fat mass.

To date, only the study of Gray and colleagues (2018) compared the effects of low- and high-velocity resistance training on body composition in older adults. After 48 weeks, they found no significant changes between and within groups in terms of total body fat mass and percentage body fat (Gray et al., 2018). Other authors have demonstrated the same results in the elderly population after applying power training programs for 12 to 22 weeks (Binns et al., 2017; Coelho-Júnior et al., 2019; Dulac , Pion et al., 2018; Roberson et al., 2018), while in other studies, only baseline values of body composition were reported (Jin et al., 2015). Conversely, Mero et al. (2013) reported significant improvements in body fat percentage, but not in absolute values of fat mass, in older men after 21 weeks of resistance training with around 20% of the exercises performed at high velocity.

These findings could lead to the conclusion that high-velocity resistance training is not an effective training method for improving body composition in terms of producing changes in fat mass. However, the lack of studies that specifically analyzed the effect of this type of training modality on body composition in the medium and long term (training intervention lasting more than 12 weeks) in the elderly population makes it difficult to draw firm conclusions.

In summary, further studies are required to establish the best multi-component and high-velocity resistance training for reducing fat mass in the elderly population.

II.VIII. NEUROMUSCULAR STRENGTH

II.VIII.I. Definition of neuromuscular strength

Strength is a term that can be defined in different ways based on the research area or scientific field to which it is applied or in which it is studied. The classic and physic definition of strength is that it is a measure of force production. It is an influence that, when acting on an object, causes it to change its state of motion, being expressed as the result of the product of mass and acceleration (F = m x a) (Manso et al., 1996). Applying this definition to human beings, movement and the exercise field, muscle strength is defined as "*the force-producing capacity of the muscle"* (Buckinx et al., 2019), or, more specifically, the *"amount of force a muscle can produce with a single maximal effort or in a muscle contraction under specific conditions"* (Beaudart et al., 2019; Brady & Straigth, 2014). It refers to the capacity of skeletal muscles to generate force (Knuttgen & Komi, 2003), being determined by structural and neuromuscular systems (Aagaard et al., 2010).

As the Britain neurophysiologist Charles Scott Sherrington said in the Gifford Lectures in 1937, "*All man can do is to move things, and his muscular contraction is his sole means thereto"* (Greig & Jone, 2016). That means that the skeletal muscles along with the nervous system (central and peripheral) – hence the term "neuromuscular" – through the muscle contractions produce muscle strength, also named "neuromuscular strength."

II.VIII.II. Types of neuromuscular strength

A. Muscle contraction types. Isotonic, isometric, isokinetic and isoinertial concepts

Skeletal muscles work under the control of the nervous system and muscle contraction only occurs when the central nervous system transmits a signal to the muscle fiber (Greig & Jones, 2016). If there are enough energy (ATP) and calcium availability, the muscle fibres generate tension by the interaction of the two proteins, actin and myosin, and the muscle may generate force and movement by shortening, lengthening or remaining the same size,

although when a muscle contracts, from a molecular and physiological point of view, it can only be shortened (because the generation of the actin and myosin cross-bridges implies a shortening) (Gomes et al., 2012; Greig & Jones, 2016).

Accordingly, in all species, when skeletal muscles are activated by action potentials, they can perform three different types of contractions, depending on the interaction between the resistance/load that the muscle is trying to move and the force of the muscle contraction (Faulkner, 2003): isotonic concentric contraction, isotonic eccentric contraction and isometric contraction. During isotonic concentric contraction, the external load is less than the force developed by the fibers within the muscle, and consequently the muscle produces force while shortening (Faulkner et al., 2007; Wernbom et al., 2007). Importantly, during a shortening contraction, the velocity of shortening is load dependent, which means the higher the load, the lower the velocity of shortening (Faulkner et al., 2007). Conversely, when the load is greater than the force developed by the muscle fibers, the muscle produces force while lengthening (Faulkner et al., 2007; Wernbom et al., 2007), performing an isotonic eccentric contraction. Finally, if the load and force are equal or if the load is immovable, the fibers will remain at the same length; an isometric muscle action is taking place, where the length of the muscle-tendon complex does not change (Faulkner et al., 2007; Wenbom et al., 2007).

In addition, training methods or modalities in resistance training can be classified according to the type of resistance or load used (Atha, 1981) and they are going to be related to the type of contraction and muscle strength performed. In this sense, resistance training modes can be classified into four categories: isotonic, isometric, isokinetic and isoinertial. In isotonic training, dynamic exercises are performed in which the muscles exert a constant external tension during shortening (concentric) or lengthening (eccentric) against a constant load (Knuttgen & Pomi, 2003; Pipes & Wilmore, 1974). This is the most popular type of resistance training and it is performed with machines or free weights which facilitate constant

loading. Thus, in theory a constant force or strength is performed by the muscle. However, the strength produced by muscles is influenced by several factors, such as the contraction mode, velocity, range of motion, force vector, muscle group used and also by the biomechanical factors (sticking point, accelerations and decelerations that occur during dynamic exercise, lengths of the lever arms of the muscle and of the resistance) (Wernbom et al., 2007). Due to these factors, the muscle will not develop a constant level of force, even if the external resistance remains constant (Fleck & Kraemer, 1997; Knuttgen & Pomi, 2003). In fact, for this reason, the term "dynamic constant external resistance" is often used in preferance to the term "isotonic" (Fleck & Kraemer, 1997), because the absolute load is constant throughout the movement, as when lifting a free weight or a load in a cable pulley system.

By comparison, isometric resistance training involves static actions where the tension of the muscle is increased without shortening or lengthening of the muscle fibers (Smith & Melton, 1981). Some authors have questioned this terminology, in the sense of whether or not an isometric contraction is indeed an actual "contraction" in terms of physiology, since the length of the sarcomere does not change. However, at molecular level the contraction exists (Gomes et al., 2012; Greig & Jones, 2016).

As muscle strength (force) is the product of load (mass) and velocity (acceleration), two more types of resistance training can be performed. Isokinetic training (can also be defined as a kind of muscle contraction) is a type of strength training that refers to a dynamic muscle action (concentric or eccentric), conducted at a fixed and constant angular velocity (Pipes & Wilmore, 1974). The velocity of the muscle contraction remains constant while the length of the muscle changes. The force exerted by the muscle is not fixed, and can vary based on the position of the joint in its range of motion and the participation effort of the subject. This kind of training makes it possible to exert a continuous maximal concentric or

eccentric muscular contraction throughout the full range of motion or the range of motion prefixed in the isokinetic dynamometer. This equipment controls the pace of an exercise by fluctuating resistance throughout the range of motion. However, the typical human movement is characterized by acceleration and deceleration of a constant mass of the body. Thus, forces or torques produced against a constant mass, rather than at constant velocity, are more specific to the dynamic actions of human beings. In this sense, isoinertial resistance training appears as an alternative (Caruso et al., 2005; Tesch et al., 2004). In this kind of training the inertia (= mass) is maintained constant throughout the range of motion, facilitating a constant resistance and maximal muscle force in every angle of motion.

Therefore, it is necessary to take into account the different types of muscle contractions and strength training methods used in the training protocols in older people, because these can produce different kinds of neuromuscular adaptations.

B. Maximum strength, power strength and endurance strength

Muscular fitness and function encompass several interrelated components, where the amount of force, the speed of the force produced and the time during the force generated highlight the three main components of neuromuscular strength: maximum muscle strength, power or explosive muscle strength and endurance muscle strength (Garber et al., 2011; Ratamess et al., 2009).

The former is defined as the highest level of muscle force that can be produced by recruiting and engaging the maximum motor units possible to generate the maximum tension against an external resistance. It is characterized by being performed at low velocities and high loads. Power strength or muscle power is referred to as the ability to exert a maximal force in as short a time as possible (Beaudart et al., 2019). It is characterized by being performed at high velocities and with low to moderate loads. It is possible to carry out with

high loads but the speeds are lower. Lastly, endurance muscle strength or muscular endurance is defined as the ability of muscles to exert force against resistance over a sustained period of time (Beaudart et al., 2019). It involves the ability to resist muscular fatigue, usually when the resistance is submaximal (Deschenes, 2004). It is characterized by being performed at moderate to high velocities (can also be performed at low velocity) and low to moderate loads during a "long" period of time.

As with the type of muscle contraction, the type of orientation to one component or another of the strength through the implementation of a strength training program can produce a wide range of neuromuscular adaptations in the elderly population that will need to be taken into account.

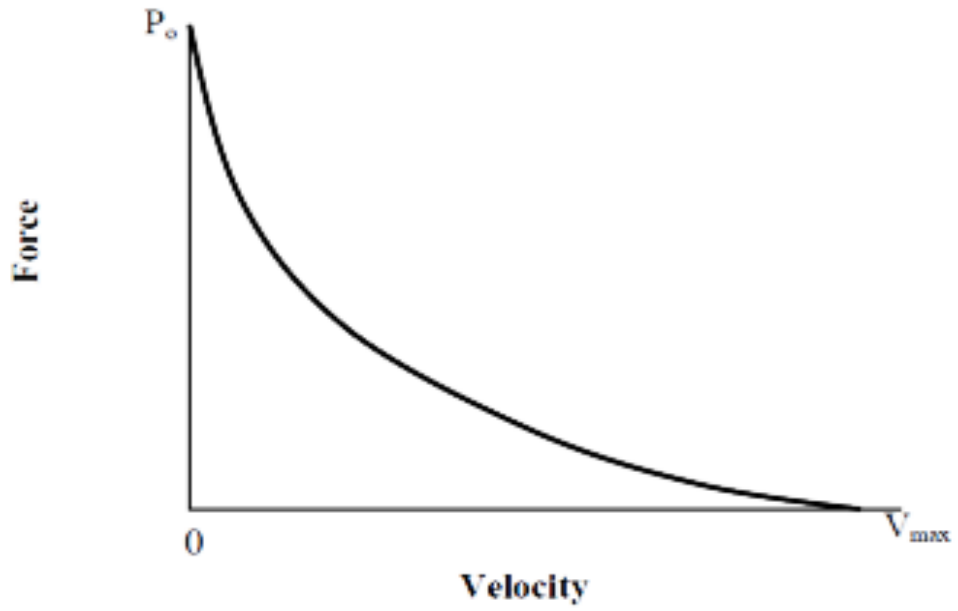
C. Power strength. Force-velocity and power-velocity relationship

In comparison to muscle strength, muscle power is an attribute of muscle function that reflects the ability to generate mechanical-muscular work per unit of time (work rate: word done per unit time) and can be defined as the product of muscle force generated by a muscular contraction and the velocity of shortening at which the muscle fiber contractions occur (product of muscle force and contraction velocity) [Power = Force x Velocity] (Foldvari et al., 2000; Knuttgen & Kraemer, 1987; Harridge et al., 1999; Kawamori & Haff, 2004; Maud & Foster, 1995).

The relationship between the muscle force and the shortening velocity in a skeletal muscle was first described by Archivald Vivian Hill in 1938 in a frog's muscle (Hill, 1938), when he described the muscle's force-velocity (F-V) hyperbolic-curvilinear relationship (Figure 57) (Hill, 1938; Wickiewicz et al., 1984). This equation supposed a huge advance, first in the field of muscle physiology, and later in the sport science field, since it helps to understand the relationship between muscle force production, muscle contraction velocity

and muscle power output. It has been widely used. The muscle's F-V relationship describes how, at increasing muscle contractile velocities, force production decreases in a hyperbolic path in an isolated muscle (Hill, 1938; Wickiewicz et al., 1984). The maximum force (torque) produced by a skeletal muscle is generated at zero velocity, in an isometric contraction, when the load/resistance is at least equal to the force produced, and therefore, the joint is maintained in a static position. For that reason, in the research field, the maximal force that a subject can generate is commonly assessed by a maximal isometric voluntary contraction (Doherty, 2003). Conversely, at maximum shortening velocity, the force generated is close to zero (Doherty, 2003).

Figure 57. *The Force-Velocity relationship in a isolated muscle.*



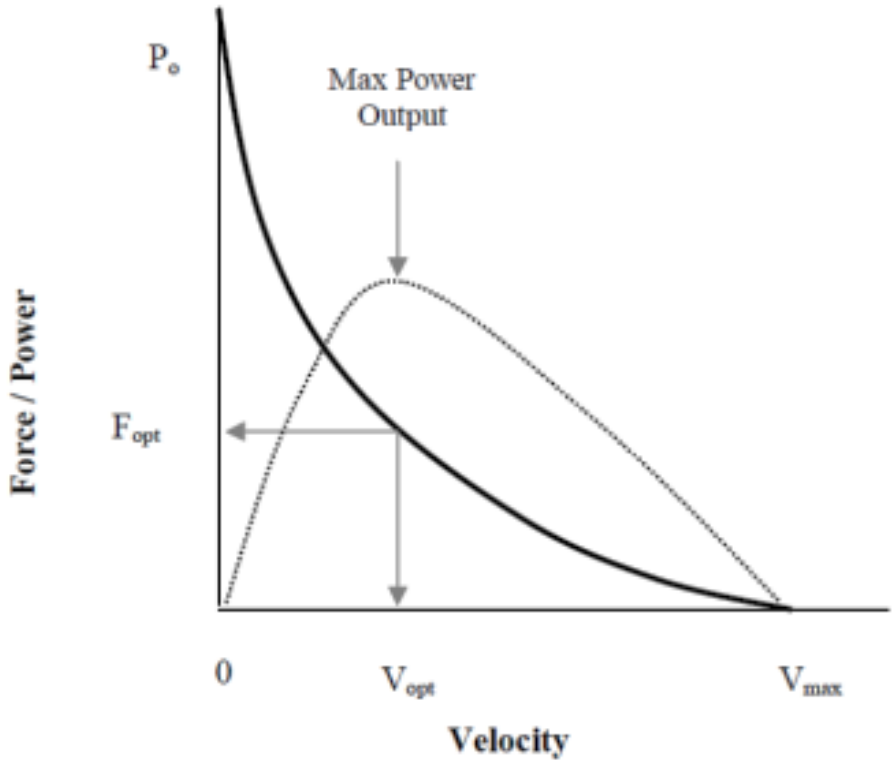
Note. P_0: maximal isometric contraction force , V_{max}: maximal shortening velocity of muscle. Reproduced and adapted from "The heat of shortening and the dynamic constants of muscle" (p. 177), by Hill, 1938, *Proceedings of the Royal Society of London. Series B-Biological Sciences, 126*(843).

As muscle power is dependent upon the force and velocity of shorthening, the muscle power output of an isolated muscle can be calculated from the F-V relationship and represented by the power-velocity (P-V) relationship (Figure 58). In this case, the relationship between power and velocity draw a parabolic instead of a curvilinear association (Macaluso & De Vito, 2003a). The maximal power output occurs at an optimal force and velocity beyond which power output exhibits a parabolic decline. Hill (Hill, 1938) established that peak power occurs at ~33% maximum contraction velocity, one third of the maximum contractile velocity from a single isolated muscle fiber. Above or below this point, power declines in a parabolic curve to a rate of zero when the velocity arrives at 100% (the force component is zero or close to zero), and also when the velocity is zero, in the static positions (the velocity component is zero or close to zero). This is because power is the product of force and velocity. Some studies comparing both extreme conditions, isometric training at maximum strength (100% maximum force) and training at maximum velocity with zero load (100% maximum velocity), have suggested that isometric contractions could be more effective to increase muscle power by increasing the force component, than movements where it is not possible to apply force (Toji et al., 1997).

However, the peak power threshold established at 33% of the maximum contraction velocity during *in vitro* assessments may differ from in vivo measurements, as the muscle peak power output is not the same when it is generated by a single joint movement or in a multiple joint exercise, or also differs between the upper and the lower limb muscles (Izquierdo et al., 1999; Macaluso & De Vito, 2003a; Wickiewicz et al., 1984), due to the involvement of multiple factors such as the muscle-tendinous components, muscle architecture, muscle mass, and predominant fiber types between muscle groups (Cronin & Sleivert, 2005; Driss et al., 2002; Lieber & Friden, 2000; Martin, Wagner & Coyle, 1997; Wickiewicz et al., 1984). For instance, Wendt and Gibbs (1974) suggested that type II fibers

are more related with the power production at higher velocities, while type I fibers are more efficient producing force during isometric and isotonic low-velocity contractions.

Figure 58. *The Force and Power – Velocity relationships in a isolated muscle*.



Note. The dotted line represents the Power-Velocity relationship and the solid line represents the Force-Velocity relationship. The arrows represent the optimal velocity (V_{opt}) and force (F_{opt}) on the Force-Velocity curve where maximum power output occurs. P_0: maximal isometric contraction force , V_{max}: maximal shortening velocity of muscle. Reproduced and adapted from "The heat of shortening and the dynamic constants of muscle" (p. 177), by Hill, 1938, *Proceedings of the Royal Society of London. Series B-Biological Sciences, 126*(843).

The molecular mechanism behind the decrease of muscle power output at higher muscle contraction velocities is that the faster the movement, the more cross-bridges fail to detach in time, providing an internal resistance **(**Greig & Jones, 2016). In other words, as a muscle fiber contracts faster, the cross-bridges have to detach more quickly, and this reduces force. The net force and power generated are the sum of the bridges that are generating force minus the bridges that have not been able to detach. Thus, the optimum velocity of movement at which maximum power is generated is when the affinity and detachment of the cross-bridges in a muscle fiber are in the most efficient balance.

II.VIII.III. Dynapenia

Often the loss of muscle strength has received far less attention than the loss of muscle mass in the process of aging. As was mentioned in a previous section, the term "sarcopenia" defines age-related loss of muscle mass. However, the term "sarcopenia" encompasses complex interactions between muscle mass, muscle strength, and muscle function due to its multifactorial etiology.

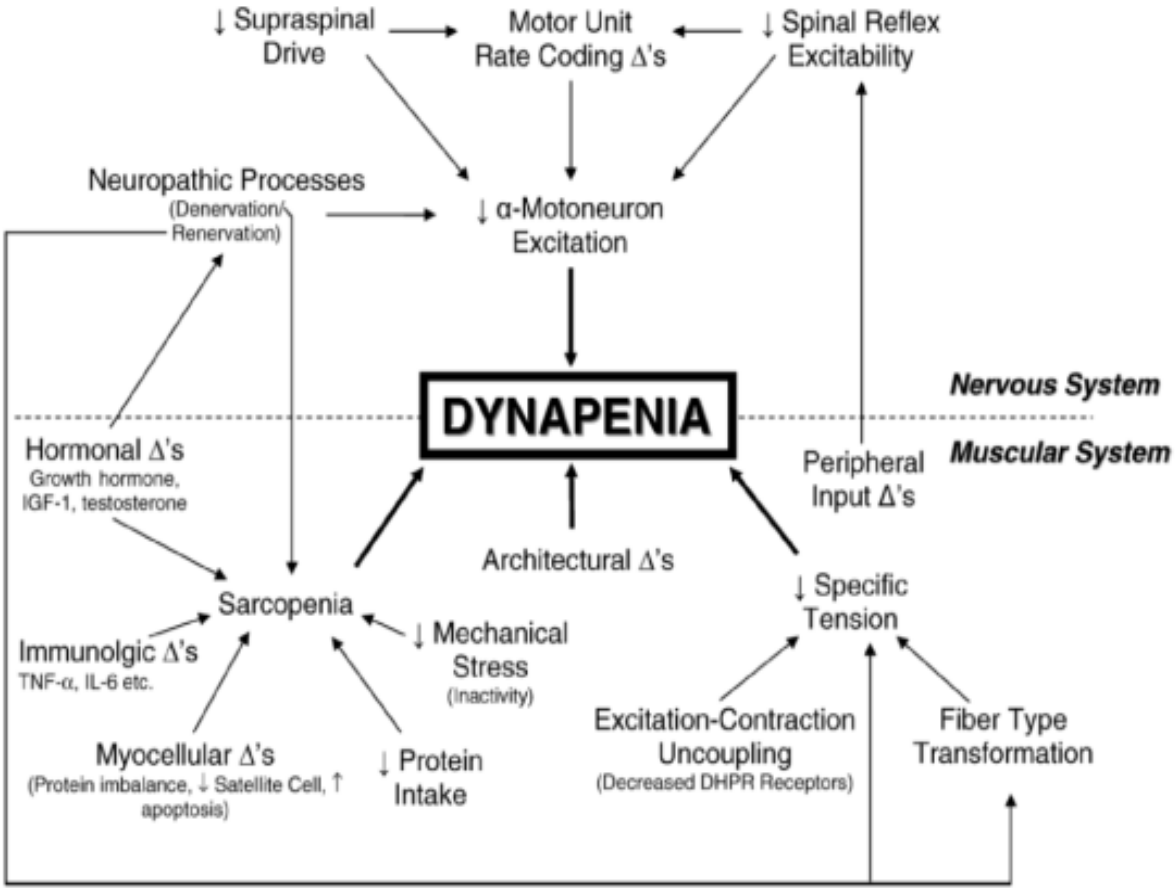
In order to distinguish between the age-related loss of muscle mass and the age-related loss of muscle strength, in 2008 Clark and Manini suggested the alternative term "dynapenia" to specifically define age-related loss of muscle strength and function (Clark & Manini, 2008). This Greek term, which means "poverty of strength," is consistent with other previous terms or definitions used in a similar descriptive manner to define age-related losses (i.e., sarcopenia, osteopenia).

The definition of this condition was necessary, since evidence, based on longitudinal studies, supports that muscle strength does not correlate directly with muscle mass, that the relationship may not be linear and even that the changes or losses of muscle mass and strength with aging do not follow the same time course (Clark & Manini, 2008; Doherty,

2003; Goodpaster et al., 2006; Manini & Clark, 2012). However, despite its usefulness, this term has not yet been uniformly incorporated into clinical use.

The mechanisms by which muscle strength, and therefore the dinapenic condition, can be modified, can arise from two main categories: neurological and skeletal muscle factors. The specific mechanisms proposed by Clark and Manini (2008) and Manini and Clark (2012) are displayed in Figure 59.

Figure 59. *Scheme with the factors that may lead to dynapenia*.



Note. IGF-1:insulin-like growth factor 1; DHPR: dihydropyridine receptors; TNF: tumor recrosis factor; IL-6: interleukin 6. Reproduced from "Sarcopenia≠ dynapenia" (p.832), by Clark and Manini, 2008, *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63*(8).

II.VIII.IV. Age-related changes in neuromuscular strength

A. Effects of aging on muscle strength

Problems with muscle function in general and muscle weakness in particular are very common in the elderly population. Although initially they could seem less relevant than failures in other vital organs, such as the brain, heart or lungs, ultimately our ability to breathe, speak and of course our mobility and independent life depend on the proper function of the skeletal muscles. In fact, in elders (< 60 years), muscle strength is inversely associated with mortality risk (Ruiz et al., 2008), being an indicator of frailty (Syddall et al., 2003) and a predictor of cause-specific mortality (Newman, Kupelian et al., 2006; Sasaki et al., 2006), hospitalization, and disability (Legrand et al., 2014).

Age-related declines in strength and power strength have been well documented by cross-sectional and longitudinal studies, both in the upper and lower limbs (Clement, 1974; Goodpaster et al., 2006; Hughes et al., 2001; Hurley, 1995; Metter et al., 1997, 1999). Aging negatively affects different levels of the pathway between the central nervous system and muscles, reducing the capacity of the elderly to generate force (da Rosa Orssatto, Moura et al., 2018; da Rosa Orssatto, Wiest & Diefenthaeler, 2018). The age-associated decrease in muscle strength was commonly and initially attributed to the age-related reduction in skeletal muscle mass (Frontera et al., 1991), based on the approach of bone health, where the decrease of bone mass explains bone weakness. For this reason, researchers focused on developing diagnostic criteria based on the classification of individuals according to their muscle mass (Baumgartner et al., 1998; Janssen et al., 2000). However, three decades later, numerous studies have demonstrated that muscle mass and muscle strength are not as closely linked as initially thought (Clark & Manini, 2008; Manini & Clark, 2012), due to the wide variation in their decrease rates.

While muscle mass decreases at a rate of 1% to 2% per year above the age of 50, greater declines are observed in muscle strength, which decreases by approximately 1.5% per year between the ages of 50 and 60 and 3% thereafter (von Haehling et al., 2010). In fact, there is a clear dissociation between the age-related changes of these two variables, due to which muscle strength can even be reduced at a rate two to five times faster than muscle mass (Delmonico et al., 2009). Only 5% of the age-associated changes in muscle strength can be explained by changes in muscle mass (Hughes et al., 2001; Miljkovic-Gacic et al., 2008). As such, currently thresholds of clinically relevant muscle weakness have been established through grip strength as the principal biomarker of sarcopenia (Alley et al., 2014; Cruz-Jentoft et al., 2019). For this reason, it is well recognized that strength is a better predictor of adverse outcomes and physical limitation than muscle mass (Barbat-Artigas et al., 2011; Dulac, Carvalho et al., 2018; Ibrahim et al., 2016; Leong et al., 2015; Schaap et al., 2013, 2018).

During life, maximum strength is reached between the 20^{th} and 30^{th} years (Baumgartner et al., 2004), and plateaus or declines slightly in those aged 40 (Lindle et al., 1997; Metter et al., 1997). In sedentary adults, a marked reduction in muscle strength begins in middle age (50^{th} year of age) (Lynch et al., 1999) and accelerates beyond the onset of the sixth decade (Deschenes, 2004; Frontera et al., 1991). During this period, a loss of muscle strength of 1.5–5% per year can be observed (Frontera et al., 1991; Goodpaster et al., 2006).

Multiple cross-sectional and longitudinal studies have tried to establish the rate of muscle strength loss throughout life or to compare the muscle strength of young and older adults (Clement, 1974; Hughes et al., 2001; Metter et al., 1997; Goodpaster et al., 2006). In summary, studies have demonstrated a rate of decline of approximately 2–4% per year (Bassey & Harries, 1993; Frontera et al., 2000; Goodpaster et al., 2006; Delmonico et al., 2009), from 0.8% to 3.6% specifically in healthy older adults (Fragala et al., 2019), to more

pronounced in very old adults (> 90 years of age) (Frontera et al., 1995; Goodpaster et al., 2006). Compared to healthy adults in their thirties, people older than 70 and 80 have 45–50% less muscle strength (Edwén et al., 2014; Leyva et al., 2016) and are only able to produce approximately 20–40% of the quadriceps maximal voluntary contraction of that of younger adults in their third decade (Dean et al., 2004; Doherty, 2003; Lanza et al., 2003; Larsson et al., 1979; Lauretani et al., 2003; Macaluso et al., 2003; Morse et al., 2005; Short et al., 2005; Skelton et al., 1994). In general, results from longitudinal studies suggest that cross-sectional studies often underestimate the rate of decline of muscle strength, because they do not take into account the influence of physical activity, nutritional habits, and quality of health care between the different generations compared, making the assumption that the strength of the elderly population analyzed is similar to when they were the same age as the younger population.

Regarding areas, it has been well documented that the age-related loss of muscle strength is more pronounced in lower than in upper limbs (Amaral et al., 2014; Landers et al., 2001; Lynch et al., 1999). For instance, Hughes et al. (2001) demonstrated a decline of isokinetic strength of 16% vs 2% of the lower and upper limbs, respectively, in older women between the fifth and eighth decades, while Frontera et al. (2000) found that the isokinetic strength of the knee extensor muscles declined by 23.7% in male and female participants after a period of 12 years after 65 years of age, a significantly greater decrease rate than that of the elbow flexor muscles, which decreased by 19.4% over the same period. Moreover, studies have demonstrated that even in lower or upper limbs, the aging effect on muscle strength is different between individual muscles, with elbow extensor decline being greater than elbow flexor (26% and 17%, respectively), or plantar flexor compared to dorsi flexor (63% vs 48%, respectively) (Klein et al., 2001; Vandervoort & McComas, 1986).

It is important to note that rates of decline of muscle strength vary by sex. Evidence suggests that sex differences may exist in muscle strength. Sex can explain between 40–74% of the variance in muscle strength throughout life, which means that a strong association between sex and muscle strength exists (Leblanc et al., 2015). Previous works, mainly cross-sectional studies, have demonstrated that men tend to possess significantly greater absolute maximal muscle strength than women throughout all ages of the life span (Doherty, 2003; Lanza et al., 2003; Lauretani et al., 2003; Vandervoort & McComas, 1986). In fact, specifically data from the Health ABC study indicated that knee extensor isokinetic strength torque is 38.1% lower in older women compared to their male counterparts (81.85 Nm vs 132.15 Nm, respectively) (Newman et al., 2003). Other studies have established that women are approximately 52% and 66% as strong as men in the upper and lower body, respectively (Miller et al., 1993), or have 42.2–62.8% of the isokinetic quadriceps torque of males between the ages of 65 and 70 years (Frontera et al., 1991; Short et al., 2005). Even when muscle strength is normalized for fatfree mass, the differences in muscle strength between older men and women have been reported as significant (Frontera et al., 1985; Newman et al., 2003).

Due to men in general having higher levels of strength than women, they have more to lose with aging. Men tend to lose a greater proportion of strength compared to women. Longitudinal studies have reported a larger magnitude of decrease in strength over time (Charlier et al., 2016; Goodpaster et al., 2001), with men experiencing a 13% decline per decade compared to 8% in women from the third to the ninth decade (Short et al., 2005). Annually, declines in muscular strength have been reported as up to 3–4% and 2.5–3% in men and women, respectively (Delmonico et al., 2009; Frontera et al., 2000; Goodpaster et al., 2006), with men losing strength almost at the same pace in upper and lower extremities, while women have a greater rate of decline in the lower limbs relative to their upper

extremities (Lynch et al., 1999; Hughes et al., 2001). In comparison with younger adults, older women have 58–78% less concentric quadriceps strength than young women (Murray et al., 1985) and 17.6% less knee extensor strength compared to women aged 45–54 (Frontera et al., 1991), while in older men this loss amounts to 20% (Frontera et al., 1991). However, despite what it may seem, the most relevant finding based on these data is the confirmation that older women reach significantly lower levels of muscle strength than men at a similar age. As a consequence, women experience greater loss of functional ability and independence than men, making it necessary to apply new exercise strategies to counteract this biologically adverse situation.

Although the physiological processes responsible for the decline of muscle strength have not been elucidated, different factors potentially influencing muscle strength decline and its relation with functional capacities have been identified in the literature. It seems that the age-related decline of muscle strength is influenced by structural, neural and musculotendinous/connective tissue factors (Doherty, 2003; Frontera et al., 2000). Structural muscle changes, which can be classified into macro (morphological and contractile) and micro (biochemical and cellular) structural changes (da Rosa Orssatto, Wiest & Diefenthaeler, 2018), contribute to the loss of muscle function with aging through muscle fiber atrophy (especially type II myofibers) (Joseph et al., 2012; Lexell et al., 1988; Lexell & Taylor, 1991; Nilwik et al., 2013), increase of accumulation of inter- and intramuscular non-contractile components (adipose and connective tissues which can account for 15% of total muscle CSA) (Alnaqeeb et al., 1984; Delmonico et al., 2009; Goodpaster et al., 2008; Kent-Braun et al., 2000), changes in muscle architectural properties (decrease of CSA, muscle thickness, pennation angle, fascicle length) (Kubo et al., 2003a; Kubo et al., 2003b; Narici et al., 2003; Thom et al., 2007), and declines in protein synthesis (reduced concentration of myosin proteins per unit of muscle area) (Dardevet et al., 2000; Ditroilo et al., 2012; Hasten

et al., 2000; Rooyackers et al., 1996) and in the activity of satellite cells (Madaro et al., 2015; Verdijk et al., 2007).

In addition, at the neuromuscular level, impairments in neural activation via reduction in the number of motor units (McNeil et al., 2005; Piasecki, Ireland, Coulson et al., 2016; Vandervoort, 2002), decreased motor unit firing rates (Kamen et al., 1995), greater variability in motor unit discharge (Christou, 2011), changes in agonist-antagonist co-activation (Clark & Manini, 2008, 2010; Häkkinen et al., 1998a, 1998b), impaired excitation-contraction coupling processes through impairments in calcium release from the sarcoplasmic reticulum (Delbono, 2011; Payne & Delbono, 2004), degeneration of neuromuscular junctions (Gonzalez-Freire et al., 2014), denervation of fibers belonging to a single motor unit (Lexell et al., 1983), loss of the regenerative capacity of the muscle fiber to be reinervated (Distefano & Goodpaster, 2018), incomplete reinnervation of previously denervated muscle fibers (Aagaard et al., 2020; Larsson et al., 2019), decreased rate of axonal transport and conduction velocity (Larsson et al., 2019), and decreases in the excitability of spinal pathways (Kido et al., 2004) contribute to reductions in muscle strength (Clark, 2019; Clark & Manini, 2010).

Another important contributor to the reduction of muscle strength is the changes in body composition and structure of the tendon. During aging, the tendinous stiffness decreases by approximately 15% (da Rosa Orssatto, Wiest & Diefenthaeler, 2018), which means that the muscle contraction has to be longer in time so that the tendon can transmit force from muscles to bones. As the tendon is more compliant and will elongate more during muscle contractions, the force-length relationship will be altered. Furthermore, other factors such as vascular changes (Groen et al., 2014; Tanaka et al., 2000) and low-grade chronic inflammation (inflammaging) (Baylis et al., 2014; Kalinkovich et al., 2017) are present as strong mechanisms of muscle weakness.

All of these mechanisms are behind the reduction of muscle strength in older adults, which is significantly related to increased disability and the loss of functional independence and institutionalization (Phillips et al., 2009; Wall et al., 2013). In fact, in older women, leg muscle strength is correlated with physical function measures such as normal or maximum gait speed and the chair stand test (Barbat-Artigas et al., 2013; Rantanen et al., 1998).

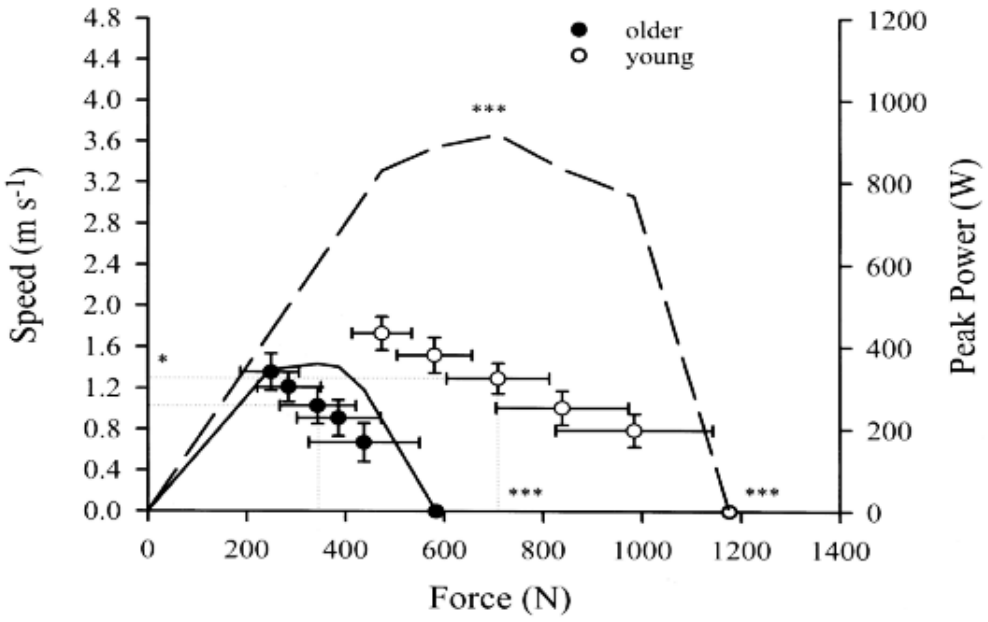
In summary, the age-related loss of muscle strength can negatively impact the physical function of older women, making it necessary to apply training protocols to prevent and avoid as long as possible the adverse effects produced by the muscle strength weakness.

B. Effects of aging on muscle power

It is well-known that muscle power, which is defined as the product of muscle force and movement velocity (i.e., the ability of the muscle to generate forceful contractions quickly), declines at a faster rate and earlier in life compared with muscle strength and muscle mass (De Vito et al., 1998; Izquierdo et al., 1999; Lauretani et al., 2003; Macaluso & De Vito, 2003a; McNeil et al., 2007; Metter et al., 1997; Pearson et al., 2002; Reid, Pasha et al., 2014; Reid & Fielding, 2012; Runge et al., 2004; Siglinsky et al., 2015; Skelton et al., 1994; Zengin et al., 2017), which is believed to be due to, along with the strength (force) component, the velocity component decreasing too (Figure 60) (De Vito et al., 1998; Pojednic et al., 2012). Evidence suggests that muscle power increases from childhood until reaching the peak value at the age of 20–30 years (Bosco & Komi, 1980; Mercier et al., 1992), after which it remains almost constant up to 40–50 years (Samson et al., 2000), and then declines to the end of life (De Vito et al., 1998; Edwen et al., 2014; Izquierdo et al., 1999; Macaluso & De Vito, 2003a; Metter et al., 1997; Reid, Pasha et al., 2014). The reduction in muscle power with age has been reported at a rate of up to 6% per year (Clark et al., 2013; Skelton et al., 1994), or also ~8–9% over a three-year period (Reid, Pasha et al., 2014), diminishing twice as fast as muscle strength (Aagaard et al., 2010; Cruz-Jentoft et al.,

2010; Fielding et al., 2002; Skelton et al., 1994). Several investigations have found this age-related reduction of muscle power to be linear (De Vito et al., 1998; Edwen et al., 2014; Macaluso & De Vito, 2003a; Pearson et al., 2002; Runge et al., 2004; Samson et al., 2000; Siglinsky et al., 2015), but other studies have demonstrated that muscle power decline increases at higher rates with advancing age, drawing a curvilinear relationship (Alcazar et al., 2020; Metter et al., 1997; Lauretani et al., 2003).

Figure 60. *Force-Velocity and Force-Power relationships between younger and older women in their 3rd and 8th decades taken during single lex extension*.



Note. The Force – Velocity curve is represented by circles while the Force- Power relationship is represented by solid line for older and broken line for younger women. The lighter broken lines represent the corresponding optimal force and velocity for maximal power. Reproduced from "Comparison between young and older women in explosive power output and its determinants during a single leg-press action after optimisation of load" (p. 460), by Macalyso and De Vito, 2003, *European Journal of Applied Physiology, 90*(5).

Very recently, Alcazar and colleagues (Alcazar et al., 2020) determined the age- and sex-specific changes in lower-limb muscle power throughout the life span in 1,305 adults (20–93 years) from Denmark. Their main findings were that the onset of muscle power decline is manifested in the fourth decade of life in both women and men, while the lower absolute, relative (normalized to body mass), and specific (normalized to leg lean mass) muscle power levels' decline can be detected from the age of 50 years (Alcazar et al., 2020), with older individuals (both men and women) demonstrating significant decreased values of relative, absolute and specific muscle power than young adults. Other authors arrived at the same conclusion, finding that elders in their 70s and 80s have significantly lower power (~44–52%), and rate of force development (~74%) (Edwén et al., 2013; Leyva et al., 2016) compared with adults of 30 years of age, or even compared with healthy middle-aged adults (~19–44%) (Pojednic et al., 2012).

As happened with muscle strength, the decline in muscle power is not uniform throughout the body, with the leg extensor muscle power being affected more than the distal muscles of the lower and upper limbs (Candow & Chilibeck, 2005; Izquierdo et al., 1999; Lanza et al., 2003). For instance, peak power in the knee extensor muscles declined by 33% from the third to the eighth decade, while in the dorsi flexor muscles decline was only 26% (Lanza et al., 2003).

Regarding the sex-specific changes in muscle power, similar to the relationship between muscle strength and sex, muscle power produced by women is significantly lower in comparison to that of men of similar ages throughout the life span (Bosco & Komi, 1980; Lanza et al., 2003; Lauertani et al., 2003; Petrella et al., 2005; Skelton et al., 1994; Trappe et al., 2003). Alcazar et al. (2020) corroborated this finding and found that men demonstrated not only significantly higher levels of absolute muscle power, if not also relative and specific muscle power compared to women of all age groups, except for specific muscle power above

the age of 80, where women exhibited similar values to men. The difference in peak muscle power between men and women is approximately 16% in their third decade of life, while this difference can increase to 30–50% and more by the eighth decade (Bosco & Komi, 1980; Brady & Straigth, 2014; Lauertani et al., 2003; Skelton et al., 1994). Trappe et al. (2003) even reported that the peak muscle power of young women (third decade) is similar to that produced in the eighth decade by older men.

Furthermore, as happend with muscle strength, the rate of decline in muscle power is lower (1.7% vs 3.0%, respectively) and starts later (45 vs 40 years) in older women compared to men (Alcazar et al., 2020; Skelton et al., 1994), independently of the type of muscle power analyzed (absolute, relative or specific power) (Alcazar et al., 2020). However, this phenomenon demonstrates how vulnerable older women are, because for elderly women it is more difficult to reach the threshold required to maintain functional independence, because their absolute, relative and specific muscle power is lower than that of men, and therefore they are more prone to functional disability and institutionalization (Lanza et al., 2003; Macaluso & De Vito, 2003b; Skelton et al., 1994).

In addition, it is necessary to take into account that, despite the fact that both muscle strength and muscle power are important components of health and function (Cheema et al., 2014; Davies et al., 2017; de Vos et al., 2005; Fielding et al., 2002; Newman, Kupelian et al., 2006), muscle power is a better and stronger predictor of functional performance, disability, and physical impairment than muscle strength in older people (Bean et al., 2003; Cuoco et al., 2004; Foldvari et al., 2000; Macaluso & De Vito, 2003a; Martinikorena et al., 2016; Metter et al., 1997; Reid & Fielding, 2012), being more related to the ability to perform daily activities such as rising from a chair or climbing a flight of stairs (Bassey et al., 1992; Izquierdo et al., 1999). It seems that the velocity component of power is related to physical impairment in older adults, independently of the strength component of power (Bean et al., 2003; Pojednic

et al., 2012), which may be the reason why power has been demonstrated to be a stronger predictor of physical limitations than strength.

Specifically, the maintenance of leg extensor power could be particularly important, due to its implication for ambulation in older adults. If fact, this parameter has been identified as a predictor of mobility disability (inability to ascend a flight of stairs or to walk one km) in older men and women (Brady & Straight, 2014), with a higher risk to develop mobility disability in women in the next three years if the leg extensor power is below 64 watts (W) (47.2% vs 15.7%) (Hicks et al., 2012). Moreover, a large body of evidence links these age-related reductions in power strength to severe functional consequences, such as an increased risk of falls (Bassey et al., 1992; Suzuki et al., 2001), hip fractures (Dean et al., 2004; Foldvari et al., 2000), decreased walking speed (Cuoco et al., 2004; Himann et al., 1988; Skelton et al., 1994), and ultimately increasing the risk of dependence and institutionalization in later years (Christensen et al., 2008). Furthermore, muscular weakness is also related to other negative health situations, including cognitive decline (Alfaro-Acha et al., 2006; Boyle et al., 2009; Buchman et al., 2009; Taekema et al., 2010), osteoporosis (McGrath et al., 2017), diabetes (Peterson, Zhang, Choksi et al., 2016), and early all-cause mortality (McLean et al., 2014; Metter et al., 2004; Wu et al., 2017).

Regarding the explanation for the reduction of muscle power, as power is the product of force and contractile velocity, there are several reports indicating that the age-related loss of muscle power is determined by factors influencing the force component and also by factors affecting the contraction velocity component (Alcazar et al., 2020; Mckinnon et al., 2017). Thus, anything that will affect force production or speed of shortening of a skeletal muscle will affect the power output generated. Therefore, all the factors previously reviewed in the muscle strength section to explain the loss of muscle strength in the elderly population can be transferred to power. However, what must be taken into account is all the special interest

factors that may affect the speed of the muscle contraction, because some authors have reported that the velocity component of muscle power is more relevant for age-related decline in muscle power than the force component (De Vito et al., 1998; Edwen et al., 2014; Reid, Martin et al., 2014), although the mechanism leading to impaired muscle power might vary between subjects (Alcazar, Rodriguez-Lopez et al., 2018).

In this sense, muscle atrophy does not explain the entire muscle power decline, because when muscle power is adjusted for muscle mass (relative muscle power), it continues to reduce with advancing age (Petrella et al., 2004; Piaseki, Ireland, Stashuk et al., 2016; Reid, Pasha et al., 2014; Roberts et al., 2018), suggesting the enrollment of neurological factors. Several of these potentially affect the velocity of muscle contraction, such as the preferential atrophy of type II muscle fibers (Larsson et al., 1979; McPhee et al., 2018), the transition of type II muscle fibers to type I (Hepple & Rice, 2016; Kelly et al., 2018; Ling et al., 2009; Roberts et al., 2018), reductions in the neuromuscular excitation rate (Reid, Pasha et al., 2014), decreased capacity of reinnervation of the muscle fibers (Clark & Manini, 2010), decreased reciprocal inhibition and its effect increasing the agonist-antagonist co-activation and co-contraction (McKinnon et al., 2017), and the smaller number of motor units (~30–40%) compared with young adults (Kelly et al., 2018; Krantic et al., 2005; Nilwik et al., 2013; Piaseki , Ireland, Coulson et al., 2016; Piaseki, Ireland, Coulson et al., 2016). In addition, the decreased speed of contraction may also be due to a decreased volume of the sarcoplasmic reticulum and a reduction in the number of T-tubule dihydropyridine receptors (Fielding, 2002).

In summary, muscle power declines with age and this relationship is particularly important to physical function, with older women being the first group to be considered for interventions that aim to reverse or attenuate the effects of aging on muscle power and which are able to improve muscle power through exercise.

II.VIII.V. Methods to assess neuromuscular strength

There is considerable variety in the tools and protocol assessments of muscle mass and muscle power. It is necessary to have reliable, sensitive, valid and objective tools and field tests to assess both parameters in different populations, especially in older adults, to detect and quantify muscle weakness. The most common and well-validated tests for assessing muscle strength and muscle power are discussed in the following sections.

A. Methods to assess muscle strength

According to Horlings et al. (2008), muscle strength measures can be classified into two groups: direct and indirect. Direct strength measures are those that provide a pure strength parameter or outcome, such as newton (N) or newton per second for example (Horlings et al., 2008), while indirect strength measures evaluate muscle strength by testing aspects of physical function through field tests, such as the five times sit to stand test (5STS). In these tests, the outcomes obtained are not giving pure and direct information of strength, because they indicate, for example, the time duration in seconds or the number or repetitions that have been carried out and they also imply other functional aspects such as coordination (Horlings et al., 2008). Therefore, direct assessments are more appropriate for research while indirect measures are more appropriate for the clinical field, although both can be implemented in both areas.

Muscle strength may be measured using a variety of methods. The review by Mijnarends et al. (2013) evaluated the most common equipment and methods that provide quantitative outcomes of strength in terms of repeatability, validity and practical feasibility in older adults (Mijnarends et al., 2013). Although the muscle strength of different muscle groups can be assessed, handgrip and knee extensor strength are the most commonly evaluated muscle groups in older adults (Sirola & Kröger, 2011; Buckinx & Aubertin-Leheudre, 2019). Three methods are mainly used: 1RM, dynamometry and field tests

(Buckinx & Aubertin-Leheudre, 2019). The assessment of maximal muscle strength in older adults during dynamic contractions is typically performed using the 1RM test, where the maximal amount of weight or the higher resistance that a subject can move or lift for a given exercise in a single repetition and with a predetermined range of motion is evaluated (Hass et al., 2001). It could be calculated for upper and lower muscle groups such as using the chest press (LeBrasseur et al., 2008), leg press (Jones et al., 1999; LeBrasseur et al., 2008), and pull down (Rydwik et al., 2007) exercise machines or also with elastic bands (Manor et al., 2006), or dumbbells (Manor et al., 2006). Different methods are used to find the 1RM (using more or fewer repetitions), repeating the exercise several times at increasing resistance until failure to complete a single repetition (Beaudart et al., 2019). However, there is no consensus and standardization protocol regarding which kind of equipment and techniques are more appropriate, reliable and valid to assess muscle strength using the 1RM in the elderly (Alcazar et al., 2017). Even though it continues to be a valid measure to evaluate muscle strength, in the elderly population and patients with pathologies, it could be advisable to use other tests that could be less harmful and more comfortable for this population.

Probably the most common method to assess muscle strength is by using a dynamometer. There are two main types of dynamometers: portables (handgrip dynamometer and handheld dynamometer) and non-portables (isokinetic dynamometer). The former provides only isometric measurements of strength, while the latter provides both isokinetic (concentric and eccentric) and isometric measures of muscle strength (Benfica et al., 2018). In contrast to 1RM, which is typically confined to the laboratory or the gym, the assessment of grip strength by using a handgrip dynamometer is the gold standard measure for the upper limbs and overall strength in older adults (Beaudart et al., 2019; Buckinx & Aubertin-Leheudre, 2019). In addition, it is the most common measure of muscle strength used in clinical daily practice (66.4% vs 24.2% (1RM leg press), 9.4% (1RM chest press) and 7.4%

(isokinetic dynamometer)) (Bruyère et al., 2015). It is a simple (Beaudart et al., 2016; Fried et al., 2001; Lauretani et al., 2003), inexpensive, non-invasive and reproducible method (Taekema et al., 2010) and does not require specialist trained staff (Ploegmakers et al., 2013). The hydraulic Jamar dynamometer is the gold standard tool for this measurement. In addition, standardized protocols along with validated cut-off values are available, which is not the case for all lower-limb muscle strength measures (Cruz-Jentoft et al., 2010, 2019; Lauretani et al., 2003; Roberts et al., 2011). Accordingly to the EWGSOP, values below 16 kg are considered low for women (Cruz-Jentoft et al., 2019). Indeed, isometric hand grip strength indicates a good correlation with leg strength (knee extension torque) (Stevens et al., 2012) and is also a powerful predictor of decline in cognition, mobility, functional status, longer hospital stays, poor health-related quality of life, higher incidence of cardiovascular diseases and all-cause mortality in older people (Leong et al., 2015; Rikj et al., 2016). The disadvantages are that it is not suitable for patients with advanced arthritis (Bean, Kiely, Herman et al., 2002) and also that isometric strength is not the most representative, because most daily activities require dynamic muscle contractions.

Along with handgrip strength, isometric muscle strength in a variety of motor tasks (grip, pinch, ankle, elbow, hip, knee, trunk flexion) can be assessed by portable handheld dynamometers (Mijnarends et al., 2013). This technique consists of measuring the isometric maximum voluntary strength during contractions performed at a fixed angular position against resistance. It has a potential interest in clinical settings, but also have many limitations, such as that the skill and strength of evaluators can affect the results or that findings could be affected by the joint angle, the position of the patient, the measurement site and the type and speed of the muscle contraction **(**Buckinx & Aubertin-Leheudre, 2019**)**. Recently, Buckinx and Aubertin-Leheudre (2019) and Stark et al. (2011) proposed standardization protocols and analyzed the validity of this method, finding that it varies from

"moderate" to "good." Thus, this method is valid and also has been established as reliable (Abizanda et al., 2011; Wang & Chen, 2010), mainly when the isometric knee extensor strength is evaluated in older subjects (Brown et al., 2000; Callahan et al., 2007). However, there are limited reference data available (Goodpaster et al., 2001; Neder et al., 1999; Newman et al., 2003).

For the purposes of assessing dynamic muscle strength in the appendicular regions, isokinetic dynamometers are the most common and precise method (Arnold et al., 1993; Li et al., 1996; Lund et al., 2005; Maffiuletti et al., 2007). These commercial dynamometers allow both isometric and isokinetic measurements of muscle strength. In the isokinetic mode, the maximum muscle contraction (concentric or eccentric) is guaranteed during the entire exercise and for each degree of joint movement, due to the fact that the angular velocity at which the movement is evaluated is constant (excluding acceleration to and deceleration) and has been determined previously by the tester (Kim et al., 2002; Macaluso & De Vito, 2003b; Yamada et al., 2017).

Although isokinetic or constant speed exercises do not usually occur in nature – because the daily activities of human beings, and specifically older adults, occur against resistance at varying speeds (Harridge et al., 1999) – this method allows for the reliable and comprehensive objective assessment of maximum muscle strength throughout the entire ROM and it collects the closest reflection of the physiological reality of muscle contraction. The variable resistance constantly determined to the subject's capacity for effort and the constant speed provided by this technique throughout the entire ROM, provide isokinetic systems with optimum safety and a high degree of precision (Buckinx & Aubertin-Leheudre, 2019). In fact, the measurement of isokinetic muscle torque from the lower limbs through the assessment of knee extension is the gold standard measure for older adults (Gleeson & Mercer, 1996; Lanza et al., 2003; Macaluso & De Vito, 2003b; Pereira et al., 2019; Trappe et

al., 2003). It has been demonstrated to be a feasible, reliable and valid method to assess muscle strength in older adults and other populations (Brown et al., 2000; Callahan et al., 2007). In addition, muscle isokinetic strength is related to the functional test (5STS) in older women, because the results of knee, hip and plantar flexion and extension explain 48% and 35% of the performance of 5STS and 30sec-CS functional tests, respectively (McCarthy et al., 2004).

In the elderly population, muscle strength is usually evaluated at low speeds (60°/s), because most of the functional activities are performed at these velocities (Lima et al., 2009; Merriwether et al., 2012; Pisciottano et al., 2014). However, muscle strength can also be measured at moderate-high (± 180º/s) and high (240–300º/s) velocities (Francis et al., 2017), although in older subjects, velocities above 180º/s are rarely exceeded. Regarding normative values, some data are available for older populations (Goodpaster et al., 2003; Neder et al., 1999; Newman et al., 2003), and very recently, Pereira and colleagues (2018) established the normative values for knee extensor isokinetic strength at 60°/s for older women (Pereira et al., 2018). Lastly, isokinetic dynamometry provides large advantages over isometric and 1RM strength testing, such as that it allows for assessing the maximum voluntary strength across the resistance range, while the isometric method is only recorded at one angle, and the 1RM method only measures a constant external resistance that can be lifted at the weakest point in the range of motion of the selected movement (Verdijk et al., 2009). By contrast, a potential drawback of isokinetic dynamometry is that it requires the use of expensive, non-portable and sophisticated equipment and high technical knowledge to use the isokinetic device, which limits its feasibility in some environments (Buckinx & Aubertin-Leheudre, 2019; Coudeyre et al., 2016).

Conversely, field tests are more practical methods to assess indirect muscle strength and they are also often used in research to assess mainly lower-limb muscle strength in older

people, because they are easy to use and applicable in clinical settings (Regterschot et al., 2015). Examples of commonly used field tests for the evaluation of lower-limb muscle strength in older adults are the 5STS (Whitney et al., 2005), the 30sec-CS, the stair-climbing test (Bean et al., 2007), the SPPB (Guralnik et al., 1994), and the walking speed test (McCarthy et al., 2004; Rantanen et al., 1998). All of these tests are reliable, valid and feasible in older adults (Mijnarends et al., 2013) and represent good alternatives for measuring the muscle strength of the lower limbs in this population (Bohannon et al., 2010; Zanini et al., 2015). They have the advantage of requiring minimal facilities and equipment, along with no highly qualified personnel (Zanini et al., 2015).

Finally, although less used than the methods mentioned previously, there are other tools and techniques to assess muscle strength, such as force or dynamometric platforms, vigometers, myometers, sphygmomanometers, manual muscle testing and plates with spring gauge (Aguilar et al., 2016; Backman et al., 1989, 1995; Edwards et al., 1987; Martins, Teixeira-Salmela et al., 2015; Mijnarends et al., 2013; Souza et al., 2013). However, except for force platforms, their validity and reliability have been questioned, due to the lack of data to support these devices and methods (Mijnarends et al., 2013).

B. Methods to assess muscle power

Although improving muscle power has been proposed as the primary goal for increasing physical function in older adults through resistance training programs, there is no consensus about which protocol or method is more suitable to evaluate this important parameter in older adults. Investigations looking at muscle power in the elderly population are less numerous than those carried out on muscle strength. Muscle power can be measured in different ways, but none of these have been agreed upon as a gold standard method. Currently, the lack of feasible and standardized protocols, normative values and cut-off points to define low muscle power, along with the specialized equipment required, make the

assessment of muscle power in daily clinical settings difficult, despite being highly recommended (Beaudart et al., 2019).

Following the same classification used to assess muscle strength, a wide variety of testing protocols are available in the literature to evaluate direct (in watts) and indirect (e.g. time, number of repetitions) muscle power through a great variety of tools (Alcazar et al., 2017). Methods used are similar to those to evaluate muscle strength, with some modifications, with the following being the most common: percentages of the 1RM test or maximum isometric contraction using computer-interfaced pneumatic resistance machines, isokinetic dynamometer, Nottingham power rig, vertical jump on a force plate or field tests (Bassey et al., 1992; Cristi et al., 2014; Machado et al., 2010; Petrella et al., 2005, 2007; Reid & Fielding, 2012).

Very recently, Alcazar and colleagues (Alcazar et al., 2017) analyzed in their systematic review the testing protocols used to assess muscle power in older adults. The authors found the following methods to be the most used in the literature: computer-interfaced pneumatic resistance machine (most used: 63.1% of the studies); linear position transducer (21.5%); rotary encoder (4.6%); electro-goniometer or potentiometer plus a load cell (3.1%); tri-axial accelerometer plus a tri-axial gyroscope (1.5%), mono-axial accelerometer plus a force transducer (1.5%), and a potentiometer alone (1.5%) (Alcazar et al., 2017). Leg press was the most performed exercise analyzed for lower limbs, followed by knee extension, whereas for the upper extremities, chest press and rowing were the most reported exercises, respectively (Alcazar et al., 2017).

Of all these methods, the Nottingham power rig is the only device specifically created to assess muscle power output. It was created by Bassey and Short in 1990 and measures the unilateral power production of the leg extensor during a single leg extension, with the

participants seated in an upright position (Alcazar et al., 2020; Straight et al., 2015a, 2015b). In older adults, explosive power has also traditionally been assessed, using a vertical jump performed on a force platform (De Vito et al., 1998; Ditroilo et al., 2011). Nevertheless, this method presents some limitations. On the one hand, it may not be safe in very old individuals, in frail older adults or in elders with osteomuscular disorders (osteoarthritis). On the other hand, older people have to lift their own body weight, which represents a high percentage of their maximum strength and therefore the individual has to work in a less favorable portion of the force-velocity curve (Macaluso & De Vito, 2003b), thus performing the movement at slower velocities than the optimal for maximum power production. With regards to the isokinetic dynamometer, power can be measured in the same way as for maximum muscle strength discussed previously, just using higher speed velocities.

As an alternative, the use of field tests can provide useful indirect information about the muscle power level of an elderly individual. The 5STS and time stair climb test are the most common tests used to measure functional power in older adults (Bean et al., 2007; Henwood & Taaffe, 2006), being valid, reliable and feasible methods (Henwood & Taaffe, 2006; Csuka et al., 1985). Previous studies have evaluated the 5STS or 30sec-CS using a force platform (Cheng et al., 2014; Fleming et al., 1991; Lindermann et al., 2003, 2007; Zech et al., 2011), a 3D accelerometer (Regterschot et al., 2016; Zijlstra et al., 2010), or a linear position transducer (Alvarez-Barbosa et al., 2016; Gray & Paulson, 2014). However, these procedures reduce the possibility to apply field tests in clinical settings. A good alternative is the sit-to-stand muscle power test or the ramp power test. The former allows for collecting direct power output using the 5STS test, only using the subject's body mass and height, the chair height and the time needed to complete the five repetitions (Alcazar, Losa-Reyna et al., 2018), while the latter records the time that the subject took to walk up a ramp with a 3.66 m

run and 0.32 m rise, transforming indirect data in power output using the formula described by Signorile et al. (2007).

It is important to mention briefly that in recent years, with technology development, mobile sensing systems have become available for the measurement of muscle power in older adults. For instance, body-fixed motion sensors attached at the hip and chest have been applied in older adults to estimate leg power output during the STS test (Regterschot, Folkersmaa et al., 2014; Regterschot, Zhang et al., 2014; Zijlstra et al., 2010), providing pure power outcomes with adequate validity (Zijlstra et al., 2010).

Finally, both muscle strength and muscle power can be expressed in absolute terms, normalized to body mass (relative strength or power) or to muscle mass (specific strength or power), all of which are valid procedures, although expressed as a unit per body mass or muscle mass has been reported as more relevant for physical performance than the absolute values per se (Skelton et al., 1994; Alcazar, Lowa-Reyna et al., 2018, Alcazar, Rodriguez-Lopez et al., 2018).

II.VIII.VI. Exercise-related effects on neuromuscular strength

Because the majority of risk factors associated with lower-muscle strength and power increase with age, the adoption of regular physical activity is essential to counteract the decline in physical activity levels, which results in a concomitant decline in muscle strength and muscle power (Walston et al., 2006). Adequate muscular strength and power output is fundamental to preserving physical function, mobility and quality of life in older adults. Therefore, it is vital that clinicians, sports scientists, sports technicians and researchers understand which kinds of interventions can be designed to maximize benefit on muscle strength and power among the fastest-growing segment of our population. Accordingly, the loss of muscle strength and power in the elderly population has been an increasingly

important theme of research in recent years. Many studies have been conducted attempting to increase both parameters in older adults through pharmacological, nutritional and exercise interventions. In the following sections the main findings on training intensity and the training modalities carried out in this PhD dissertation regarding changes in muscle strength and muscle power will be discussed

A. Resistance training, variable resistance, and neuromuscular strength[12]

i. Effects on muscle strength

Over the past 30–40 years, numerous studies have been conducted to examine the effects of resistance training on measures of muscle strength in older adults. As a consequence, in 2009, the effectiveness of this kind of training modality on muscle strength in older adults was deemed by the ACSM to be supported by the highest category of evidence (Evidence Category A) (Chodzko-Zajko et al., 2009). However, the established guidelines for resistance training provide only the minimum recommendations for muscle-strengthening activities, a basis for maintaining muscular strength in the elderly population. Currently, since the publication of the ACSM guideline recommendations for exercise for older adults a decade ago, a continually growing body of research has highlighted that resistance training, following the principles of individualization, periodization, and progression, is the most common, safe, effective and preferred strategy of physical activity intervention for preventing the loss of muscle strength and elicit strength adaptations in older adults (ACSM, 2009; Boutros et al., 2019; Fragala et al., 2019; Peterson & Gordon, 2011).

Mounting high-quality evidence from systematic reviews (Hunter et al., 2004; Latham et al., 2004; Liu & Latham, 2009; Theodorakopoulos et al., 2017; Theou et al., 2011), meta-

[12] Related publication: Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

analyses (Borde et al., 2015; Boutros et al., 2019; Buch et al., 2017; Csapo & Alegre, 2016; de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Guizeli et al., 2018; Martins et al., 2013; Peterson et al., 2010; Raymond et al., 2013; Silva et al., 2014; Steib et al., 2010; Stewart et al., 2014; Straight et al., 2016; Yoshimura et al., 2017) and even an umbrella review (Beckwée et al., 2019) convincingly demonstrate that resistance training interventions are the most effective for combating age-related declines in muscle strength. Particularly, in a very recent umbrella review performed by Beckwée and colleagues (Beckwée et al., 2019), the authors recommended resistance training to improve muscle strength in older adults after collecting and analyzing the data from 14 meta-analyses and systematic reviews, summarizing the robust evidence for the effectiveness of strength training in promoting improvements in muscle strength.

The improvements obtained through strength training vary greatly between studies, from improvements of 9% to 174% (Fragala et al., 2019). Several meta-analyses have tried to provide the average amount of improvement obtained after applying a resistance training program. Peterson and colleagues (Peterson et al., 2010) found positive effects of resistance training on strength outcomes of both upper and lower limbs, with percentage changes of 29 ± 2, 24 ± 2, 33 ± 3, and 25 ± 2, respectively, for leg press, chest press, knee extension, and lat pull among adults > 50 years, and with strength increases ranging from 9.8–31.6 kg. Specifically, for the lower body, they observed a main effect equal to approximately 30% strength gain for both leg press and knee extension following 18 weeks of training, and similar increases (25%) were identified for both upper-body exercises.

In the meta-analysis by Guizelini and colleagues (Guizelini et al., 2018), the authors concluded that resistance training produces a significant increase of 18.4% in muscle strength. These results are slightly smaller when compared with other systematic reviews, which demonstrated increases of 24–33% (Borde et al., 2015; Peterson et al., 2010; Stewart et

al., 2014). This large variability between studies in the meta-analysis is mainly due to the high variety of training protocols applied, as well as the different methods used to analyze the strength outcomes in the elderly population with diverse characteristics.

Factors such as training duration, training frequency, training intensity, time under tension, rest between sets and type of training device used have a high impact on the results finally achieved on muscle strength after applying the exercise protocol in older subjects. In general, resistance training protocols composed of single or multiple sets (two to four), intensity ranging from 40% to 85% of 1RM, and performed with a weekly frequency from one to three sessions per week result in average increases of 20–70% in muscle strength after a training period of 6 to 24 weeks (Cadore et al., 2014).

However, to clarify the influence of these training parameters on muscle strength in older adults, the dose-response relationship has been analyzed by some studies (Borde et al., 2015; Cadore et al., 2014; Guizelini et al., 2018). Borde and colleagues (Borde et al., 2015) found in their meta-regression that the variables of training period, intensity and the total time under tension had significant effects on muscle strength, with the largest effects for the longest training periods (50–53 weeks), intensities of 70–79% of the 1RM and the total time under tension in each repetition of 6 s (Borde et al., 2015). They also found a tendency towards significance for the parameter "rest between sets," with 60 s indicating the largest effect on muscle strength (Borde et al., 2015). In addition, two training sessions per week, a training volume of two to three sets per exercise, seven to nine repetitions per set and a rest of four seconds between repetitions were more effective than other amounts (Borde et al., 2015). Conversely, Guizelini et al. (2018) found that training duration had no influence on the strength gains after short-to-medium periods (4–16 weeks) of resistance training.

Despite the generally consistent response of muscle strength to resistance training, little is known about the relationship between sex and strength gains. Only Peterson et al. (2010) explored this relationship in a meta-analysis and demonstrated that both older women and older men achieved significant strength improvements without significant differences between the sexes. Nevertheless, the degree of response varies considerably and the results from several studies are inconclusive. While some studies have reported similar gains among the sexes (Ivey, Roth et al., 2000; Leenders et al., 2013; Roth et al., 2001; Tracy et al., 1999), others have reported greater relative and absolute improvements in men than in women (Bamman et al., 2003; Da Boit et al., 2016; Ivey, Tracy et al., 2000; Tracy et al., 1999).

What seems clear is that in older adults, strength training has been consistently demonstrated to have potential as a strategy to mitigate age-related neuromuscular changes, because skeletal muscle remains highly malleable with exercise training, even into an advanced age, maintaining its plasticity and its ability to adapt structurally and functionally to the resistance exercise (Macaluso & De Vito, 2003b; Narici et al., 2004). The underlying mechanisms for exercise-induced improvements in muscle strength have not been elucidated and there are likely multiple factors at play. It seems that primary improvements from strength training results from neural adaptations in the first weeks of a training program by increasing the motor unit recruitment/firing rate (Arnold & Bautmans, 2014; Prevost et al., 1999), the motor neuron excitability (Hakkinen et al., 2001), muscle innervation (Messi et al., 2016) and the neuromuscular junction function (Deschenes et al., 2015). In an early to mid-phase, muscle strength improvements will be mediated by learning patterns regarding technique (Kraemer et al., 1995), as well by increasing activation of the agonist muscles and reduced coactivation of the antagonist muscles (Häkkinen et al., 1998). Finally, in a late phase, morphological and structural changes of the musculotendinous system, such as

hypertrophy (Housh et al., 1992), increased tendon stiffness and hysteresis (Narici et al., 2008; Reeves et al., 2003), and reduction of intramuscular fat (Radaelli et al., 2013) occur.

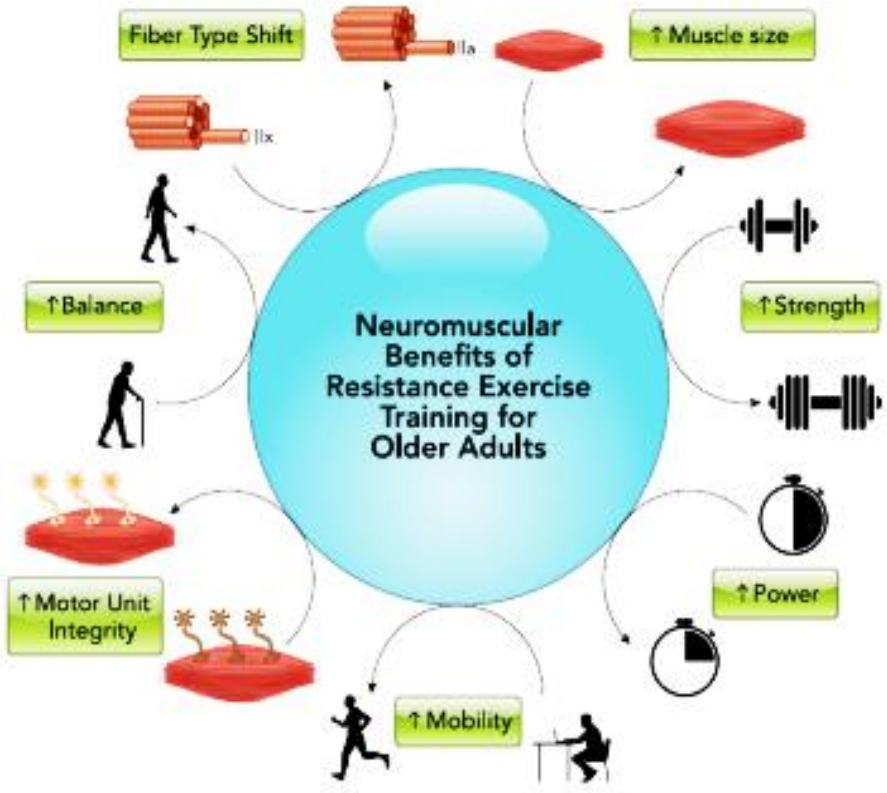
The ACSM suggests that several different types of devices can be used to improve or maintain muscle strength, including free weights, machines and resistance bands (Chodzko-Zajko, 2014; Garber et al., 2011; Ratamess et al., 2009). However, most of the resistance training protocols to improve muscle strength in older adults have been carried out with machines and free weights, but not with variable resistance such as elastic bands. Only a few studies have employed elastic resistance as equipment for older adults to improve muscle strength (Damush & Damush, 1999; Fahlman et al., 2011; Flández et al., 2020. Fritz et al., 2018; Gargallo et al., 2018; Krebs et al., 2007; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017; Ribeiro et al., 2009; Rogers et al., 2002; Thiebaud et al., 2013; Topp et al., 1996). Despite the lack of studies, two previous systematic reviews demonstrated that resistance training performed with elastic bands is an effective training method to improve muscle strength of upper and lower limbs in adults and the elderly population (de Oliveira et al., 2017; Thiebaud et al., 2014; Martins et al., 2013), particularly in "healthy" subjects and those with functional limitations, being less effective in subjects with some kinds of disorders (Martins et al., 2013). Even the addition of variable resistance, such as chains or elastic bands attached to free weights (barbell in bench press or back squat), could also be an effective method for improving muscle strength in athletes and untrained subjects (Soria-Gila et al., 2015). In addition, the results of the meta-analyses of de Oliveira et al. (2016) and Lopes et al. (2019) provided the same conclusion: elastic resistance training is not superior to other methods for improving upper and lower muscle strength in older adults. Thus, elastic resistance training is able to promote similar strength gains to conventional resistance training in different population profiles and using diverse protocols (Lopes et al., 2019).

As a consequence, most of the studies have demonstrated the effectiveness of the elastic resistance training method to increase muscle isometric, isotonic and isokinetic strength in older adults (Damush & Damush, 1999; Dancewicz et al., 2003; Fritz et al., 2018; Gargallo et al., 2018; Krebs et al., 2007; Martins et al., 2013; Oh et al., 2016; Ribeiro et al., 2009; Thiebaud et al., 2013; Webber & Porter, 2010a, 2010b; Woo et al., 2007), although there are also authors that did not observe improvements at this parameter (Krebs et al., 2007; Martins, Safons et al., 2015; Oesen et al., 2015).

Despite these favorable results, an important aspect to highlight is the low quality of the studies and the high variety of training protocols and subject population studied (Martins et al., 2013). For instance, most of the studies do not use an appropriate method to control intensity with elastic bands, or the intensity was too low for the stated objective. Usually, studies' duration ranged from 6 to 24 weeks, using one to three sets of two to 11 exercises and performing between 10 and 12 repetitions per exercise, with the female gender being the most analyzed (Martins et al., 2013).

In summary, decades of research have led to strong evidence that resistance training has a positive impact on muscle strength in older adults (Figure 61). Various forms of resistance training have the potential to improve muscle strength, such as variable resistance training. However, it is still not known how this kind of resistance training can improve muscle strength output in older adults, and particularly in healthy older women, due to the low quality of the studies conducted to date, the high variability of the population analyzed and the lack of the dose-response relationship.

Figure 61. *Neuromuscular benefits for older adults undergoing resistance exercise training*.



Note. Reproduced from "The importance of resistance exercise training to combat neuromuscular aging" (p. 113), by Lavin et al., 2019, *Physiology*, *34*(2).

ii. Effects on muscle power

A fundamental relationship exists between strength and power, since power is the product of strength and velocity. Accordingly, resistance training interventions have been designed to improve muscle power in older adults (de Vos et al., 2005; Henwood et al., 2008; Henwood & Taaffe, 2005; Holviala et al., 2012; Hruda et al., 2003; Liu-Ambrose et al., 2010; Lohne-Seiler et al., 2013; Marsh et al., 2009; Rambsbottom et la., 2004; Reid et al., 2008; Sayers & Gibson, 2010; Skelton et al., 1995). In fact, resistance training has been suggested as a safe and effective intervention strategy for preventing the loss of muscle power in adults (Evans & Campbell, 1993; Reid & Fielding, 2012), with the position statement by the ACSM

recommending it for this population (Garber et al., 2011; Kraemer et al., 2002; Nelson et al., 2007).

Despite these recommendations for adults, the effects of traditional slow-moderate velocity resistance training on power outcomes in older adults are contradictory. Some studies have reported significant improvements (Bean, Kiely, Herman et al., 2002; Behm & Sale, 1993b; Caserotti et al., 2008; Cormie et al., 2010; de Vos et al., 2005; Frontera et al., 1988; Hakkinen, Newton et al., 1998; Henwood et al., 2008; Izquierdo et al., 2001; Jozsi et al., 1999; Kaneko et al., 1983; Latham et al., 2004; Macaluso et al., 2003; McBridge et al., 2002; Miszko et al., 2003; Moss et al., 1997; Ramirez-Campillo et al., 2014; Sayers et al., 2003; Skelton et al., 1995; Stone et al., 1979; Stowers et al., 1983; Wilson et al., 1993; Toji et al., 1997; Toji & Kaneko, 2004), where the improvements in strength are accompanied by increasing power strength, while others have not (Bean, Kiely, Herman et al., 2002; Newman et al., 2003).

To determine whether traditional or power resistance training is more effective in improving power outcomes, a common empirical approach has been to compare the effectiveness of traditional resistance training vs high-velocity/power strength training on muscle power in older adults. Four meta-analyses have reviewed data from studies adopting this approach (Byrne et al., 2016; Straigth et al., 2016; Steib et al., 2010; Tschopp et al., 2011). Steib et al. (2010) and Tschopp et al. (2011) reported an SMD of 1.66 (95% CI 0.08–3.24) and 0.42 (95% CI -0.02–0.85) in favor of power training, after analyzing four and seven studies, respectively (Steib et al., 2010; Tschopp et al., 2011). The level of this evidence was considered by the authors “moderate” and “weak,” due to the low quality, small sample sizes and wide CIs (Steib et al., 2010; Tschopp et al., 2011). In addition, the findings from the meta-analysis by Straigth et al. (2016) indicated that resistance training is an efficacious intervention strategy for improving leg press and knee extension muscle power in adults aged

> 50 years (Straigth et al., 2016). However, again, high-velocity resistance training was superior to traditional training in increasing lower-extremity muscle power. The studies included in this meta-analysis involved community-dwelling, middle-aged, and older adults (Straigth et al., 2016). Lastly, the results of the recent meta-analysis by Byrne and colleagues (Byrne et al., 2016), which included 13 studies that compared power and traditional resistance training, support the evidence for the superiority of power training over traditional resistance training for improving muscle power in older adults. In fact, nine of the 13 studies reported these findings, with four of seven studies reporting significantly greater improvements in lower-limb muscle power (Balachandran et al., 2014; Correa et al., 2012; Sayers et al., 2003, 2012), two equivalent gains in lower-limb power (Pamukoff et al., 2014; Ramirez-Campillo et al., 2014), one reporting greater gains in upper-limb power, (Ramirez-Campillo et al., 2014) and one study reporting no change in power with either power or traditional resistance training (Drey et al., 2012). In general, the training programs were characterized by a training volume ranging from one to six sets, four to 20 repetitions, at intensities ranging from 20% to 80% 1RM and one to 11 exercises. The training sessions lasted from 10 to 90 min and the training duration from 6 to 52 weeks (majority 6–16 weeks), with a training frequency of two to three days per week (Byrne et al., 2016). Most of the samples analyzed were older men and women.

Especially interesting is the study by Tiggemann and colleagues (Tiggemann et al., 2016), because it is the only one to date that used the perceived exertion method to control the intensity of the traditional and power training programs in older women. They demonstrated increases in muscle strength and power of the lower limbs (leg press and knee extension) in both traditional and power training groups, following a training period using perceived exertion to control the intensity (Tiggemann et al., 2016).

It is important to note that previous works have detected some factors that act as moderators in the response obtained on muscle power after a resistance training program in older adults. Research has demonstrated that the training volume is a key determinant, with larger effects on muscle output after resistance training interventions with a moderate volume (product of sets x repetitions = 24) than low (< 24) or high (> 24) (Straight et al., 2016). However, to date no specific guidelines have been published regarding the optimal resistance training volume for improving muscle power in "healthy" older adults. In addition, the ability to increase muscle power has also been related to the previous individual level of strength of the subjects (Cornie et al., 2011). Thus, increases in maximal muscle power following resistance training are expected to be higher in untrained or moderately trained subjects than in stronger individuals. Conversely, age and sex do not seem to have an influence on the effect of resistance training on lower-body muscle power, as Straight et al. (2016) concluded in their meta-analysis.

With this background, it seems pretty clear that strength training can improve power through the strength component in the strength-velocity curve, but there is strong consensus that power resistance training or resistance training at fast velocity results in greater power improvements (2.20 ± 1.34% per week) (da Rosa Orssatto, Cadore et al., 2019) compared with traditional slow-moderate resistance training (Balachandran et al., 2014; Bottaro et al., 2007; Casertti et al., 2008; Conlon et al., 2017; Correa et al., 2012; Henwood et al., 2008; Radaelli et al., 2018; Ramírez-Campillo et al., 2014a, 2014b, 2017; Reid, Martin et al., 2014). Thus, the benefits of resistance training exceed improvements in skeletal muscle size and strength alone, thanks probably to the neuromuscular changes that it produces such as increased CSA of type I and II fibers (Campos et al., 2002; Dons et al., 1979; Hakkinen et al., 1981; Green et al., 1998; Thorstensson et al., 1976), greater pennation angle and fascicle length (Aagaard et al., 2001; Kawakami et al., 1995), and increased neural drive and inter-

and intra-muscular coordination (Kaneko et al., 1983; Komi et al., 1978; McBridge et al., 2002; Moss et al., 1997; Narici et al., 1989).

B. Exercise intensity and neuromuscular strength

i. Effects on muscle strength

There is strong evidence that resistance training can mitigate the effects of aging on muscle strength (Borde et al., 2015; Peterson et al., 2010; Silva et al., 2013; Steib et al., 2010). However, to provoke these desirable training adaptations, a training parameter that has been identified as a key or moderator in the process of improving strength through strength training must be taken into account: training intensity (Beckwée et al., 2019; Borde et al., 2015; Peterson et al., 2010; Steib et al., 2010). It is important to note that there is no standardized definition of the intensity thresholds of high, moderate, or low intensity in the literature, which makes it difficult to determine the homogeneity of the findings among the existing evidence. Previous meta-analyses have classified high intensity as loads ≥ 80% 1RM (Csapo & Alegre, 2016; Peterson & Gordon, 2011), while others ≥ 70% 1RM (Raymond et al., 2013), moderate-high intensity as 70–79% 1RM (Peterson & Gordon, 2011), moderate intensity as 50–69% 1RM (Beneka et al., 2005; Borde et al., 2015; Raymond et al., 2013), or low-moderate as 60-69% 1RM (Peterson & Gordon, 2011) and, finally, low intensity as loads lower than 50% 1RM (Beneka et al., 2005; Borde et al., 2015; Raymond et al., 2013) or lower than 60% 1RM (Peterson & Gordon, 2011; Csapo & Alegre, 2016). The training load used in resistance training interventions with older adults typically ranges from 30% to 90% of 1RM (Fragala et al., 2019), with moderate close to high intensity (69% 1RM) being the most used intensity across studies (Borde et al., 2015).

World-leading organizations in exercise have recommended that resistance training be performed at moderate-to-high intensities, which means training loads between 60% to 80% of 1RM (ACSM, 2009; Peterson & Gordon, 2011). In order to analyze the influence of

training intensity on the strength gains in older adults, 15 years ago the first studies appeared that compared different resistance training intensities in older adults (Fatouros et al., 2005; Seynnes et al., 2004). These studies observed superior increases in muscle strength when participants trained at higher intensities (~80% 1RM) compared to lower intensities (<60% 1RM). Later, more studies were performed trying to elucidate the question of the influence of training intensity in strength gains (Beneka et al., 2005; Cassilhas et al., 2007; DeBeliso et al., 2005; Fatouros et al., 2005; Fatourus et al., 2006; Harris et al., 2004; Hortobagyi et al., 2001; Hunter et al., 2001; Kalapotharakos et al., 2004, 2005; Pruitt et al., 1995; Seynnes et al., 2004; Singh et al., 2005; Sullivan et al., 2005; Taaffe et al., 1996; Tsutsumi et al., 1997, 1998; Vincent et al., 2002; Willoughby et al., 1998). In order to collect and analyze all of this information, several meta-analyses comparing the effectiveness of resistance training at different intensities in the elderly population were carried out in recent years (Borde et al., 2015; Csapo & Alegre, 2016; Peterson et al., 2010; Peterson & Gordon, 2011; Raymond et al., 2013; Silva et al., 2014; Steib et al., 2010).

These meta-analyses have produced mixed data. Peterson et al. (2010) and Silva et al. (2014) compared studies with intensities between 40% and 85% 1RM and verified a dose-response relationship between muscle strength and resistance training intensity in older adults, with higher-intensity training associated with greater improvements in muscle strength. Particularly, Peterson et al. (2010) in their meta-analysis which included 47 studies, observed that the mean percentage change in maximal strength gains when increasing intensity from one subgroup to another (low intensity: <60% 1RM, low/moderate intensity: 60-69% 1RM, moderate/high intensity: 70-79% 1RM and high intensity: ≥80% 1RM) was 5.5% (Peterson et al., 2010). Moreover, along with Peterson et al. (2010), other meta-analyses have suggested greater effects not only of high intensity compared with moderate or low intensity, but also from moderate intensity compared with low intensity (Borde et al., 2015;

Peterson et al., 2010; Silva et al., 2014; Steib et al., 2010). For instance, Steib et al. (2010) observed that intensities higher than 75% of 1RM achieved greater effect (with higher effect size (ES)) on maximal strength than moderate (55–75% of 1RM) or lower intensities (<55% of 1RM) in older adults aged 60 to 80 years of age (Steib et al., 2010). In addition, the authors also found that moderate intensity achieved greater effects on maximal strength than low intensity (Steib et al., 2010). The protocols of the trials analyzed were very similar (three times per week, mostly three sets of 6–14 repetitions). Only the duration of the interventions varied substantially (Steib et al., 2010).

However, Borde et al. (2015), analyzing an intensity range from 50% 1RM to ≥ 90% 1RM, demonstrated that the effect of intensity is not characterized by an incremental linearity but by an inversed U-shape profile (Borde et al., 2015). In this meta-analysis, which included 25 studies investigating the effects of resistance training in sedentary older adults (65 years of age and older), intensities between 70% and 79% 1RM generated greater strength gains than lower and higher intensities (Borde et al., 2015). These findings corroborate the idea that a dose-response relationship exists between muscle strength and resistance training intensity in older adults, and also support the recommendations of the ACSM position statement that states that higher intensities result in greater strength gain in older adults (Chodzko-Zajko et al., 2009). Thus, strength adaptations are influenced by training intensity, which is considered a strong moderator.

Despite these results, it is important to recognize that the efficacy of different training intensities when resistance training interventions have been carried out to improve muscle strength in older adults can be influenced and mediated by other training variables, such as volume or duration of the training period. Especially relevant seems to be the influence of volume, because some trials have reported similar strength gains with low repetitions at high intensity and with high repetitions at low intensity (Alegre et al., 2015; Léger et al., 2006;

Taaffe et al., 1996; Vincent et al., 2002), that is, when both training groups are matched for mechanical work (Raymond et al., 2013). This means that, probably, if the training volume is not taken into account, the results of the previous meta-analyses mentioned above may have been biased by the inclusion of studies that used unequal amounts of mechanical work or degrees of training-induced fatigue (Csapo & Alegre, 2016). Indeed, Csapo and Alegre (2016) have suggested that the differences between high and low intensities are minimized when the studies are matched for the total amount of mechanical work, calculated as the product of sets × repetitions × load (Csapo & Alegre, 2016). Nonetheless, even though the difference between intensities are minimized, the authors found in their meta-analysis that even matched for mechanical work, effects are more pronounced when using heavier loads (increases in strength 43% for high intensity before 35% for low to moderate intensity) (Csapo & Alegre, 2016). Another important finding was that both high- and lighter-load training programs may induce significant gains in strength, drawing the conclusion that a "strength-endurance continuum" could exist that implies that, to achieve gains in muscle strength, moderate-high intensities or high volumes have to be prescribed (Campos et al., 2002).

Rather than having to be exposed to high loads or high volumes, achieving maximal effort is also an important factor for gains in muscle strength in older adults (Goto et al., 2005; Carpinelli, 2008). Maximal effort can be defined as the momentary muscle fatigue that is achieved when a series of repetitions within a set is performed. Probably, this maximal effort might be needed to maximize the neuromuscular adaptations to enhance the muscle strength response (Goto et al., 2005; Carpinelli, 2008). In relation to this, some authors have reported that training with heavier loads has been related to a higher RPE than lower loads, even when total mechanical work is matched (Alegre et al., 2015), probably due to a greater sensation of effort. Thus, high intensity could be better, because it allows producing a greater

effort, being closer to the maximal effort. Despite the higher RPE and the characteristics of the high-intensity resistance training, it should be noted that no differences in adherence rates and dropout, as well as adverse events and injuries, were reported between high- and low-intensity resistance training in older adults (Raymond et al., 2013). In fact, this kind of training was even found to be safe in very old adults up to 96 years old (Fiatarone et al., 1990, 1994) when familiarization with proper exercise technique and structured progression were carried out.

In summary, taken together, older adults may experience strength gains in response to resistance training in a wide range of training intensities, with the higher resistance training intensities being more relevant because they elicit greater muscle strength gains, although these improvements are dependent on volume, maximal effort, and duration of the training period. Finally, it is important to note that although high intensity is generally more effective than low-to-moderate intensity, there is no expert consensus on which resistance training protocol or what exact intensity is the most optimal for increasing muscle strength in the elderly population, due to the high heterogeneity between studies and the individual variability in the training response. Furthermore, to date little is known about the effect of training intensity on the specific gender of women to improve muscle strength after a resistance training program, and even less when elastic resistance is used as a training device.

ii. Effects on muscle power

Although inconclusive, evidence on the optimal training intensity for improving muscle strength is by far more notorious than in respect of studies that have tried to identify which is the most appropriate training intensity for improving muscle power in older adults when isotonic contractions are employed. Only a few studies have compared the effects of different resistance training intensities in older adults (de Vos et al., 2005; Macaluso et al., 2003; Orr et al., 2006; Englund et al., 2017; Reid, Martin et al., 2014).

Notably, Reid, Martin et al. (2014) found that high-velocity resistance training with low external resistance (40% 1RM) yielded similar improvements in muscle power (leg extensor peak power) compared to training with high external resistance (70% 1RM), (34% vs 42%, respectively) after 16 weeks in community-dwelling older adults (Reid, Martin et al., 2014), with no significant differences between intensities. In addition, de Vos et al. (2005) compared the effects of three training intensities (20%, 50% and 80% of 1RM) on muscle strength and muscle power and observed that, while muscle strength gains were higher in the group that used the highest load (13% vs 16% vs 20%, respectively), similar muscle power improvements were found across the three levels (~15%) after 12 weeks of high-velocity power training in healthy older subjects without mobility limitations (de Vos et al., 2005). In addition, a wide range of studies have employed different training intensities (low, moderate or high) and all of them have seen improvements in power output in older adults (Earles et al., 2001; Fielding et al., 2002; Reid et al., 2008). However, in contrast to what happens with muscle strength, training intensity has not been stablished as a primary moderator parameter in the response of muscle power to resistance training in older adults, at least not in lower limbs (leg press and knee extension) (Straigth et al., 2016).

The most recent ACSM position statement indicates that intensities of 20–50% should be used if the goal is the improvement of muscle power in healthy adults through resistance training programs (Garber et al., 2011), while Kraemer et al. (2002), in a previous ACSM position statement on models of resistance training and their progression, suggested a combination of light-to-moderate (30–60% 1RM) and heavy (85–100% 1RM) loads, performed always as fast as possible to improve both components of muscle power: velocity and strength, respectively (Kraemer et al., 2002). However, others have suggested that only resistance training with heavy loads (> 60% 1RM) are effective to improve muscle power with resistance training (Hazell et al., 2007).

Very recently, in the systematic review by Katsoulis et al. (2018), the authors investigated the effects of high-intensity (≥70% of 1RM), moderate-intensity (between 51% and 69% of 1RM) and low-intensity (≤50% of 1RM) power strength training on muscle power outcomes in healthy older adults (Katsoulis et al., 2018). Leg press (Bean et al., 2004; Bottaro et al., 2007; Caserotti et al., 2008; de Vos et al., 2005; Earles et al., 2001; Fielding et al., 2002; Henwood et al., 2008; Macaluso et al., 2003; Marsh et al., 2009; Pamukoff et al., 2014; Reid, Martin et al., 2014; Sayers & Gibson, 2014), knee extension (Beijersbergen et al., 2017; Beltran-Valls et al., 2014; de Vos et al., 2005; Englund et al., 2017; Fielding et al., 2002; Henwood et al., 2008; Henwood & Taaffe, 2005; Marsh et al., 2009; Pamukoff et al., 2014; Reid, Martin et al., 2014; Sayers & Gibson, 2010; Wilhelm et al., 2014), knee flexion (Beijersbergen et al., 2017; Beltran-Valls et al., 2014; de Vos et al., 2005; Henwood et al., 2008), and dorsiflexor/plantarflexor (Beijersbergen et al., 2017; Webber & Porter, 2010b) were evaluated. In general, muscle strength improved by 22.4%, 27.2%, and 24.3% with high, moderate and low intensities, respectively, while improvements in muscle power outcomes averaged 26.8%, 33.4%, and 21.5% for high, moderate and low intensities, respectively (Katsoulis et al., 2018). All three intensities were effective to evoke clinically significant changes in muscle power, because the clinically significant change in muscle power was estimated at ~10% in leg press for healthy older adults and ~15% for mobility-limited older adults (Kirn et al., 2016). Specifically, in both the multi-joint exercise of leg press and the single-joint exercise of knee extension (the most studied), the improvements in muscle power were similar across the intensities, with high and moderate intensities indicating little enhanced benefit. The important finding from this review was that power training produced significant gains in muscle power in older men and women regardless of mobility status, age, training duration (from 6 to 24 weeks) or type of external resistance used, and these gains can be achieved using a wide spectrum of intensities (20–80% of the

1RM) (Katsoulis et al., 2018). However, it is necessary to take into account that of the 27 studies, most included men and women, but only six were conducted only on women (Bean et al., 2004; Caserotti et al., 2008; Fielding et al., 2002; Macaluso et al., 2003; Signorile et al., 2002; Webber & Porter, 2010b).

This unclear dose-response relationship found in the evidence and in the guidelines may be due to the force-velocity relationship in skeletal muscles. Despite the fact that, classically, the force-velocity relationship in isotonic concentric contractions indicates that peak muscle power is developed at 30–40% of maximal velocity and at 60–70% of maximal force (McComas, 1996), it seems that, based on the literature available, gains in muscle power can be achieved using a wide range of loads and intensities (20–80% of 1RM). Therefore, different training intensities are likely to produce adaptations in muscle power through different components of power, with higher intensities that could improve muscle strength while lower intensities could increase muscle fiber contraction velocity.

It has been suggested that there might even exist different optimal loads for different exercises, such as bench throws, power cleans, and jump squats (Soriano et al., 2015; Soriano et al., 2017). However, to date only two studies have evaluated optimal training loads among multiple exercises in older persons (Potiaumpai et al., 2016; Strand et al., 2019). Potiaumpai et al. (2016) reported exercise-specific optimal load ranges, with differences attributed to the number of joints involved during a specific lift and the nature of the lever system at each joint during exercises performed with pneumatic machines (Potiaumpai et al., 2016). Strand et al. (2019) found that optimal load ranges differ between multi-joint and single-joint exercises performed with plate-loaded machines, with no differences between the sexes (Strand et al., 2019). Specifically, multi-joint exercises demonstrated a narrow optimal load range (50–60% 1RM for leg press, 50% 1RM for chest press, 40–60% 1RM for seated row and 40–80% 1RM for shoulder press), favoring the velocity component of the force-velocity curve, while single-

joint exercises produced a wider optimal load range (50–60% 1RM for hip adduction, 40–80% 1RM for hip abduction, 50–70% 1RM for calf raise, 60–80% 1RM for biceps curl, 40–80% 1RM for leg curl and 50–80%1RM for triceps extension), including also the force component of the curve by extending the effective threshold into the upper limits of the curve (Strand et al., 2019). Moreover, it is necessary to take into account that the optimal load to produce muscle power could be determined not only in terms of the types of exercises but also by sex. Nevertheless, there are no data available for the elderly, only for the young and athlete populations (Comfort et al., 2015; Thomas et al., 2007).

It is important to note that the training device could also be an important factor in determining the optimal load to increase muscle power. However, to date no studies have been carried out in this regard, comparing different training intensities when the resistance training program is performed with elastic bands. In addition, there is a lack of knowledge regarding the effects of this kind of load (variable resistance) on power outcomes in the older population, and particularly in older women, when it is used in resistance training or high-velocity strength training programs.

In summary, based on the above-mentioned studies, it may be suggested that training at high velocities, with a wide range of intensities (20–80% 1RM), results in power improvements in older adults (Byrne et al., 2016; da Rosa Orssatto, Cadore et al., 2019). Nonetheless, lower training loads produce lower perceived exertion and fatigue rates compared with higher loads, making training more tolerable for the elderly population (Richardson, Duncan, Jimenez, Juris et al., 2018). Based on the evidence available to date, it is necessary to apply resistance training programs at different intensities and high-velocity resistance training programs in older women with variable resistance to know the effects of these kinds of training modalities on muscle power measures.

C. Exercise modality and neuromuscular strength[13]

i. Effects on muscle strength

The decline of muscle strength is a predictor of adverse health events and mobility in older adults, a phenomenon that alters the quality of life of the elderly society. It is therefore essential to assess accurately different training methods and training methodologies to know their effects in the managing of the loss of muscle strength. At present, studies are increasingly interested in understanding the dose-response relationship between different training intensities and modalities and the adaptations that these produce in muscle strength in older adults. Two of the most interesting modalities studied in recent years are multi-component training and power resistance training.

Many reviews and RCTs have demonstrated that muscle strength in older adults can be improved by exercise training, but nearly all focused on unimodal training programs (Bouaziz et al., 2016; Galvao & Taaffe, 2005; Henwood & Taaffe, 2006). Adding more information about different training modalities that can enhance muscle strength in healthy older adults, and particularly in older women, is undoubtedly necessary. Currently, multi-component training interventions, comprising at least three components i.e., strength training, aerobic endurance training, and balance, have been proposed by the current exercise guidelines as an important training modality, due to their effects on fragility and sarcopenia in older adults (Cress et al., 2006). However, there is little and poor quality evidence about the effects of this kind of training regimen in the prevention of muscle decline and the preservation of muscle strength, and even in the reversion of the decline of muscle strength in older adults (Ansai et al., 2015; Barnett et al., 2003; Binder et al., 2002; Carmell et al., 2000;

[13] Related publication: Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

Carvalho et al., 2009; Chandler et al., 1998; Freiberger et al., 2012; Justine et al., 2012; King et al., 2002; Lambert et al., 2008; Levy et al., 2012; Lord et al., 2003; Nakamura et al., 2007; Nelson et al., 2004; Puggaard, 2003; Rubenstein et al., 2000; Seguin & Nelson, 2003; Smith et al., 2012; Shubert et al., 2010; Taguchi et al., 2010; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012; Villareal, Smith et al., 2011; Worm et al., 2001).

Converse to resistance training, where its effects on muscle strength in older adults are consensually established, data regarding the role of multi-component training are often contradictory, with some authors describing positive effects (Ansai et al., 2015; Binder et al., 2002; Carmell et al., 2000; Carvalho et al., 2009; Freiberger et al., 2012; Izquierdo et al., 2016; Justine et al., 2012; Lambert et al., 2008; Levy et al., 2012; Nakamura et al., 2007; Rubenstein et al., 2000; Smith et al., 2012; Shubert et al., 2010; Taguchi et al., 2010; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012; Villareal, Smith et al., 2011; Worm et al., 2001), and others not (Barnett et al., 2003; Jessup et al., 2003; Nakamura et al., 2007; Nelson et al., 2004; Puggaard, 2003), at least not across all strength measures (Judge et al., 1993; Lazowski et al., 1999; Rubenstein et al., 2000). Especially interesting are the findings of the systematic review performed by Baker, Atlantis et al. (2007) and Bouaziz et al. (2016), which revealed that the relative ES for strength measures after multi-component interventions ranged from -0.08 to 1.67, with a mean of 0.41 across all strength measures (Baker, Atlantis et al., 2007), and also that muscle strength gains ranged from 1.4% to 95.0% (Bouaziz et al., 2016). Lopez et al. (2017) supported also the positive effects of multi-component interventions on maximum strength in their meta-analysis on frail older adults (Lopez et al., 2017).

Regarding gender, some studies have demonstrated positive effects of multi-component training interventions on muscle strength in women (Marques, Mota, Machado et al., 2011; Marín- Cascales et al., 2015; de Resende-Neto et al., 2019; Karikanta et al., 2007;

Otero et al., 2017), improving different muscle strength measurements, such as handgrip strength (Marques, Mota, Machado et al., 2011), dynamic or static isokinetic strength of knee flexor and extensor muscles (de Resende-Neto et al., 2019; Marques, Mota, Machado et al., 2011; Marín-Cascales et al., 2015), or functional tests (Marques, Mota, Machado et al., 2011; Otero et al., 2017). Nevertheless, despite the possible beneficial effect of multi-component training on muscle strength, the results, as have been pointed out by the reviews and meta-analyses previously mentioned, are highly affected by the heterogeneity of the exercise interventions and the outcome measurements of strength among studies. For instance, strength measurement methods varied between the 1RM test (Jessup et al., 2003; Judge et al., 1993; Lambert et al., 2008; Lazowski et al., 1999; Levy et al., 2012; Nelson et al., 2004; Smith et al., 2012; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012; Villareal, Smith et al., 2011; Worm et al., 2001), maximum isometric contractions (Barnett et al., 2003; Englund et al., 2005; Lazowski et al., 1999; Taguchi et al., 2010; Lord et al., 2003), handgrip strength (Barnett et al., 2003; Englund et al., 2005; Justine et al., 2012; Nakamura et al., 2007; Nelson et al., 2004; Taguchi et al., 2010), isokinetic dynamometry (Binder et al., 2002; Chandler et al., 1998; Rubenstein et al., 2000), and field tests such as the chair stand (Carvalho et al., 2009; Nakamura et al., 2007; Rubenstein et al., 2000; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012), or arm curl tests (Carvalho et al., 2009; Justine et al., 2012; Levy et al., 2012; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012).

Moreover, another vacuum in the literature that it is necessary to highlight is the lack of evidence regarding comparison interventions between multi-component training and other training modalities. Thus it is not possible to know whether multi-component training could be superior or not to other types of training programs with respect to strength gains in older adults. Therefore, future research should include robustly designed RCTs that particularly

involve multi-component training in older adults, and especially older women, and compare their effects with other training modalities such as resistance training or high-velocity strength training.

Regarding this last training modality, several RCTs have investigated the effects of high-velocity resistance training vs traditional resistance training on muscle strength in older adults (Bean et al., 2009; Bottaro et al., 2007; Drey et al., 2012; Fielding et al., 2002; Henwood et al., 2008; Henwood & Taaffe, 2005; Hruda et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Lopes et al., 2014, 2016; Orr et al., 2006; Pamukoff et al., 2014; Reid et al., 2008; Signorile et al., 2002), and particularly in older women (Bottaro et al., 2007; Caserotti et al., 2008; Fielding et al., 2002; Häkkinen et al., 1998; Henwood et al., 2008; Henwood & Taaffe, 2005; Pereira et al., 2012; Tiggmann et al., 2016; Webber & Porter, 2010b).

As a result, in general, the findings obtained from these studies indicate that power resistance training is an effective exercise modality, leading to gains in upper- and lower-extremity muscle strength in a manner similar to traditional strength training (Bottaro et al., 2007; Henwood et al., 2008; Marsch et al., 2009; Müller et al., 2020; Ramirez-Campillo et al., 2014; Tiggmann et al., 2016; Wallerstein et al., 2012), although especially in the lower limbs. In fact, the similarities of the effects between both training modalities on muscle strength have been reported in both dynamic (Balachandran et al., 2014; Bottaro et al., 2007; Correa et al., 2012; Fielding et al., 2002; Henwood et al., 2008; Lopes et al., 2015; Ramírez-Campillo et al., 2014) and isometric strength (Henwood et al., 2008; Lopes et al., 2015), and the same conclusion has been reached when the studies evaluated only traditional (Walker et al., 2015, 2017; Walker & Hakkinen, 2014) or power modalities (Caseroti et al., 2008; Conlon et al., 2017; Flández et al., 2020; Radaelli et al., 2018; Ramirez-Campillo et al., 2017; Reid et al., 2005). However, it seems that power resistance training could be more efficient

for improving isometric (1.80 ± 0.86% weekly improvement for power vs 1.23 ± 0.86% for traditional) rather than dynamic muscle strength (2.16 ± 0.94% weekly improvement for power vs 1.95 ± 0.90% for traditional) (da Rosa Orssatto, Cadore et al., 2019).

Very recently, Guizelini et al. (2018) supported the previous findings mentioned, when in their meta-analysis they found that the training type did not have an effect on muscle strength gains, indicating similar improvements for high-intensity, low-velocity resistance training and low-intensity, high-velocity resistance training (Guizelini et al., 2018). For instance, in elderly women, Pereira et al. (2012) reported similar gains in dynamic and isometric leg press and bench press muscle strength after a 12-week training period of power resistance training vs traditional resistance training. In addition, Marsh et al. (2013) found that there was no difference between groups (power vs traditional strength training) in isometric quadriceps strength after 16 weeks of resistance training in older women. Finally, Tiggemann et al. (2016) compared the effects of 12 weeks of traditional resistance training and power training using RPE in 30 healthy elderly women and found that after 12 weeks, both groups had significant increases in 1RM for leg press (56.3 ± 14.5% for the traditional group and 60.3 ± 20% for the power group) and knee extension (16.1 ± 5.9% and 22.9 ± 11.6% for traditional and power groups, respectively) (Tiggemann et al., 2016). Intensities in the power resistance training groups of the studies usually ranged between low and moderate (40–60% of 1RM), and most of the studies lasted less than 16 weeks.

These data suggest that, in older people, high loads are not necessary to induce greater muscle strength improvements due to resistance training programs using high velocity of movement during the concentric phase with moderate intensities (i.e., 40–60% of 1RM) induce increases in muscle strength (Bean et al., 2009; Bottaro et al., 2007; Cadore et al., 2014; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Steib et al., 2010). Thus, it seems that the velocity of contraction is a key determinant involved in strength gains. Indeed, in

terms of adaptive mechanisms, both high-intensity resistance training at slow-moderate velocity and high-velocity resistance training at light-moderate intensities could induce similar neuromuscular adaptations, such as enhanced neural activity (by high load or fast contraction), increased motor unit recruitment, elevated spinal motor neuronal excitability, changes in agonist coactivation, enhanced maximal motor unit firing rates and increased efferent motor drive (Aagaard et al., 2010), along with the contribution of morphological adaptations such as muscle hypertrophy (Nogueira et al., 2009; Wallerstein et al., 2012). Both neural and structural muscle changes are essential for muscle strength gains, but neural adaptations are especially relevant during the first weeks of training for the elderly population (Guizelini et al., 2018). Moreover, although both fast and slow-moderate contractions are able to enhance the maximum voluntary muscle contraction, fast contractions elicit a greater motor unit activation level than slow contractions (Desmedt & Godauz, 1977). In this way, the option of power resistance training to increase maximum strength in older people may be a good alternative training modality because, compared to traditional resistance training, lower intensities achieve similar results on muscle strength with a lower RPE, which may increase the adherence of participants.

However, most of the studies conducted training programs that lasted less than 16 weeks, and none of them used variable resistance as a device for the power resistance training program. Thus, it is still necessary to conduct further research to know the effects of a medium-long, high-velocity resistance training program performed with elastic bands in older adults, and more specifically in older women.

ii. Effects on muscle power

If little and poor quality evidence exists in relation to the effects of multi-component training on muscle strength in older adults, studies that analyzed its effects on muscle power are almost nonexistent. The most common parameters assessed when using multi-component

training with the elderly population have been muscle strength, balance, mobility, ADLs, walking speed, or other physical function variables. However, despite the importance of muscle power in the autonomy and independence of the elderly, little is known about the effects of this training regimen thereon, with only one study to date. De Resende-Neto et al. (2019) evaluated the effects of a 12-week functional training program (similar to multi-component but performing strength exercises at fast velocity) on muscle power (evaluated through leg press and rowing machines at 50% of 1RM) in physically active older women. The authors concluded that this kind of training was effective in improving muscle power in the same manner as traditional resistance training. However, much more research is needed to elucidate the impact of this modality on muscle power in older adults.

Along with multi-component training, in the last decade, the number of studies employing power resistance training in the elderly population has increased as the importance of muscle power and its influence on physical functioning and disability has emerged (Clark et al., 2010; Pereira et al., 2012; Reid et al., 2012). These studies generally involve the major lower-extremity muscle groups, as they are highly activated during mobility and ambulation.

Recent literature has concentrated on the importance of high-velocity resistance training because although traditional strength training (slow to moderate velocity of muscle contractions) is an effective modality for improving a wide range of physiological outcomes, particularly muscle strength, its effects seems to be more limited in regard to improving muscle power in older adults (Walker et al., 2015). In general, the effectiveness of traditional resistance training on power outcomes is controversial, with some authors reporting no changes (Correa at al., 2012; Walker et al., 2015, 2017) and others supporting its beneficial effects on power output measures (Balachandran et al., 2014; Bottaro et al., 2007; Fielding et al., 2002; Henwood et al., 2008; Ramirez-Campillo et al., 2014). Nevertheless, it seems that low-volume interventions comprising just one or two exercises with multiple sets are

associated with greater improvements in muscle power through resistance training (Byrne et al., 2016).

Several studies have made direct comparisons between power strength training and traditional resistance training to determine their effects on muscle power (Balanchadran et al., 2014; Bean et al., 2009; Bottaro et al., 2007; Correa et al., 2012; Drey et al., 2012; Fielding et al., 2002; Henwood et al., 2008; Henwood & Taaffe, 2005; Hruda et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Onambele et al., 2008; Orr et al., 2006; Pamukoff et al., 2014; Pereira et al., 2012; Ramirez-Campillo et al., 2014; Reid et al., 2008; Sayers et al., 2003; Sayers et al., 2008; Signorile et al., 2002; Tiggemann et al., 2016; Wallerstein et al., 2012). Some found no differences between training modalities (Drey et al., 2012; Henwood et al., 2008; Miszko et al., 2003; Reid et al., 2008; Wallerstein et al., 2012), but most studies demonstrated an advantage (not always significant) of high-velocity resistance training compared with traditional resistance training and control groups for power enhancement in older adults (Bottaro et al., 2007; Correa et al., 2012; Fielding et al., 2002; Henwood et al., 2008; Ramirez-Campillo et al., 2014).

Recent reviews and meta-analyses have corroborated the finding that power resistance training may be more effective at improving muscle power when compared with traditional resistance training (Byrne et al., 2016; Steib et al., 2011; Straight et al., 2016), particularly for the lower limbs (Straight et al., 2016). The percentage of gains of muscle output vary among studies, with a mean percentage improvement in lower-extremity muscle power (measured in watts) reported in the meta-analysis by Straight et al. (2016) of +16.96%. Interestingly, in the same meta-analysis, no effects of training intensity were observed for gains in lower-body muscular power. The characteristics of the power and traditional resistance training studies that analyzed power outcomes were reported by Byrne et al. (2016). The number of sets ranged from 1 to 8, the number of repetitions ranged from 8 to 20, frequency ranged from 2

to 3 days a week, and duration of intervention ranged from 5 to 52 weeks, with a mean of 16 weeks (Byrne et al., 2016).

In addition, numerous studies that analyzed high-velocity resistance training in older adults compared with a control group have consistently reported on the high benefits of this kind of training modality on various muscle power outcomes in this population (Bean et al., 2002, 2004; Beltran Valls et al., 2014; Cadore et al., 2014; Caserotti et al., 2008; Chen et al., 2012; de Vreede et al., 2005; Earles et al., 2001; Gianoudis et al., 2014; Henwood et al., 2008; Henwood & Taaffe, 2005; Hruda et al., 2003; Jozsi et al., 1999; Lohne-Seiler et al., 2013; Paul et al., 2014; Pereira et al., 2012; Portegijs et al., 2008; Ramsbottom et al., 2004; Skelton et al., 1995; Webber & Porter, 2010a, 2010b; Wilhelm et al., 2014), with some studies reporting gains of more than 60% (Henwood et al., 2008; Sayers et al, 2003). One very interesting characteristic of high-velocity resistance training is that both higher and lower intensities provide similar increases in power output in the elderly (Byrne et al., 2016). These data suggest that contraction velocity, rather than external load or intensity, may be a relevant factor in achieving muscle power adaptations, with fast contractions being the key, in contrast with what happens to maximal strength and muscle mass, which are both stimulated at either slow or fast velocity. In summary, there is a consensus that high-velocity resistance training performed with a wide range of intensities (20% to 80% of 1RM) results in power improvements (da Rosa Orssatto, Cadore et al., 2019), although moderate intensities (i.e., 40% to 60% of 1RM) could be the most appropriate (da Rosa Orssatto, Cadore et al., 2019; Fragala et al., 2019).

Notably, studies involving older women have demonstrated significant improvements in muscle power when high-velocity resistance training was applied (Bean et al., 2004; Fielding et al., 2002; Marsh et al., 2013; Pereira et al., 2012; Sayers et al., 2003; Tiggemann et al., 2016). Gains have been observed across different populations as well, including

healthy, mobility-limited, and community-dwelling older women (Bean et al., 2004; Fielding et al., 2002; Sayers et al., 2003; Tiggemann et al., 2016). For instance, Pereira et al. (2012) found that after a 12-week training period, muscle power increased from 17.2% (ball throwing distance) to 40.2% (vertical jump height), while Tiggemann et al. (2016), after the same training period, noted significant increases in muscle power (≈30%) evaluated through squat jumps and counter movement jumps in healthy older women. In addition, Fielding et al. (2002) reported a 97% improvement in leg press peak muscle power after 16 weeks of power training at 70% of 1RM in older women. All the studies performed with older women used a wide range of resistance equipment, such as machines, weighted vests, or body weight. However, the effects of elastic resistance in high-velocity resistance training programs are still unknown.

Power strength training should be considered an alternative to traditional resistance training to produce greater improvements in muscle power in older adults. It is important to note that this training modality can achieve enhancements in maximal strength, muscle size, and power strength at low to moderate intensities (40% to 60% of 1RM; Cadore et al., 2014; Ramírez-Campillo et al., 2014), facilitating access to exercise for older people with comorbidities. However, further research is still needed on the effects of high-velocity resistance training in older women when applied with variable resistance and for a period longer than 16 weeks.

II.IX. PHYSICAL FUNCTION

II.IX.I. Physical function and disability concepts

Physical function, also called physical performance or physical fitness, is a term that has evolved since its appearance and does not have a unique definition. When first used, physical function was an objective measure of how an individual performed various ADLs and appeared in place of ADLs scales based on questionnaires (Beaudart et al., 2019). Currently, physical function is defined as a multidimensional and integrative concept, an objectively measured whole-body function related to various systems: locomotion, balance, muscle strength and power, central and peripheral nervous function, and cardiovascular responses (Beaudart et al., 2019; Cruz-Jentoft et al., 2019). Thus, physical function is a strong indicator of an individual's health status. In the last decade, some measures of physical function, such as gait speed, have been introduced as clinical parameters to detect frailty and sarcopenia in older adults (Cruz-Jentoft et al., 2019). Beaudart et al. (2019) offer the simple yet complete definition of physical function as "an objectively measured whole body function related with mobility."

Impairments in physical function can result in disability, as the two concepts are highly linked. The definition of disability also varies across populations and studies. For instance, the Established Populations for Epidemiologic Studies of the Elderly study defines disability as a self- or proxy report of needing help with or being unable to perform one or more instrumental activities of daily living (IADLs; Mendes de Leon et al., 1997), while the National Long-Term Care Study describes it as the inability to perform an IADLs or basic activity of daily living (BADLs) due to aging or health (Manton et al., 1995). In addition, the NHANES defines disability as having any difficultly performing IADLs or BADLs. Based on these definitions, disability can be defined as the inability to perform IADLs or BADLs.

Following the concept of physical function as proposed by Beaudart et al. (2019), a lower level of physical function is evident not only when subjects are not able to perform IADLs or BADLs. Impairments in any of the systems evaluated as part of physical function may be evident long before disabilities appear, allowing for the detection of vulnerability in persons in the first stages of clinical disability syndromes.

II.IX.II. Physical function, disability, and aging

Physical function, mobility, and the ability to perform various IADLs and BADLs, such as chair standing, walking, and stair-climbing, decline with aging (da Silva et al., 2018). Increasing age is associated with a decline in function of all systems: musculoskeletal, neuromuscular, and cardiovascular. These age-associated impairments in physical function can hinder the ability of older adults to perform the basic tasks required for independent living (Ahlqvist et al., 2016; Hyatt et al., 1990). However, it is necessary to differentiate between declines purely associated with normal aging, which do not generally impact daily activities and independence, and declines associated with health conditions (diseases), environmental factors, and behavioral constraints (e.g., sedentary lifestyle), which can have substantial impacts on function and independence at younger stages of old age **(**Hill et al., 2017).

Among the issues associated with aging, the maintenance of physical function has been considered extremely important because one of the most important components of successful aging is the ability to independently perform ADLs such as walking, standing from a seated position, climbing stairs, and simple lifting (Hazell et al., 2007). In 2015, the WHO in its World Report on Ageing and Health established a new paradigm of healthy aging in two ways. First, it redefined the concept of healthy aging as the process of "developing and maintaining the functional ability that enables well-being in older age" (WHO, 2015). Second, the WHO proposed a new integrated care model centered on elderly people in which

the immediate priority is achieving the healthy aging goals of building and maintaining functional ability in the second half of life, as opposed to traditional approaches focused on multimorbidity (WHO, 2015). This change of vision proposed by the world's preeminent health organization occurred after numerous studies found that limitations in functional ability are more strongly associated with health-care costs and mortality than multimorbidity (Grundstrom et al., 2012; Kumar et al., 2017; Landi et al., 2010). Based on the WHO approach, functional ability depends on the intrinsic capacity of the individual (composed of physical and cognitive capacities), relevant environmental factors, and the interactions between them (WHO, 2015). Although all these factors are vital in fostering healthy aging, intrinsic capacity is the greatest determinant of functional ability. For this reason, the WHO pronounced that the main role of health-care systems is to optimize intrinsic capacity, particularly in the elderly population (WHO, 2015).

It is important to consider this new vision of healthy aging proposed by the WHO, since the prevalence and incidence rates of disability have increased continuously in the last decades, becoming a public health problem. According to the NHANES, among adults aged 60–69, 23% have IADLs disability, 20% have ADL disability, 48% have functional limitations, and 30% have mobility disability (Seeman et al., 2010). The percentage of individuals reporting limitations increases with age, with 31.4% in adults aged 70–79 and 42.9% for individuals 80 and older (Holmes et al., 2009). More than 20% of older adults reported difficulty performing at least one aspect of daily living, including walking 100 m, ascending 10 steps, stooping, bending, kneeling, or lifting and carrying 10 kg (Fried et al., 2004). More recently, the US Disability Status Report from 2013 reported a prevalence rate of disability of 25.8% among adults aged 64–74 years and 50.7% in adults aged 75 years and older (USABAC, 2013). Moreover, the prevalence rate of disability related to independent living was 7.9% and 25.6%, respectively, while the prevalence rates of self-care disability

and ambulatory disability were 4.5% and 15.8% for those aged 64–74 and 13.8% and 33.3% for those over 75 (USABAC, 2013). However, the high prevalence rates related to disability are not unique to the United States. The WHO Global Burden of Disease Study, which collected data from 59 countries, estimated that the overall disability prevalence among adults aged 60 and over is 38.1% (WHO, 2011c). These data indicate that the prevalence of disability is a global phenomenon. This is concerning due to the projected growth of the world aging population, particularly in Europe, and the related increase in health-care services and health-care costs associated with being disabled or dependent (Stuck et al., 1999).

It is important to note that women tend to be a greater risk for disability (Newman & Brach, 2001) and report more BADLs and IADLs disabilities than men (47% vs 35%; FIFoA-R, 2010). This disparity between sexes seems to be related to the fact that life expectancy and the types of diseases that precipitate disability in men and women differ (Newman & Brach, 2001). For instance, women tend to live longer with disability than men and also experience more diseases such as arthritis, obesity, osteoporosis, and sarcopenia that present comorbidities related to physical disability (Fried et al., 1997; Guralnik, 1997; Newman & Brach, 2001). Men tend to have cardiovascular diseases, which mainly end in death or in a new health condition without disability or with a low grade of disability (Adams et al., 1999; Guralnik & Ferrucci, 2002). Therefore, aging will likely result in a greater number of women than men living with physical disabilities, negatively impacting health-care systems across the world, especially those with higher rates of elderly population, as is the case in Spain. In fact, between 1990 and 2017, the number of years lived in poor health or disability has increased by 1.2 years (from 8.5 to 9.7 years) in men and by 1.1 years (from 11.1 to 12.2 years) in women living in Spain (Kyu et al., 2018).

On average, people aged 50–70 experience a decline in gait speed and chair stand ability of around 30%, while in people over 70, this decrement can reach 50% compared with their younger counterparts (Suetta et al., 2019). Functional declines in elderly people can affect their abilities to perform BADLs and IADLs. Reduced levels of functional capacity in older adults have proven to be an independent risk factor for number of hospitalizations, duration of hospitalizations, and number of medical visits (Hennessy et al., 2015; Millán-Calenti et al., 2010; Na et al., 2017; Nascimento et al., 2018). Reduced levels of functional capacity are also related to lower quality of life (Öztürk et al., 2011), nursing home admission, and mortality (Guralnik et al., 1994; Studenski et al., 2011; Stuck et al., 1999). Physical function is a long-term predictor of physical disability (Idland, Pettersen et al., 2013), and older adults who have lower physical function (i.e., slow walking speed) are at increased risk for disability (4.2 to 4.9 times more likely to develop disability) compared to typically functioning older adults (Botoseneanu et al., 2013; Chen et al., 2016; Dunlop et al., 1997; Harris et al., 1989; Guralnik et al., 1995). Importantly, impaired physical function is related to a higher risk of functional decline over 10 years of follow-up (Forrest et al., 2006), and declines in the level of physical function in midlife predict the incidence of disability in old age (Dodds et al., 2018).

Particularly important are the consequences of the loss of ability to balance in older adults. Diminished ability to maintain balance may be linked with an increased risk of falling (Rossat et al., 2010), increased dependency, and early death (Howe, Rochester et al., 2011). In older adults, the short- and long-term effects of fall-related injuries, foremost among which are hip fractures, include prolonged hospitalization (Rabin, 1995), mobility limitations, loss of independence, associated illness, reduced quality of life, and increased risk of early death (Rubenstein & Josephson, 2002; Tiedemann et al., 2008; WHO, 2011a). Furthermore, poor

balance has been determined to be a predictor of cognitive decline (Rolland et al., 2009) and of higher all-cause mortality (Cooper et al., 2010).

Factors contributing to the age-related decline in physical function are numerous and can be explained by several mechanisms, although most are multifactorial and unclear. Deteriorating neuromuscular function, in terms of low muscle strength and power, is well documented to be associated with low walking speed, mobility limitations, falls, and physical disability among older populations (Bean, Kiely, Herman et al., 2002; Bouchard et al., 2010; Foldvari et al., 2000; Manini et al., 2012; Newman, Simonsick et al., 2006; Reid & Fielding, 2012; Stenholm et al., 2009). Muscle strength has been determined to be an independent risk factor for disability (Visser et al., 2005). As an example, knee extensor strength is related to gait speed over 20 m (Manini et al., 2007), with low knee extensor strength being associated with gait-speed declines of 0.24 m/s and 0.06 m/s over a three-year period in men and women, respectively. Handgrip strength is also a strong predictor of physical disability in older adults (Rantanen, Guralnik, Foley et al., 1999; Xue et al., 2011). Low muscle power was associated with a nine- and threefold greater risk of developing mobility disability in men and women, respectively (Visser et al., 2005). Muscle power is strongly associated with physical function in older adults, being one of the most important indicators of disability (Bean, Kiely, Herman et al., 2002; Bean et al., 2003; Foldvari et al., 2000).

The age-related decline in physical function can be only partly explained by the loss of muscle strength and muscle power. Changes in body composition, including losses in lean mass coupled with increases in fat mass (sarcopenia and obesity), have also been identified as significant contributors to physical decline in older adults (Alley et al., 2008; Janssen et al., 2002, 2004; Schaap et al., 2013; Villareal et al., 2005). Another essential factor that strongly influences older adults' functional performance of ADLs is the deterioration of the sensorimotor and neuromuscular systems that directly negatively affect performance in static

and dynamic balance and coordination (Maki & Mcllroy, 1996; Seider et al., 2010). For instance, older adults demonstrate larger center of pressure displacements and sway velocity in unipedal and bipedal static and dynamic postures under various situations (e.g., balance with eyes closed or opened; balance on stable or unstable surface) compared with young adults (Abrahamova & Hlavacka, 2008; Era et al., 2006; Hytonen et al., 1993). Poor values in field tests designed to measure balance and gait speed, such as the modified Romberg test (< 19 s), the TUG test (> 13.5 s), or walking speed (< 0.8 m/s) are associated with a two- to threefold increased risk of falls in older adults (Lesinski et al., 2015).

High levels of strength, power, and balance, especially in the lower limbs, along with an adequate body composition are important prerequisites for achieving successful performance of ADLs such as climbing and descending stairs or standing up from a chair. Cardiorespiratory function is also a main factor related to physical impairments. Individual peak oxygen consumption (VO_2peak) declines approximately 10% per decade after age 25–30 years in healthy sedentary adults (Tanaka & Seals 2008) and is greatly attenuated in elderly individuals. Reduced VO_2max is attributable to both central (respiratory, cardiovascular, and neural changes) and peripheral (neuromuscular changes) factors (Saltin & Calbet, 2006). Regarding the peripheral factors, maximal oxygen extraction is reduced along with skeletal muscle (Saltin & Calbet, 2006). Of the central respiratory and pulmonary factors, it is worth highlighting the lower expiratory volume due to higher chest wall stiffness and lower strength in the respiratory muscles presented in older adults (Knudson et al., 1983). Moreover, the alveolar surface available for gas exchange decreases during aging (Thurlbeck & Angus, 1975). Regarding the central cardiovascular factors, increases in left ventricular wall thickness, calcification and fibrosis of the cardiac valves, stiffness of arteries, and number of predisposed sites for lipid deposition contribute to reductions in cardiac output, maximum heart rate, and capillary density in older adults (Lye & Donnellan, 2000). Lastly,

deficits in cognitive function have also been suggested as an independent risk factor for physical function in older adults (O'Connor et al., 2011).

It is important to note that the pattern of decline in physical performance differs by sex. Compared to age-matched men, women show lower levels of muscle strength (Boudard et al., 2011) and muscle power (Reid et al., 2012), increased adiposity (Vincent et al., 2010; Tseng et al., 2014), and higher loss of skeletal muscle mass (Jankowski et al., 2008; Valentine et al., 2009), which can negatively impact physical function and place older women at increased risk for disability. However, all these factors are modifiable and could be targets for interventions to promote physical function among older adults, particularly among older women. Only female sex, older age, genetic factors, and some chronic diseases are considered important risk factors that are not modifiable (Ferrucci et al., 2000).

Several syndromes are associated with disability and physical function in older adults, the most common of which is frailty. Frailty is an age-associated biological syndrome characterized by a decreased reserve of intrinsic capacity and resistance to minor stressors, instead indicating an extreme vulnerability to these stressors (Cadore et al., 2014; WHO, 2015). This syndrome is the main risk factor for disability in the elderly population (Casas-Herrero & Izquierdo, 2012; Xue, 2011), being present in approximately one in 10 (from 7% to 16.3%) older adults (Collard et al., 2012; Garcia-Garcia et al., 2011). Moreover, one in three older adults demonstrate physical function corresponding to prefrailty, the state that precedes frailty (Collard et al., 2012). Frailty is associated with higher rates of hospitalization, institutionalization, fall death, and mortality (Clegg et al., 2013; Cesari et al., 2016; García-García et al., 2014; Rockwood & Mitnitski, 2007). The diagnosis of frailty is based on several factors, including low level of physical activity, weight loss, and physical impairments such as low gait speed or low grip strength (Fried et al., 2001).

Along with frailty syndrome, Binkley et al. (2013) recently described dysmobility syndrome as a new approach to identify older people at risk of poor health outcomes, considering potential interactions between a more diverse range of factors that may be better predictors. Osteoporosis, low lean mass, obesity or high fat mass, slow gait speed, low grip strength, and falls in the preceding year are the six factors evaluated to diagnose dysmobility syndrome (Binkley et al., 2013). A person is classified as having this syndrome if three or more of these factors are present (Binkley et al., 2013). The cutoff criteria proposed by Binkley et al. (2013) for each factor were collected in their work. From 2013, when Binkley first described dysmobility syndrome, it has been associated with increased falls and fractures, reduced function, and mortality (Hill et al., 2017).

In summary, healthy aging and disability are two different sides of the same coin. The risk for physical disability is greater among those with lower levels of physical function. Although the prevalence of disability rates worldwide are concerning, the incidence of disability is lower for older adults who exercise (resistance and/or aerobic) at 37.1% than for non-exercisers at 52.5% (Penninx et al., 2001), because most factors behind the impairment of physical function are modifiable with exercise. As the proportion of older adults rises globally, identifying and understanding the biological causes and underlying mechanisms behind the decline of physical function are increasingly important, as is identifying strategies to prevent the loss of intrinsic capacity with age. Therefore, there is a need for widespread implementation of effective exercise programs to mitigate age-related declines in various physical function areas (strength, power, balance, walking speed, cardiovascular capacity, muscle mass, adiposity) in older adults, particularly in older women, to prevent and avoid the occurrence of frailty or dysmobility syndromes.

II.IX.III. Methods to assess physical function in older adults

Over the last decades, many tools have been developed to objectively assess physical function in older adults with the aims of identifying people at risk of disability, predicting unhealthy events, and assessing the effectiveness of therapeutic interventions (Beaudart et al., 2019; Bennell et al., 2011). These tools to measure the physical performance of older adults are described in the literature and include questionnaires (Cress et al., 1996; Tager et al., 1998), batteries (Tager et al., 1998; Wilkins et al., 2010), and field tests (Beaudart et al., 2019; Bennell et al., 2019). Some tools measure single performance items, such as balance or muscle strength, whereas others, such as the batteries, include the assessment of multiple items (Mijnarends et al., 2013). The use of functional fitness tests provides a more specific evaluation of the changes induced by the training program that can measure the impact of the training stimulus on the ability to perform some task of daily living. Since physical function is the result of the integration of various physiological systems, it is necessary to examine the specific components or parts that could be affected by the training program. As field tests of muscle strength and endurance, muscle power, balance, cardiovascular function, and cardiorespiratory endurance are increasingly used for research and practice, descriptions of these evaluation tools are presented in the following sections.

A. General batteries

Test batteries are required to report the age-related decline in functional capability over a wide range of abilities. The two most widely used physical performance test batteries that have been applied in clinical and research settings for older adults are the SPPB and the Senior Fitness Test (SFT).

i. Short physical performance battery

The SPPB was originally developed by Guralnik and colleagues in 1994 as a method of safely assessing the ability of older people with or without disability to perform ADLs

(Guralnik et al., 1994). This test battery evaluates balance, gait speed over a short distance, and lower extremity muscle power through three tests performed in this order: a hierarchical standing balance test, walking speed in a 4-m course, and a chair stand test five times (5STS). In the first balance test, the subject is asked to maintain three standing positions for at least 10 s each to obtain the full score for the item, following a hierarchical difficulty: side-by-side, semitandem, and tandem positions **(**Beaudart et al., 2019). For the walking speed test, the subject is asked to walk at their usual speed for a distance of 4 m, recording the shortest time. The subject is allowed to use walking aids (e.g., cane, walker) if necessary, but no assistance from another person can be provided. Finally, in the repeated chair stand tests, the subject is asked to stand up and sit down five times as quickly as possible with arms crossed over the chest, recording the time to complete five stands. Performance for each of the components is given a score of 0 to 4, where 4 indicates the best performance and 0 the worst, resulting in a global test battery score ranging from 0 to 12 points (Beaudart et al., 2019).

Meaningful changes in the SPPB score have been defined by subsequent researchers (Kwon et al., 2009; Perera et al., 2006). Estimates for a small meaningful change in SPPB range from 0.27–0.55, with 0.5 representing the most commonly referenced small change (i.e., clinically detectable, potentially important) and 1 point denoting a substantial change (i.e., clinically detectable, definitely important; Beaudart et al., 2019; Perera et al., 2006). Generally, for older adults, high performance on the SPPB is a score of 10 or greater. A score lower than 10 points has been demonstrated to be a strong predictor of the loss of ability to walk 400 m with a specificity of 0.84 and a sensibility of 0.69 (Vasunilashorn et al., 2009), while scores lower than 8 and 6 points have been associated with mobility-related disability (Guralnik et al., 2000) and increased risk of death (Pavasini et al., 2016; Rolland et al., 2006), respectively. In addition, the SPPB is a valid and reliable measure of physical performance that can predict future risk of mobility impairment, lower body functional limitations, care

dependence, institutionalization, hospital admission, rehospitalization, length of hospital stay, and mortality across diverse populations of older adults (Ostir et al., 2002; Pavasini et al., 2016; Vasunilashorn et al., 2009; Volpato et al., 2011). Moreover, the SPPB is one of the tests proposed for the assessment of sarcopenia, with a cutoff score of <8 (Cruz-Jentoft et al., 2019).

Despite the positive and relevant information that this test battery provides about the physical function of older adults, it is necessary to consider that there may be ceiling effects, because the majority of physically active older adults may achieve the maximum test score. This means the test cannot detect differences among those older adults with good to excellent performance. Conversely, it is also possible to find floor effects in the case of a subject who is unable to walk 4 m or unable to complete five chair rises. These ceiling and floor effects, along with the ordinal rather than continuous-scale scoring used in the SPPB, limit the test's ability to detect gradual changes in individual performance. In fact, the too easy (side-by-side balance) or too difficult (five chair stands) tests that the SPPB contains have been found to be effective discriminators for only 75% of assisted living care patients (Giuliani et al., 2008) and 20% to 50% of community living older adults (Guralnik et al., 1994; Seeman et al., 1994).

Despite these negative aspects, the easy application of the SPPB (only 10 min, a 4-m track, ground marks, a chronometer, and a straight-backed chair are needed) along with its excellent test-retest reliability (intraclass correlation coefficient [ICC] = 0.83–0.92; Gómez et al., 2013; Freire et al., 2012; Ostir et al., 2002) and inter-rater reliability (ICC = 0.91; Bodilsen et al., 2015) make this tool one of the most widely used in clinical and research settings (although data on healthy populations are limited). For more information about this battery, see articles by Beaudart et al. (2019) and Mijnarends et al. (2013).

ii. Senior Fitness Test

With the intention of improving the SPPB, Rikli and Jones (2001) designed the SFT battery, a valid field-based (nonlaboratory) tool for assessing different physical function parameters in older adults. It applies to people over 60 with various levels of physical and functional abilities, and it does not require sophisticated equipment and spaces. Prior to developing the SFT, Rikli and Jones (1999a, 1999b) published the normative values of the tests that would later become part of the SFT based on a nationwide study of 7,183 older Americans aged 60–94 years. In 2013, the same authors published the fitness standards of the tests collected in the SFT that predict the level of capacity needed for maintaining physical independence into later life (Rikli & Jones, 2013a, 2013b). The SFT uses seven tests to assess various components of functional capacity, including lower and upper body muscle endurance, lower and upper body flexibility, agility and dynamic balance, and aerobic endurance. In order, lower and upper body endurance strength is measured by the 30sec-CS and 30sec-AC tests, respectively. Then lower and upper body flexibility is measured through the chair sit-and-reach and back scratch tests, respectively. Agility and dynamic balance are evaluated by the 8-foot up-and-go and finally aerobic endurance is assessed through the 6-min walk test (6MWT) or 2-min step test. The strength, balance, and aerobic tests are explained in more detail in the following sections. In the case of the flexibility tests, the chair sit-and-reach test assesses the flexibility of the lower extremities, mainly the biceps femoris (correlation ranging between .61 and .89 with hamstring flexibility; Paterson et al., 1999). From a sitting position at the front of a chair, with legs extended and hands reaching toward the toes, the number of centimeters from the extended fingers to the top of the toe or the amount by which it is exceeded is recorded. The back scratch test evaluates the flexibility of the upper body, mainly the shoulders. In a standing position, with one hand reaching over the shoulder and one up the middle of the back, the participant tries to touch both hands. The

number of centimeters between the extended middle fingers or the number of centimeters that are exceeded is measured (Rikli & Jones, 2001).

The excellent test-retest reliability (ICC = 0.80–0.98; Rikli & Jones, 2013a), validation in a wide range of populations and contexts (Rikli & Jones, 2013b), validation of the SFT scores with "gold standard" measures such as 1RM or treadmill VO_2 tests (Rikli & Jones, 2013a), easy application, and high number of physical function components measured in the same battery make this tool one of the most widely used in both clinical and research contexts.

iii. Others batteries

Other less common test batteries that can be used to evaluate physical function in older adults are the Fullerton Functional Fitness Test (Miotto et al., 1999), the 4-item physical performance test (Wilkins et al., 2010), the 7-item physical performance test (Beissner et al., 2000), and the 13-item self-reported physical function test (Tager et al., 1998).

Due to the high utility of the SPPB and SFT, some of their tests have been used in the present PhD dissertation along with other tests. In the following sections, specific descriptions of the most important field tests used to measure the physical function components assessed in the two projects of the thesis are explained.

B. Muscle strength-endurance tests

i. Thirty seconds chair stand test

The 30-second chair stand test (30sec-CS), or also called 30-second sit-to-stand test, developed by Rikli and Jones (1999a) is the most important field test to assess lower body strength in older adults and has been widely used in many studies. This test is simple and quick to perform (< 1 minute) since it consists of registering the number of sit-stand-sit

cycles (with their arms folded across their chests, individuals stand up from a standard chair of 43 cm height to a fully extended position, then sit back down as quickly as possible) completed during the 30 s of the test (Jones et al., 1999). This test is highly feasible in clinical practice and research because it requires minimal equipment (conventional chair with armrests and straight back and a chronometer) and only 1–2 min to administer and does not require highly qualified personnel (Beaudart et al., 2019; Zanini et al., 2015).

It is important to note that although this test is commonly described as a tool to measure the muscle endurance of lower limbs in older women due to the total work time used and represents a good alternative for measuring muscle strength of the lower limbs (Bohannon et al., 2010; Zanini et al., 2015), sit-to-stand performance is influenced by a number of physiological and psychological processes (Lord et al., 2002). This suggests that this test is a composite measure of several components of physical function, such as muscle power (the movement has to be performed as quickly as possible) and dynamic balance (Beaudart et al., 2019). Moreover, this test was designed to combat the floor effect of the 5STS proposed in the SPPB (some older adults cannot complete the five attempts and are therefore not assigned a score), since subjects unable to perform it are given a score of 0. It also allows for the evaluation of wider variations in ability levels compared to the 5STS (Martin, Engelberg et al., 1997). Furthermore, the test-retest reliability has been established as between good and excellent (ICC = 0.84–0.92) in healthy older adult, subjects with knee arthroplasty or mild to moderate dementia, and hospitalized patients with strokes (Jones et al., 1999; Lyders et al., 2015; Telenius et al., 2015; Unver et al., 2015). However, limited data have been reported for the inter-rater reliability, with only one study showing very strong reliability (ICC = 1) in older adults with mild to moderate dementia who lived in nursing homes (Telenius et al., 2015).

Very limited data are available regarding the minimal detectable changes (MDC) values for this test. An MDC value with 95% confidence of 3.49 sit-stand-sit cycles in older people with dementia has been established (Blankevoort et al., 2013), while an MDC value with 95% confidence of 1.64 cycles was found in 82 older people with end-stage hip and knee osteoarthritis (Gill et al., 2008). An improvement of more than this value during the 30sec-CS test is considered to be a true change in performance. No MDC value has been defined for the healthy older population. Importantly, the cutoff point of 10 sit-stand-sit cycles in 30 s has been determined to indicate an increased risk for falls in older women (CDC, 2016), while the reference values for maintaining physical independence proposed by Rikli and Jones (2013b) range between 15 and 13 repetitions in women between 60 and 79 years of age. In addition, the normal range scores, defined as the middle 50% of the population, described by Rikli and Jones (2001) for different age female groups were as follows: 12–17 repetitions (60–64 years), 11–16 repetitions (65–69 years), 10–15 repetitions (70–74 years), 10–15 repetitions (75–79 years), 9–14 repetitions (80–84 years), 8–13 repetitions (85–89 years), and 4–11 repetitions (90–94 years). Moreover, normative values have been proposed for Korean and US older adults (Macfarlane et al., 2006), with means of 10.1 and 13 stands during the 30sec-CS test for Korean and US older adults of 70–74 years, respectively.

The 30sec-CS test has been shown to be a predictor of falls in a population of older nursing home residents (Applebeum et al., 2017). A sit-stand-sit cycle that took more than 3.5 s was found to be a significant predictor of falls in ambulatory frail older people (Lipsitz et al., 1991). In addition, a positive correlation was found with the timed stair-climbing test ($r = 0.59$) and with walking speed ($r = 0.66$) in patients after knee arthroplasty and frail older adults, respectively (Almeida et al., 2010). A moderate correlation between the 30sec-CS test

and the leg press test of lower limb strength in community-dwelling older women (r = 0.71) has also been found (Jones et al., 1999).

Other versions of the 30sec-CS test included the maximum number of times a subject can stand up and sit down on a regular chair in 1 min (Zanini et al., 2015) or recorded the total time to complete five or 10 sit-to-stand maneuvers (Yanagawa et al., 2016).

ii. Thirty seconds arm curl test

To assess the muscle endurance of the upper body, Rikli and Jones (2001) designed the 30sec-AC test, in which the participant starts by sitting in a chair with a straight back, feet flat on the floor, with an extended elbow lifting a weight of 2 kg in the case of women or 3 kg in the case of men in the dominant hand, which is oriented toward the body. From this position, the number of biceps curls the participant can perform in 30 s is recorded. In this case, the reference values for maintaining physical independence proposed by Rikli and Jones (2013) range between 17 and 15 repetitions in women between 60 and 79 years of age. In addition, the normal range scores, defined as the middle 50% of the population, described by Rikli and Jones (2001) for different age female groups were as follows: 13–19 repetitions (60–64 years), 12–18 repetitions (65–69 years), 12–17 repetitions (70–74 years), 11–17 repetitions (75–79 years), 10–16 repetitions (80–84 years), 10–15 repetitions (85–89 years), and 8–13 repetitions (90–94 years).

C. Muscle power tests

During the last decade, studies have revealed the importance of muscle power in older adults, since the performance of functional tasks in this population is characterized by the combination of varied manifestations of muscle strength across a wide range of angular velocities (Reid & Fielding, 2012). Along with the tools that can be used to measure muscle

power mentioned in previous sections, two field tests are the most common: the 5STS test and the timed stair-climbing test.

i. Five sit-to-stand test

The 5STS test is an easy, rapid, and commonly used functional performance measure that is collected in the SPPB and recommended by the EWGSOP for the assessment of muscle power in older adults (Cruz-Jentoft, et al., 2019). This test measures the amount of time needed for individuals to complete five repeated chair stands without using their arms. During the test, the participants have to perform five sit-to-stand cycles as rapidly as possible from the sitting position with their buttocks touching the chair to the full standing position. The material, time, and space requirements to perform this test are very low, facilitating its application in many different contexts. This test is a valid predictor of poor health conditions, such as hospitalization events, lower limb limitation, and death, when the participants exceed the cutoff value of 17 s to perform the 5 repetitions (Cawthon, 2015; Cesari et al., 2009). The 5STS also shows a strong correlation with the gait ability of elderly people (Cesari et al., 2009). Previous studies determined that the peak angular velocities for the knee and hip extensor muscles with sit-to-stand movements performed quickly were 186°/s and 224°/s, respectively (Gross et al., 1998; Hortobagyi et al., 2003; Schenkman et al., 1996), corroborating the high demand for lower limb muscle power in this test.

Several studies have evaluated direct muscle power using this test and a linear position transducer (Alvarez Barbosa et al., 2016; Glenn et al., 2015, 2016; Glenn, Gray & Binns, 2017; Glenn, Gray, Vincenzo et al., 2017; Gray et al., 2016; Gray & Paulson, 2014; Kato et al., 2015), 3D accelerometers (Regterschot et al., 2016; Zijlstra et al., 2010), or force platforms (Alvarez Barbosa et al., 2016; Chen et al., 2012; Cheng et al., 2014; Drey et al., 2012; Fleming et al., 1991; Lacroix et al., 2015; Lindemann et al., 2003, 2007; Regterschot et al., 2016; Zech et al., 2011, 2012). However, these procedures have high technical, economic,

and personnel costs, making their implementation in a clinical setting or with a large number of participants difficult. Two different procedures have been proposed to directly obtain muscle power output through this test or a variant. Takai et al. (2009) described an easy procedure to assess muscle power in which only the time needed to complete 10 sit-to-stand repetitions, chair height, leg length, and body mass of the subject are required to calculate the mean muscle power produced by the subject. Alcazar, Losa-Reyna et al. (2018) proposed the sit-to-stand muscle power test, where the velocity and muscle power were calculated using the subject's body mass and height, chair height, and the time needed to complete 5 sit-to-stand repetitions.

ii. Timed stair- climbing test

Stair-climbing is an essential ADL that contributes to functional independence. The timed stair-climbing test, also known as the stair climb power test, has been proposed as a clinically relevant field tool to assess the ability to ascend and descend a flight of stairs, providing information about the lower extremity muscle power in older adults (Sipers et al., 2016). The test consists of measuring the time to ascend and descend or just the time to ascend a determined number (which varies between studies) of stairs (Bennell et al., 2011). The time taken to walk up the stairs, turn around, and walk back down as quickly as possible without using the handrails or any other aid but safely is recorded (Zaino et al., 2004), with a shorter time representing a better performance. Only a flight of a preselected number of stairs and stopwatch are needed to perform this test. Along with the time, the stair-climbing speed (SCS), measured as the number of steps per second, and the stair-climbing power (SCP) can also be calculated using the formula described by Lazowski et al. (1999).

The test-retest reliability of this test has been previously established as high in people with end-stage hip and knee osteoarthritis (ICC = 0.90; Kennedy et al., 2005) and in older adults with symptomatic hip and/or knee osteoarthritis (ICC = 1; Lin et al., 2001). The inter-

rater reliability between three clinicians was also previously reported as high (ICC = 0.94; Almeida et al., 2010). Formal normative values for this test in older adults have not yet been developed. Some authors have reported that an SCS of 1.2 steps per second for ascent and descent of stairs is normal for healthy community-dwelling older women (Hinman et al., 2014). However, other authors reported an average stair ascent speed of 1.6 steps per second and descent speed of 1.7 steps per second (Tiedemann et al., 2007), although it seems that SCSs range from 1.1 to 1.7 steps per second for older adults (Hinman et al., 2014). The MDC value with 90% confidence was established as 5.5 s and 2.6 s in samples of people with end-stage hip and knee osteoarthritis and with lower extremity osteoarthritis following knee arthroplasty, respectively (Almeida et al., 2010; Kennedy et al., 2005). No MDC value has been established in the healthy elderly population.

It is important to note that there is strong evidence that correlates the ability to climb stairs with lower limb strength and power (Bean, Kiely, Leveille et al., 2002; Ploutz-Snyder et al., 2002; Salem et al., 2000). In addition, results from this test are highly related to other leg power measures (double leg press at 40% and 70% of 1RM), gait speed, standing balance, and chair stand time (Bean et al., 2007). For instance, Bassey et al. (1992) reported that leg-extensor power was significantly related (r = 0.65–0.88) to stair-climbing test in nonagenarians. Moreover, the muscle activation of the knee extensor during stair ascent and descent is estimated at 78% and 88% of maximum strength, respectively (Hortobagyi et al., 2003). Mean and peak velocities have been measured at 134°/s and 230°/s for the knee extensor muscles during maximal velocity stair ascent. However, along with the muscle strength and power of the lower limbs, many other physiological and psychological factors have been significantly associated with SCS. The psychological variables of pain, anxiety, fear of falling, and vitality (Lord et al., 2002; Tiedemann et al., 2005) and some physiological

components, such as lower limb proprioception, balance, and vision, also influence the outcomes of this test (Tiedemann et al., 2007).

Finally, it is necessary to remark that a wide number of variations of the timed stair-climbing test have been developed for different populations and contexts. The variations include the number of steps, the task recorded (only the ascent period or both ascent and descent), the use of a handrail, the normal or the fastest pace, or whether the step count is recorded for a set period of time or the test is timed over a set number of steps. Some of the variations include a nine-step ascent/descent (Kennedy et al., 2005; Maly et al., 2006; Rejeski et al., 1995), a 12-step, 30-second test (Kreibich et al., 1996; Madsen et al., 1996), a three-step ascent cycle duration (Parent & Moffet, 2002), a four-step ascent/descent (Lin et al., 2001), and a six-step self- and fast-paced test (Pua et al., 2010).

D. Balance tests

From a technical standpoint, balance is defined as the ability to maintain the projection of the body's center of mass (CoM) within manageable limits of the base of support during different specific tasks, such as in a static standing or sitting position, or changing the base of support in dynamic postures, such as walking (Winter, 1995). The base of support is described as the defined area drawn between the points of contact of the body or extensions of the body, such as assistive devices, with a surface. From a more informal point of view, balance can be defined as the ability to stay steady in static and dynamic tasks thanks to the interaction of several physiological sensory systems, including neuromuscular, visual, vestibular, and somatosensory.

Based on Lacroix et al. (2017), balance can be divided into four categories: static steady-state balance (e.g., single leg stance), dynamic steady-state balance (e.g., walking), proactive balance (e.g., reaching forward while maintaining a fixed base of support), and

reactive balance (e.g., displacements after an unexpected perturbation). All are essential to the successful performance of most ADLs as well as recreational activities for older adults. The biological changes related to aging, such as degenerative processes in the muscular and neural systems, including reductions in muscle strength, loss of type II muscle fibers, reductions in reaction time, proprioception, and joints of motion, and loss of sensory and motor neurons (Aagaard et al., 2010; Daubney & Culham, 1999; Nevitt et al., 1989), along with physical inactivity negatively affect balance control and impact the functional ability and performance of BADLs and IADLs in the elderly population. The loss of ability to maintain balance is linked with a higher risk of falling (Rossat et al., 2010), loss of independence, illness, and early death (Howe, Rochester et al., 2011).

This situation highlights the importance of assessing balance as an essential component of physical function in the elderly. As balance is a complex and multifactorial ability and, as was mentioned above, different kinds of balance exist, there is a wide range of tools available to measure balance in different situations (e.g., when the body has a constant or static base of support or during movement) by direct (quantifying the position of the body's CoM in relation to the base of support) or indirect (observation, self-reporting, or functional field tests) methods. The most common tests are detailed below.

i. Timed up and go test

The TUG test (also known as the 8-foot up-and-go test) is used to measure dynamic balance and agility (Podsiadlo & Richardson, 1991). Originally developed in 1986 as the get-up and go (GUG) test by Mathias et al. (1986) for frail elderly people, the GUG test requires the subject to stand up from a chair, walk 3 m, turn around 180°, return, and sit down again. The performance of the individual in this test was initially evaluated in a subjective way by the observer, based on the perception of the patient's risk of falling, on a five-point ordinal scale: "normal," "very slightly abnormal," "mildly abnormal," "moderately abnormal," and

"severely abnormal." However, Podsiadlo and Richardson (1991) adapted the GUG test to a timed version called the TUG test. The authors maintained the protocol of the GUG test but included the time component as an objective measure, recording the total time in seconds to complete the tasks. Thus, the TUG test is a single test measuring the time a person takes to complete a complex series of four different motor tasks (rising from sitting, walking, turning, and sitting back down). The participant sits in a chair with a straight back, hands on the thighs and feet resting on the floor with one more advanced, wearing regular footwear and using their customary walking aid. No physical assistance is given. At the signal of the tester, the participant has to complete the tasks mentioned above, walking at their usual pace or at maximal speed without running, depending on the variant of the test selected. To perform this simple test, minimal equipment is necessary (standard arm chair, 3-m track with floor marks, and stopwatch). The TUG test is included in the SFT described by Rikli and Jones (2001).

The test-retest reliability of the TUG test has been established as moderate (ICC = 0.53) to good (ICC = 0.97–0.99) across studies (Podsiadlo & Richardson, 1991; Rockwood et al., 2000; Schoppen et al., 1999; Steffen et al., 2002). Moreover, evidence for inter-rater reliability shows it is excellent in the older population (ICC = 0.98–0.99; Podsiadlo & Richardson, 1991; Shumway-Cook et al., 2000). The reliability with frail older people was also excellent within the same day (ICC = 0.99) and in consecutive sessions (ICC = 0.99) when measured by different health professionals (Podsiadlo & Richardson, 1991).

The time to perform the task is compared to normative values for age, gender, and type of population. Reference values for the TUG test scores have been suggested for different populations (Bischoff, Stähelin, Monsch et al., 2003; Bohannon, 2006; Kamide et al., 2011), since the TUG test is used with subjects ranging from children to the elderly and for many conditions, including osteoarthritis, joint arthroplasty, rheumatoid arthritis, hip fractures, strokes, and cerebral palsy (Bennell et al., 2011**)**. The performance of the individual

can also be summarized into a five-point scaled score (Mathias et al., 1986). For older adults, the normal range of scores, defined as the middle 50% of the population, described by Rikli & Jones (2001) for different age female groups were as follows: 6.0–4.4 s (60–64 years), 6.4–4.8 s (65–69 years), 7.1–4.9 s (70–74 years), 7.4–5.2 s (75–79 years), 8.7–5.7 s (80–84 years), 9.6–6.2 s (85–89 years), and 11.5–7.3 s (90–94 years). Furthermore, Gusi , Prieto et al. (2012) and Pondal and Del Ser (2008) established normative data in a sample of community-dwelling older adults and elderly individuals without gait disturbances in Spain, respectively, showing values similar to those reported by Rikli and Jones (2001). The following ranges have been established in frail, elderly people: < 10 s = normal; 10–19 s = good mobility (can go out alone and move without a gait aid); 20–29 s = bad mobility (cannot go outside alone, requires a gait aid); and ≥ 30 s = increased functional dependence (Podsiadlo & Richardson, 1991). Importantly, reference values for maintaining physical independence proposed by Rikli and Jones (2013b) range between 5.0 and 6.0 in women between 60 and 79 years of age. In addition, a TUG test score ≥ 14 s is sensitive (87%) and specific (87%) for identifying older individuals who are at risk for falls (Gusi, Carmelo Adsuar et al., 2012; Pondal & Del Ser, 2008; Shumway-Cook et al., 2000), while the cutoff value of 10 s was predictive of near falls in older people with hip osteoarthritis (Arnold & Faulkner, 2007). Moreover, a cutoff value of > 20 s is recommended for assessing sarcopenia (Cruz-Jentoft et al., 2019). Regarding the MDC value for this test, no data are well defined for older populations. Only a reduction in time greater than or equal to 0.8, 1.2, and 1.4 s has been determined as the MDC values for individuals with hip osteoarthritis (Wright et al., 2011), while a reduction of 2.49 s seems to be the MDC value in a sample of people with end-stage hip and knee osteoarthritis. In addition, Mangione, Miller & Naughton (2010) established the clinically relevant threshold at 1.09 s after reviewing 12 studies with a total of 691 participants who performed progressive resistance training.

Several clinical trials and studies have demonstrated that TUG test scores have a high correlation with other physical function components, such as gait speed, upper and lower muscle strength, static balance, lower limb muscle power, and aerobic capacity (Coelho-Junior et al., 2018). Variability in TUG test scores (~20%) can be explained by lower limb muscle strength (13%) and power (1%), balance (4%), mobility (2%), and aerobic capacity (< 1%; Coelho-Junior et al., 2018). Some authors have demonstrated an association between TUG test scores and the risk of falls (Alexandre et al., 2012; Rydwik et al., 2011; Shumway-Cook et al., 2000; Viccaro et al., 2011), physical function (Rydwik et al., 2011; Van Iersel et al., 2008; Viccaro et al., 2011), health status (Viccaro et al., 2011), risk of hospitalization (Viccaro et al., 2011), cognitive function (Donogue et al., 2012), nursing home placement (Nikolaus et al., 1996), ambulatory abilities (Cole & Basmajian, 1994), and ability to perform ADLs (Rydwik et al., 2011; Viccaro et al., 2011). In addition, a recent study confirmed the TUG test's validity as a mortality predictor in older adults (Bergland et al., 2017).

Despite the several evident benefits of the TUG test, it is not without some limitations that must be considered. For instance, the time measure is not always sensitive to fall risk in healthy older populations, because 3 m is probably not long enough to produce high reliability (Frenken et al., 2011; Palmerini et al., 2013; Salarian et al., 2010; Shahar et al., 2009; Weiss et al., 2011). In addition, the test is fairly sensitive to the type of footwear and chair used (Arnadottir et al., 2000; Higashi et al., 2008; Wall et al., 2000). This test does not suffer from ceiling effects (Herman et al., 2011), but floor effects can be observed, as the person's walking ability is involved (Beaudart et al., 2019). For instance, a floor effect has been found in hospitalized older people, with one-quarter of the patients tested unable to complete the test (De Morton et al., 2007).

Finally, several modified versions of the original TUG test have been proposed to address the limitations of the standard TUG test and to perform additional assessments, such

as rising from the chair without using hands, walking at maximum pace, or adding a second task, thus producing a timed up-and-go dual task (Barry et al., 2014; Kamide et al., 2011; Rydwik et al., 2011; Shumway-Cook et al., 2000).

ii. Functional reach test

To assess proactive balance, the FRT is a simple balance test designed by Duncan et al. (1990) that consists of analyzing the ability of a person to move their CoM to the anterior limits of their base of support by measuring the distance (in centimeters) an individual can reach forward beyond arm's length while maintaining a fixed base of support in a standing position. This test has been shown to be a valid tool for assessing proactive balance for healthy older adults (Duncan et al., 1990; Newton, 2001), with good test-retest reliability (ICC = 0.92) and inter-rater reliability (ICC = 0.98; Duncan et al., 1990). In addition, it is a sensitive measure strongly connected to physical frailty in the elderly population (Weiner et al., 1992). This test has been validated as a fall risk predictor in older adults (Duncan et al., 1990; Duncan et al., 1992; Shumway-Cook et al., 2000). Results obtained in the FRT can be transformed to a gradable scale from 0–3 regarding the relative risk of falling, where 0 = unable or unwilling to reach (28 times more likely to fall); 1 = reach ≤ 15.2 cm (four times more likely to fall); 2 = reach between 15.3 and 25.4 cm (two times more likely to fall); and 3 = reach ≥ 25.4cm (not likely to fall; Duncan et al., 1990).

iii. Others balance measures

Along with the tests mentioned above, a wide number of test and tools exist to measure the different types of balance. Static steady-state balance can be assessed using the Romberg test and its variations, such as the sharpened, tandem, or mobile Romberg test (Galán-Mercant & Cuesta-Vargas, 2014; Gras et al., 2017; Khasnis & Gokuda, 2003). In addition, static balance can be measured by the single leg stand test and the tandem and semitandem tests (Springer et al., 2007). These tests can be performed with eyes open or

closed and on various surfaces. In the case of the single leg stand test, the risk of fall is high when the older person fails to maintain the position for a time shorter than or equal to 5 s (Eladio et al., 2015; Ortega, 2016).

In the case of dynamic balance, gait speed over a short distance is one of the most widely used measures in clinical practice and research because gait is an intrinsic function in the human being, and its deterioration determines the loss of independence (Guest, 2020). There is no standardized assessment consensus to evaluate this parameter, and according to the systematic review by Graham et al. (2008), there is great variation in the methodology of walking speed measurement. Generally, gait speed is measured over a short distance (e.g., 2.4 m, 4 m, 6 m, or 10 m), but since gait speed is usually assessed in accordance with the instructions in the SPPB, the 4-m distance is the most commonly used (Beaudart et al., 2019). Gait speed tests are quick and easy to administer because only a stopwatch is needed, and they are reliable, valid, and sensitive measures (Green et al., 2002). Generally, the tests consist of recording the time that the participant takes to walk the predefined distance at their usual or maximal speed. The maximum or average gait speed over this time is calculated and expressed as meters walked per second, or m/s. A systematic review found that gait speed is a valid and sensitive outcome for a broad range of individuals with different characteristics, from patients with cancer to persons with neurological and osteomuscular problems (Graham et al., 2008). However, a floor effect appears in subjects who are unable to walk, while a ceiling effect has also been reported in specific populations, such as older people with very high physical functioning (Beaudart et al., 2019).

The test-retest reliability for walking speed tests over 4- and 10-m distances has been shown to be excellent for healthy older adults (ICC = 0.96–0.98; Peters et al., 2013) and for specific populations, such as in stroke and cardiac rehabilitation patients (Green et al., 2002; Puthoff & Saskowski, 2013). In addition, the inter-rater reliability has been reported to be

very strong in older adults with COPD (ICC = 0.99; Bisca et al., 2017; Kon et al., 2013). The values obtained in these kinds of tests require a comparison with reference values that vary between 0.6 and 1.70 m/s (Guest, 2020). The limit considered for a healthy walking speed is 1.0 m/s, and anything above 1.2 m/s or 1.4 m/s is exceptional (Fritz & Lusardi, 2009; Studenski et al., 2011). However, it is necessary to consider that the reference values of gait speed vary between countries due to differences in anthropometric measures. For example, the normative values for Japanese people differ by 1.44 s from those of Caucasians (Mikos et al., 2018), so it is important to choose the specific normative values according to the population evaluated.

Various cutoff points to define poor health or increasing risk of disability have been proposed for these walking speed tests. For instance, a walking speed ≤ 0.8 m/s for 4 m was proposed by EWGSOP as an indicator of severe sarcopenia (Cruz-Jentoft et al., 2019), but this also identifies subjects with poor physical performance (Lauretani et al., 2003). This same gait speed threshold was revealed as highly sensitive for identifying frailty (Clegg et al., 2015). Furthermore, gait speed lower than 0.6 m/s has recently been proposed for the dysmobility condition (Cummings et al., 2014), although some authors demonstrated that gait speeds lower than 1 m/s for a 6-m distance identify older persons at high risk of health-related negative events (Cesari et al., 2009). Other cutoff values have been adapted to the height and gender of participants and have been calculated on a distance of 15 ft (4.572 m) (Freire et al., 2012; Wang & Chen, 2010). The cutoff values were established in gait speeds lower than 0.65 m/s (≥ 7s) and 0.76 m/s (≥ 6s) for women of a height ≤ 173 cm and > 173 cm, respectively (Freire et al., 2012; Wang & Chen, 2010). Regarding the MDC value, for the 4-m distance, changes of 0.05 m/s are recognized as small but clinically detectable and potentially important changes (Perera et al., 2006), while improvements between 0.08 and 0.14 m/s are considered significant changes (Perera et al., 2006). All changes of 0.1 m/s and

above are indicative of a substantial change that is clinically detectable and definitely important (Perera et al., 2006).

The assessment of gait speed over a certain distance has proven to be positively associated with muscle strength of the lower limbs (Buckinx et al., 2016; Cesari, Kritchevsky, Penninx et al., 2005). However, the relationship between usual gait speed and lower limb strength is nonlinear, since small changes in lower limb strength may have substantial effects on gait speed in adults with poor physical function (i.e., prefrail or frail adults), but large changes in lower limb strength may have no effect or only little effect on gait speed in healthy older adults (Buchner et al., 1996). One of the reasons for the usefulness of these tests is that gait speed has been previously identified as a prognostic factor for falls, cognitive impairment, disability, severe mobility limitation, sarcopenia, institutionalization, fractures, hospitalization, significant morbidity, and mortality in community-dwelling older adults (Abellán et al., 2009; Guralnik et al., 2000; Peel et al., 2013; Studenski et al., 2011).

Other tests aimed at evaluating dynamic balance are the tandem walk test and the Star Excursion Balance Test. The former involves walking 15 steps placing your feet heel-to-toe in a narrow beam (Robertson & Gregory, 2017), and the latter involves standing on one leg while using the other leg to reach maximally to touch a point along a designated line (Gribble et al., 2012). Finally, different types of balance can also be registered using computerized posturography (Orr et al., 2008) or balance tests batteries such as the Berg balance scale (Berg et al., 1995; Steffen et al., 2002) or the Tinetti scale (Tinetti et al., 1986), also called the performance-oriented mobility assessment scale (Lin et al., 2004).

E. Aerobic endurance tests

The last component of physical function that is routinely assessed in research studies is aerobic capacity, usually through performance on long-distance walks. Generally,

cardiorespiratory fitness has been measured through VO_2max or VO_2peak, this second measure being a submaximal value due to the risks that a maximum test may pose among older adults (Myers et al., 2002). To obtain these values, a continuous and incremental test on a treadmill or stationary bicycle in a controlled environment (laboratory) is used, and older adults first need a familiarization phase to be able to complete the test, which entails time and economic expenses (Myers et al., 2002). However, for older adults, long-distance walk tests have proven valid for evaluating aerobic capacity and have been used to measure outcomes in clinical trials (Bennell et al., 2011). There are two main long-distance walk tests: the 400-m walk test and the 6MWT. In the first, the instructor asks the participant to walk as quickly as possible over the specific distance of 400 m (Newman, Simonsick et al., 2006), while in the second, the tester asks the participant to walk as far as possible in the given time of 6 min (American Thoracic Society statement, 2002). In both cases, a corridor of at least 20 m as well as a minimum time for execution of 15 min is required. In contrast to short-distance walk tests, long-distance walk tests are extremely useful in differentiating categories of risk among older individuals in healthy conditions (Beaudart et al., 2019).

i. Six minute walking test

The first test similar to the 6MWT was described as a field test to evaluate general physical fitness (Balke, 1963) and was later transformed into a 12-min walk test in people with chronic bronchitis (McGavin et al., 1976). The final 6MWT emerged as an adaptation from the 12-min walk test for those individuals with respiratory disease who could not complete this test (Southard & Gallagher, 2013). The 6MWT was found to be as valid and reliable as the 12-min walk test (Butland et al., 1982) and is useful in assessing submaximal levels of functional performance, since the outcomes obtained represent a submaximal exercise level that is equivalent to 80% of VO_2max (ATS statement, 2002; Kervio et al. 2003). The 6MWT consists of measuring the distance an individual is able to walk in 6 min

on a hard, flat surface. Participants have to walk as quickly as possible for 6 min in a marked circuit (30-m corridor). To perform this test, a 30-m premeasured flat walking area with interval markings every 3 m, cones to mark boundaries, and a stopwatch are needed. This test has been widely used in many types of populations with various disorders, such as patients with cardiac and pulmonary diseases, older people with osteoarthritis, Parkinson's disease, and Alzheimer's disease, and in elderly populations and children (ATS statement, 2002; Bennell et al., 2011). Its test-retest reliability was excellent (ICC = 0.91–0.97) in community-dwelling elderly people (ages 61–89 years) with independent functioning (Rikli & Jones, 1999a; Steffen et al., 2002).

For older adults, the normative range scores, defined as the middle 50% of the population, described by Rikli and Jones (2001) for different age female groups were as follows: 545–660 m (60–64 years), 500–635 m (65–69 years), 480–615 m (70–74 years), 430–585 m (75–79 years), 385–540 m (80–84 years), 340–510 m (85–89 years), and 275–440 m (90–94 years). An important advantage that the 6MWT presents is that there are regression formulas to predict the VO_2max values based on the final result (in meters) obtained in the test (Mänttäri et al., 2018). Therefore, it is possible to compare the values obtained in the 6MWT with reference values of VO_2max collected in the literature, such as those reported by Myers et al. (2017), which indicated reference values of 20.7 ± 5.0 ml/min/kg and 18.3 ± 3.6 ml/min/kg for groups of women aged 60–69 and 70–79 years, respectively.

The reference values for maintaining physical independence proposed by Rikli and Jones (2013b) range between 625 m and 550 m in women between 60 and 79 years of age. The MDC value at 90% was established as 61.3 m in people with end-stage hip and knee osteoarthritis (Kennedy et al., 2005), while the minimum clinically important differences (MCIDs) were determined to be 20 m (small) and 50 m (substantial) in community-dwelling elderly people with mobility dysfunction (Perera et al., 2006). Previous studies also

established 24–54 m as the clinical significance for older adults (Holland et al., 2010; Mangione, Craik et al., 2010). In addition, the smallest change associated with a noticeable clinical difference in the perceptions of the patients about their exercise performance was 54 m in patients with severe COPD (Redelmeier et al., 1997). A possible ceiling effect can be found in people with high exercise capacities (Bennell et al., 2011). Research has shown that a distance of 300 m or less is associated with increased risk of mobility and mortality (Rostagno et al., 2003; Salzman, 2009). In addition, the 6MWT has been found to highly correlate with heart rate, dyspnea response, oxygen saturation, maximum oxygen consumption, and quadriceps and hamstring strength in middle-aged and older adults (Enright et al., 1998; Maly et al., 2006; Mizner et al., 2011; Price et al., 2001).

ii. Others aerobic endurance tests

In the case of the 400-m walk test, participants are asked to complete 20 laps of 20 m, each lap as fast as possible, and are allowed up to two rest stops during the test (Cruz-Jentoff et al., 2019). This test is feasible for the assessment of sarcopenia (cutoff > 6 min for the completion of 400 m) (Bean et al., 2007). Participants unable to complete the walk, or those who cannot complete the walk in 15 min, are considered to have mobility disability. Other tests available for the assessment of the older adult's aerobic capacity are the 2-min step test and 3-min step test with preset cadence. In the former, which is part of the SFT, participants have to raise each knee to a point midway between the patella and iliac crest. The final score is the number of full steps (times both knees reach the required height) completed in 2 min (Rikli & Jones, 2001). In the latter, participants are asked to climb up and down a 25-cm-high step at a pace of 20 times per minute for 3 min, recording the pulse rate in each minute. The cardiorespiratory fitness is then calculated with a specific formula (Chen et al., 2009).

Although there is a wide range of assessment field tests available for monitoring the different components of physical function in older adults, there remains no consensus on the

most appropriate method. Accordingly, practitioners and researchers selecting tests must base their decisions on the characteristics of the population (ceiling and floor effects can appear in older adults with high levels of physical function or frailty) and on practical and logistical issues (e.g., time, equipment, and space requirements). It is also necessary to select the tests based on whether the objective is to assess isolated fitness components or composite measures of performance. It seems that a combination of different physical function field tests could be the most effective means of obtaining a global view of the physical fitness of the elderly population.

II.IX.IV. Exercise-related effects on physical function

The 2020 *WHO Guidelines on Physical Activity and Sedentary Behaviour* (WHO, 2020) provide recommendations on the amount and types of physical activity for various age groups, including older people. They recommend that older adults engage in at least 150 min of moderate-intensity aerobic physical activity (e.g., brisk walking) per week, or at least 75 min of vigorous-intensity activity per week, or an equivalent combination of moderate- and vigorous-intensity activity. The physical activities that an older person can perform vary according to their level of physical function, but they include transportation (e.g., walking or cycling), occupational activities (if they are still working), leisure time physical activities, household chores, and planned or structured activities in the daily, family, and community contexts (WHO, 2011a, 2020). Unfortunately, it is estimated that the number of older adults meeting these guidelines ranges from less than 4% when objectively measured to less than one-third when based on self-reported questionnaires (Carlson et al., 2010; Troiano et al., 2008), underscoring the importance to increase physical activity levels in this population.

Despite the lower rates of physical activity in the elderly population, there is strong evidence to suggest that engaging in physical activity and exercise training programs is associated with better physical function, better quality of life, and longer life expectancy in

older adults compared with those who are sedentary (Ferrucci et al., 1999; Keysor, 2003; Leveille et al., 1999). Maintaining an adequate level of the various components of physical function (muscle strength, muscle endurance, muscle power, balance, agility, and aerobic capacity) is a key factor in preserving mobility and independence in later years and is needed to perform BADLs and IADLs, such as lifting and carrying objects, climbing steps, getting in and out of chairs or vehicles, and walking any distance (Rikli & Jones, 2013a). For that reason, physical activity and structured exercise are often recommended to prevent disability and maintain physical function in older adults (Chodzko-Zajko et al., 2009). Disability, dependency, and poor health do not have to be inevitable consequences of aging. Research has demonstrated that physical activity is related to prolonged independent living in older adults (Spirduso & Cronin, 2001) and to restored independent functioning (Bray et al., 2016). Skeletal muscle function deficits are treatable with exercise interventions. As an example, the incidence of disability is lower for older adults who engage in resistance and/or aerobic activities (37.1%) than for those who are sedentary (52.5%; Penninx et al., 2001). Similarly, the Women's Health and Aging Study reported that physical activity is inversely associated with physical disability among older community-dwelling disabled women (Rantanen, Guralnik, Sakari-Rantala et al., 1999).

Therefore, identifying and promoting effective strategy interventions to maintain and improve physical functioning among older adults is needed. In the following sections, current evidence about the effects of traditional strategies, such as resistance training performed at different intensities with variable resistance, and the effectiveness of new exercises approaches, such as multi-component and power strength training, on physical function in older adults are detailed.

A. Resistance training, variable resistance, and physical function[14]

Many studies have been conducted on attempts to increase physical functioning in older adults, including nutritional, pharmacological, physical activity, and exercise interventions. As many ADLs require muscle strength, resistance training has been the most common exercise intervention implemented and studied (Liu & Latham, 2009). However, the literature investigating resistance training and physical performance in older adults is characterized by high heterogeneity in the populations studied, the types of training regimen applied in terms of mode, dose, and progression, and the kinds of physical components and field tests evaluated (Papa et al., 2017). Consequently, despite the high number of studies highlighting the positive impact of resistance training on muscle strength and power (two of the main components of physical function) in older adults, the effects of this type of exercise strategy on physical function are not well understood.

Some reviews and meta-analyses, including an umbrella review, have examined the effectiveness of resistance training on overall physical function and its specific components in older adults (Beckwée et al., 2019; Borde et al., 2015; Byrne et al., 2016; Csapo & Alegre,

[14] Related publications:

1. Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877

2. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

3. Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High- and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press)*

4. Fritz, N. B., Juesas, Á., Gargallo, P., Calatayud, J., Fernández-Garrido, J., Rogers, M. E., & Colado, J. C. (2018). Positive effects of a short-term intense elastic resistance training program on body composition and physical functioning in overweight older women. *Biological Research for Nursing, 20*(3), 321-334. https://doi.org/10.1177/1099800418757676

2015; Fiatarone et al., 1990; Jadczak et al., 2018; Latham et al., 2004; Liu & Latham, 2009; Mangione, Miller & Naughton, 2010; da Rosa Orssatto, De la Rocha Freitas et al., 2019; Papa et al., 2017; Paterson & Warburton, 2010; Skelton et al., 1995; Steib et al., 2010; Theodorakopoulos et al., 2017; Tschopp et al., 2011; Yoshimura et al., 2017).

The recent umbrella review of Beckwée et al. (2019) reported that there is high-quality evidence for a positive and significant effect of resistance training on physical performance in older adults based on their analysis of two systematic reviews and one meta-analysis. Likewise, another recent umbrella review demonstrated that resistance training could significantly enhance physical performance in pre-frail and frail older adults (Jadczak et al., 2018). The Cochrane review by Liu and Latham (2009), which included 121 trials and more than 6,700 older adults, making it the most comprehensive review to date, compared pooled data from 33 RCTs (progressive resistance training vs control group) and found a small but significant effect of progressive resistance training for improving physical function and decreasing physical disability (SMD = 0.14; 95% CI = 0.05 to 0.22) in older adults. Others systematic reviews and meta-analyses also found resistance training to be an effective exercise strategy to improve functional capacity in the elderly (Borde et al., 2015; Byrne et al., 2016; Csapo & Alegre, 2015; Fiatarone et al., 1990; Mangione, Miller & Naughton et al., 2010; da Rosa Orssatto, Cadore et al., 2019; Papa et al., 2017; Skelton et al., 1995; Steib et al., 2010; Tschopp et al., 2011). A few previous reviews and meta-analyses noted that resistance training results in modest improvements or reported no impact on physical disability or functional performance (Latham et al., 2004; Paterson & Warburton, 2010). However, the reasons why there were no positive effects found may be because these studies were conducted many years ago when not enough data was available or on older adults with functional limitations.

Various findings have been reported on the effectiveness of progressive resistance training on specific components of physical function, depending on the component studied and the field test used. A meta-analysis by Liu and Latham (2009) that focused on muscle strength reported a significant moderate to large effect of resistance training on chair rise time compared to control groups (SMD = -0.94, 95% CI = -1.49 to -0.38, 384 participants, 11 trials). Curiously, the same authors had found only modest improvements in the same task in a previous systematic review (Latham et al., 2004). In the later meta-analysis, the authors also found that the resistance training interventions had positive effects on muscle power strength through improvement in the stair-climbing test (eight trials; Liu & Latham, 2009).

The most analyzed component of physical function in older adults after application of a resistance training program is balance. The Cochrane review by Liu and Latham (2009) found that strength training performed two to three times per week had a small positive effect on balance (SMD = 0.12; 95% CI = 0.00 to 0.25). Specifically, the data available from 12 trials with a total of 691 participants indicated that progressive resistance training significantly improved the time to complete the TUG test by 0.69 s compared with a control group (SMD = -0.69 s, 95% CI = -1.11 s to -0.27 s). This change, although considered statistically significant, may not be clinically meaningful, because the MDC values in people with hip and knee osteoarthritis have been reported to be between 0.8 and 2.5 s (Kennedy et al., 2005; Mangione, Craik et al., 2010; Wright et al., 2011). Previous reviews and meta-analyses also reported positive effects of resistance training on the TUG test in older adults (Lopez et al., 2018; Papa et al., 2017; Vlietstra & Hendrickx, 2018). For instance, in the Cochrane review by Howe et al. (2011), the resistance training programs achieved a statistically significant reduction of 4.30 s in the time taken to perform the TUG test (MD = -4.30 s; 95% CI = -7.60 s to -1.00 s, 71 participants, three studies) and an increase in single leg stance time with eyes closed (MD = 1.64 s; 95% CI = 0.97 to 2.31 s, 120 participants,

three studies). However, no statistically significant difference was found between the exercise and control groups for single leg stance time with eyes open (187 participants, three studies) or the Berg balance score (20 participants, one study; Howe, Rochester et al., 2011).

Papa et al. (2017) did a systematic review on the effects of resistance training in older adults with skeletal muscle function deficits and found significant effects on physical performance tests (11 studies), including the FRT. Likewise, Howe et al. (2011) reported that resistance training achieved a statistically significant improvement compared with controls in the same test, with mean changes of 3.27 cm (MD = 3.27 cm, 95% CI = 1.39 to 5.15 cm). However, they did not find significant differences for the tandem stance (Howe, Rochester et al., 2011).

Along with improvements in the TUG and FRT tests, previous meta-analyses have also reported a significant effect of resistance training on usual and maximum walking speed (Howe, Rochester et al., 2011; Liu & Latham, 2009; Lopez et al., 2017; Yoshimura et al., 2017). Yoshimura et al. (2017) noted significant improvements of 0.11 m/s and 0.26 m/s in the usual and maximum gait speed, respectively. Similarly, Liu and Latham (2009) found a modest improvement (0.08 m/s) in gait speed (MD = 0.08 m/s, 95% CI = 0.04 to 0.12 m/s, 1,179 participants, 24 trials) for resistance training compared with a control group. Although small, the MDC value for this test has been reported to be 0.05 m/s, and a substantial change has been reported to be 0.1 m/s in older adults (Perera et al., 2006). Likewise, Howe et al. (2011) reported a significant increase of 0.25 m/s in gait speed for resistance training programs (SMD = 0.25, 95% CI = 0.05 to 0.46 m/s, 375 participants, eight studies). Conversely, Vlietstra and Hendrickx (2018) did not find significant improvements on gait speed in their meta-analysis involving older adults with sarcopenia.

Despite the apparent positive effect of resistance training on various balance outcomes, some studies show minimal or no effect of progressive resistance training on balance (Daubney & Culham, 1999; Judge et al., 1994; Wolfson et al., 1993, 1996). These differences between studies could be controversial since the improvements in balance function after strength training are usually related to tasks where muscle strength is a dominant component (Bouisset & Zattara, 1990), but in tasks with less call for muscle strength, the improvements decrease (Oddsson et al., 2007). Nevertheless, progressive resistance training is widely accepted as an appropriate modality to improve different types of balance.

If balance has been the most studied component of physical function, the opposite is true of aerobic capacity. Although resistance training may also improve aerobic capacity in older adults, with previous work reporting improvements in VO_2max following strength training (Frontera et al., 1990; Ozaki et al., 2013), its effects as measured by field tests have been less studied. Only the meta-analysis by Liu and Latham (2009) examined data about the effects of resistance training on the 6MWT and found a significant average increase of 52.37 m in the resistance training group compared with a control group (325 participants, 11 studies). Since this exceeds the MCIDs of 20 m (small) and 50 m (substantial) determined by Perera et al. (2006), it seems that resistance training could be an effective strategy for improving aerobic capacity in older adults.

Interestingly, in an attempt to identify the best resistance training protocol for improving physical function in the elderly population, Fragala et al. (2019) noted in the NSCA position statement on resistance training for older adults that a supervised progressive resistance training program performed two to three times per week at 55% to 80% of 1RM, using large muscle groups for 30–60 min with 2-min rests between sets, could be the most appropriate (Bray et al., 2016; Ku et al., 2016; Papa et al., 2017). Greater functional fitness

benefits may be achieved by participating three times per week (Nakamura et al., 2007), but one training session per week may be sufficient to achieve improvements (Barbalho et al., 2017). However, the heterogeneity in experimental design across studies in terms of the participants' characteristics, training variables (volume, intensity, duration), and assessment methods make it difficult to determine the best type of resistance training to combat physical function declines in older adults. Nevertheless, when looked at collectively, the evidence suggests that progressive resistance training can play a fundamental role in improving and/or maintaining physical function in older adults, or at least some components thereof.

The underlying mechanisms by which resistance training attenuates the decline in physical function of older adults are likely multifaceted and have yet to be fully clarified. Despite established relationships between muscle mass, muscle strength, muscle power, and physical function in older adults, the role of each component in facilitating improvements is difficult to establish. Low muscle mass and strength are associated with poor physical function (Visser et al., 2002), but the relationships between muscle strength and physical function and especially between muscle power and physical function are more robust than the relationship between muscle mass and physical function (Newman et al., 2003).

Although numerous studies have indicated a strong and significant relationship between muscle strength and performance in various physical function tasks, such as walking speed or chair stands (Hairi et al., 2010; Ostchega et al., 2004; Sayers et al., 2005), some research suggests that higher volumes of strength training or muscle strength gains do not have additional benefits for functional capacity (Turpela et al., 2017). Studies have noted that once muscle strength has reached a certain threshold, additional gains may not provide additional benefits for physical function and performance of ADLs (Boshuizen et al., 2005; Damush & Damush, 1999; Keysor, 2003; Keysor & Jette, 2001; Latham et al., 2003; Liu, Shiroy et al., 2014; Liu & Latham, 2011; McMurdo & Johnstone, 1995; Skelton et al., 1995).

These data suggest that strengthening the muscle may not necessarily provide a proportional increase in functional performance. One possible explanation of this phenomenon is the nonlinear relationship between strength and function (Buchner et al., 1996). It is thought that the relationship between strength and function is curvilinear, exhibiting a ceiling effect or threshold for improvements in function with increases in strength and power (Buchner et al., 1996). Therefore, individuals with low levels of muscle strength or power would likely achieve greater improvements in function performance from resistance training compared to individuals with high physical functioning and high levels of muscle strength. In the former, even a very low volume of strength exercise (one session per week) appears to be beneficial for physical function (Barbalho et al., 2017). Another possible cause of the lack of improvements in physical function through resistance training is the low level of transfer between the strength exercises prescribed and functional tasks, because the muscle activation patterns may differ notably between strength-related movements and function-related movements (Barry & Carson, 2004). For example, functional tasks require variable speed and force requirements; some may rely on movement speed while others may be more strength related. However, traditional strength training exercises are performed at slow velocity and usually near maximal effort.

Despite the widespread use of conventional devices, such as weight machines and dumbbells, and their positive results regarding physical function improvements, a high percentage of older people who adopt this type of training give up during the first year of practice due to factors related to economic and logistical difficulties (Lopes et al., 2019). In trying to find a more accessible alternative, several studies have investigated whether elastic resistance training achieves similar improvements in physical function in older adults as resistance training performed with machines or free weights (Frantke et al., 2015; Flández et al., 2020; Fritz et al., 2018, 2021; Gargallo et al., 2018; Hoffman et al., 2016; Kwak et al.,

2016; Liao et al., 2018; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2016; Oliveira et al., 2018; Park et al., 2016; Silva et al., 2020; So et al., 2013; Straight et al., 2012; Yamauchi et al., 2005). Additionally, previous systematic reviews have demonstrated that elastic resistance training was considered effective for improving muscle strength in older adults (Martins et al., 2013; Thiebaud et al., 2014) and physical function in healthy adults (de Oliveira et al., 2017).

Some of these studies analyzed the effect of elastic resistance training on muscle strength of the lower limbs through the 30sec-CS test (de Oliveira et al., 2018; Frantke et al., 2015; Fritz et al., 2018; Hoffman et al., 2016; Liao et al., 2018; Oesen et al., 2015; Park et al., 2016; So et al., 2013; Yamauchi et al., 2005) or the upper limbs through the 30sec-AC test (de Oliveira et al., 2018; Fritz et al., 2018; Park et al., 2016; So et al., 2013; Yamauchi et al., 2005). Others have studied the muscle power of the lower limbs through the 5STS test included in the SPPB (Martins, Safons et al., 2015; Oh et al., 2016; Straight et al., 2012) or through the timed stair-climbing test (Oh et al., 2016). Most have studied the effects of elastic resistance training on different types of balance through the TUG test (de Alencar et al., 2020; de Oliveira et al., 2018; Fritz et al., 2018; Kwak et al., 2016; Liao et al., 2018; Park et al., 2016; Straight et al., 2012; Yamauchi et al., 2005), the FRT (Kwak et al., 2016; Liao et al., 2018; Oesen et al., 2015), and field tests of walking speed (Oesen et al., 2015; Oh et al., 2016). Finally, the effects of elastic resistance training on aerobic capacity have been evaluated through the 6MWT (Frantke et al., 2015; Oesen et al., 2015; Fritz et al., 2018). Only a few studies have focused on the effects of this type of exercise training strategy in older women (de Oliveira et al., 2018; Fritz et al., 2018; Liao et al., 2018; Oh et al., 2016; Park et al., 2016), although the samples analyzed presented very different characteristics, such as older women with overweight (Fritz et al., 2018), sarcopenic status (Liao et al.,

2018), or sarcopenic obesity (de Oliveira et al., 2018) or community-dwelling elderly women (Oh et al., 2016).

Interestingly, despite the heterogeneity between studies with regard to the population studied, the length of the training interventions (from eight weeks to six months), and the characteristics of the elastic resistance training programs in terms of intensity, volume, number, and type of exercises selected, all the studies that analyzed the effects of elastic resistance training mentioned above found significant positive results on the various components of physical function. Moreover, most found significant differences when resistance training was compared to control groups. Thus, it seems that elastic resistance training may facilitate greater adherence and accessibility with similar results on the various components of physical function in older adults than resistance training performed with machines and free weights.

In summary, resistance training offers numerous benefits beyond improvements in physical function in older adults, including positive changes in muscle strength and endurance, muscle power, various types of balance, gait speed, and aerobic capacity. Resistance training can attenuate age-related changes in muscle function and improve performance in ADLs such as stair-climbing, standing from a sitting position, and walking long distances. However, additional research is needed to determine the most efficacious resistance training interventions to improve physical function and prevent disability in older women. Moreover, future research should focus on exploring the use of variable resistance as training equipment to achieve functional improvements in older adults, specifically in older women.

B. Exercise-intensity and physical function[15]

Notwithstanding the numerous well-known advantages of resistance training on physical function in older adults, how to achieve these improvements may be relevant for some types of patients or individuals, especially in the elderly population. One important parameter that must be controlled properly is training intensity. Previous meta-analyses have examined whether high, moderate, or low intensity produces greater positive effects on physical function in older adults (Liu & Latham, 2009; Mcleod et al., 2018; Raymond et al., 2013; Steib et al., 2010). All agree that progressive resistance training is a successful strategy for improving functional outcomes in older adults, but these gains are independent of training intensity. Specifically, in the meta-analysis by Steib et al. (2010), no differences were found in functional outcomes in the three studies included that directly compared different intensities. Likewise, the meta-analysis by Raymond et al. (2013) concluded that although for lower limb strength gains, high-intensity resistance training seems to be more effective than lower intensities, functional outcomes improved similarly across all intensities. The physical function outcomes analyzed were stair climb time, sit-to-stand time, habitual and maximal safe walking speeds, and 6MWT distance (Seynnes et al., 2004; Sullivan et al., 2005, 2007). In the case of stair climb time and 6MWT distance, high intensity achieved greater improvements with small and moderate but not significant effects over moderate and low intensities, respectively. The gains obtained in sit-to-stand time and habitual and maximal walking speeds were similar between intensities.

[15] Related publications:

1. Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877

2. Fritz, N. B., Gargallo, P., Juesas, Á., Flandez, J., Furtado, G. E.,Teixeira, A. M., & Colado, J.C. (2021). High- and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly. *Journal of Human Sport and Exercise (In Press).*

On the other hand, Mcleod et al. (2018) suggested that although high intensity (≥ 70% of 1RM) is generally more effective than low to moderate intensity (30% to 69% of 1RM) in combating physical function impairments in older adults with chronic diseases, the heterogeneity between studies makes it difficult to establish the optimal resistance training intensity. In fact, there is no consensus regarding the optimal training intensity for achieving improvements in functional status in older adults. One reason is the small number of studies that have compared the effects of different resistance training intensities on physical function outcomes in older adults in the same study (Beneka et al., 2005; de Vos et al., 2005; Fatouros et al., 2005; Harris et al., 2004; Hortobagyi et al., 2001; Hunter, 2001; Kalapotharakos, 2005; Seynnes et al., 2004; Singh et al., 2005; Sullivan et al., 2005; Taaffe et al., 1996; Tsutsumi et al., 1997; Vincent et al., 2002).

The findings obtained in these studies indicate that high-intensity resistance training is better than training at low intensities for strength outcomes but may not be required for improvement of functional outcomes, where lesser intensities may suffice, especially when older adults have low levels of physical function or relevant comorbidities. Some authors reported that subjects with the lowest scores at baseline had the greatest improvements, independent of training intensity (Sullivan et al., 2007). It should be noted that even when only one's own body weight is used for resistance, physical function in older adults can improve to a similar extent as using conventional resistance training with machines or free weights (Mcleod et al., 2018). One possible explanation for the lack of difference in functional outcomes between intensities is that there may be a threshold above which strength gains do not lead to further functional improvements (Steib et al., 2010). Another frequently used argument is that the relatively high volume of low- or moderate-intensity training (10–15 repetitions) compared with high-intensity training (4–8 repetitions) might considerably impact the physical function adaptation when the number of sets and exercises is equal

between groups (Steib et al., 2010). Therefore, high intensity may not be required to improve functional performance, and lesser intensities with similar volume may suffice.

Finally, it is important to note that there are no previous studies that have analyzed the effects of progressive elastic resistance training at different intensities on physical function in older adults. Thus, based on the evidence available to date, it is necessary to test resistance training programs at different intensities using variable resistance in older adults, more specifically in older women, to determine the effects of this kind of exercise strategy on physical function outcomes.

C. Exercise modality and physical function[16]

To optimize improvements in older adults' physical function, the most effective type of exercise program should be identified by considering what kind of training modality would be most appropriate to develop the various components of physical function. Training strategies involving exercises that stimulate several components of physical health, such as multi-component exercise programs, could be an interesting alternative to traditional progressive resistance training. Furthermore, because muscle power is an important predictor of functional capacity in older adults, strategies to develop skeletal muscle power in this population must also be discussed. In fact, two of the most interesting modalities studied recently for improving physical function in older adults are multi-component training and power resistance training.

Several reviews and meta-analyses have certified, with a good level of evidence, the positive effects of the multi-component training modality on the functional status of older

[16] Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

adults (Baker, Atlanis et al., 2007; Bouaziz et al., 2016; Cadore et al., 2014; Howe, Rochester et al., 2011; Lopez et al., 2017; Mcleod et al., 2018). It appears to be the best strategy for attenuating declines in physical mobility (Cadore et al., 2014; de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Jadczak et al., 2018; Theou et al., 2011) and one of the most effective interventions for improving the overall physical function status of elderly individuals because various components of physical function, including balance, strength, and cardiorespiratory capacity, are trained in the same session (Freiberger et al., 2012; Izquierzo et al., 2012; Villareal, Smith et al., 2011).

This statement is supported by the literature, in which positive effects on overall or specific components of physical function are observed in older adults (Ansai et al., 2015; Arai et al., 2007; Baker, Kennedy et al., 2007; Barnett et al., 2003; Beyer et al., 2007; Binder et al., 2002; Bird et al., 2011; Campbell et al., 1997; Carvalho et al., 2009, 2010a, 2010b; Casas-Herrero et al., 2019; Clemson et al., 2012; Freiberger et al., 2012; Hara et al., 2007; Iwamoto, 2009; Jessup et al., 2003; Justine et al., 2012; Kamide et al., 2009; Karikanta et al., 2007; King et al., 2002; Kovacs et al., 2013; Levy et al., 2012; Lin et al., 2007; Liu-Ambrose et al., 2008; Lord et al., 1995, 2003, 2005; Losa-Reyna et al., 2019; McMurdo & Rennie, 1993; Marques et al., 2009, 2013; Marques, Mota, Machado et al., 2011; Means et al., 2005; Nakamura et al., 2007; Nelson et al., 2004; Oliveira et al., 2019; Otero et al., 2017; Park et al., 2008; Pope et al., 2019; Ramsbottom et al., 2004; Rubenstein et al., 2000; Shubert et al., 2010; Suzuki et al., 2004, 2012, 2013; Sykes & Ling, 2004; Taguchi et al., 2010; Tolomio et al., 2010; Toraman et al., 2004; Toraman & Sahin, 2004; Toto et al., 2012; Trape et al., 2017; Vaughan et al., 2014; Villareal, Smith et al., 2011; Worm et al., 2001).

Positive effects on overall function or specific components of physical function are more often observed when the exercise intervention includes two or more physical-conditioning components (i.e., strength, endurance, or balance) compared to exercise

programs that only include one component (Barnett et al., 2003; Lord et al., 2003; Villareal, Smith et al., 2011). Evidence from systematic reviews, meta-analyses, and umbrella reviews (de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Jadczak et al., 2018; Theou et al., 2011) have demonstrated that exercise interventions combining resistance training and aerobic training are more effective for combating age-related declines in physical mobility than unimodal exercise. Along this line, the review by Bray et al. (2016) reported that components of strength, balance, aerobic, and flexibility training should be incorporated into the exercise prescription to prevent the onset of disability and frailty in the elderly population, emphasizing balance and strength training exercises.

Interestingly, the meta-analyses by Bouaziz et al. (2016) and Howe et al. (2011) examined the impact of multi-component training programs on overall physical function and on various components thereof. Bouaziz et al. (2016) found significant improvements on muscle strength of the upper and lower limbs, as measured by the 30sec-AC and the 30sec-CS tests, respectively, as a result of multi-component exercise programs at the end of the training period and compared with control groups. The muscle strength gains ranged from 1.4% to 95.0% (Bouaziz et al., 2016). Significant improvements were also observed in balance, independently of the test performed (leg stance test, Berg balance scale, FRT, TUG test, 4-m gait speed test, 10-m walking test, 8-m gait test). According to the authors' classification, improvements in balance (leg stance test, Berg balance scale and FRT, among others tests) were estimated between 5.3% and 88.9%, while improvements in gait speed (TUG, 4-m gait speed, 10-m walking test and 8-m gait test, among other tests) ranged from 7.2% to 40.0% (Bouaziz et al., 2016). Similarly, Howe et al. (2011) found that multi-component training programs achieved a statistically significant reduction in time to perform a TUG test (MD = -1.63 s, 95% CI = -2.28 s to -0.98 s, 635 participants, 12 studies), a significant improvement in FRT score (MD = 5.77 cm, 95% CI = 2.70 to 8.84 cm, 350

participants, seven trials), an increase in single leg stance time with eyes open (MD = 5.03 s, 95% CI = 1.19 to 8.87 s, 545 participants, nine studies), and an increase in single leg stance time with eyes closed (MD = 1.60 s, 95% CI = -0.01 to 3.20 s, 176 participants, two studies) immediately after intervention. However, the authors found no statistically significant difference between the exercise and control groups for single leg stance times with eyes open change scores (SMD = 0.00, 95% CI = -0.31 to 0.31), self-selected gait speed (SMD = 0.04, 95% CI = -0.10 to 0.17, 818 participants, 15 studies), or gait speed at fastest pace at the end of the intervention (Howe, Rochester et al., 2011). Furthermore, Lopez et al. (2017) found a lower effect on TUG scores when the strength component in multi-component sessions was prescribed through an RPE compared to the percentage of 1RM. Finally, Bouaziz et al. (2016) also noted a significant improvement in cardiorespiratory fitness (assessed by the 6MWT) in all the multi-component studies analyzed. The aerobic capacity gains ranged from 1% to 41.8% (Bouaziz et al., 2016).

Strangely enough, the efficacy of the multi-component training modality on physical function compared directly with other training strategies has been little studied (Leite et al, 2015). Previous work compared the effects on measures of muscle strength or body composition but not on physical function tests (de Resende-Neto et al., 2019). In addition to the lack of comparison studies between training modalities, few studies have used elastic bands as a training device in multi-component programs (Brouwer et al., 2003; Kamide et al., 2009).

Despite broad evidence for the efficacy of a multi-component exercise strategy to improve physical functioning in older adults, there is high heterogeneity between studies in term of multi-component training protocols. Some studies combine balance, strength, aerobic, and flexibility components (King et al, 2002; Kovacs et al., 2013; Lambert et al., 2008; Levy et al., 2012; Lord et al., 2003; Marques et al., 2009; Smith et al., 2012; Shubert et al., 2010;

Taguchi et al., 2010; Toto et al., 2012; Villareal, Smith et al., 2011; Worm et al., 2001), and this is the combination most widely used. Others involve only three components, mainly balance, strength, and aerobic (Ansai et al., 2015; Barnett et al., 2003; Carvalho et al., 2009, 2010; Freiberger et al., 2012; Justine et al., 2012; Rubenstein et al., 2000; Suzuki et al., 2012, 2013), but also strength, aerobic, and flexibility (Toraman et al., 2004; Toraman & Sahin, 2004). Others introduced five components: balance, strength, aerobic, flexibility, and coordination (Binder et al., 2002; Means et al., 2005; Vaughan et al., 2014). There is also high variability in the prescription of the parameters of each training component regarding the intensity (mode [maximum heart rate, heart reserve, VO_2peak, % 1RM, RPE] and dose), volume (sets and repetitions, time, and tasks), and frequency (number of sessions per week). Moreover, the intervention duration and the characteristics of the samples studied are widely heterogeneous. The quality level of most studies to date is low due to the low quality of the exercise program reported and the low sample sizes, among other aspects.

It is reasonable to suggest that despite the high heterogeneity between studies, the benefits to physical function in older adults obtained by the various multi-component training programs are related to the combination of the key components of physical activity in the same session. Since resistance training programs are recommended for improving neuromuscular function and limiting muscle atrophy (Fragala et al., 2019), aerobic programs are recommended for enhancing cardiovascular fitness and minimizing the risk of coronary diseases (Nied et al., 2002), balance training stimulates improvements in balance performance, thus reducing the risk of falling and helping to better manage the fear of falling (Gusi, Carmelo Adsuar et al., 2012), and flexibility activities enhance ROM, participants involved in multi-component training programs combine the benefits of the four major components (strength, aerobic, balance, and flexibility) recommended by the ACSM and AHA (Chodzko-Zajko et al., 2009; Cress et al., 2005; Marcus et al., 2006). In fact, these

organizations encourage the performance of balance exercises 1 to 7 days a week, muscle-strengthening activities that work all major muscle groups 2 or more days a week, 30 min of moderate-intensity aerobic physical activity (40% to 60% of HRmax) most days of the week or 20 min of vigorous-intensity aerobic activity 3 days a week, and 10 min of flexibility activities at least 2 days a week. With multi-component training sessions, these recommendations can be almost completely fulfilled.

According to the aforementioned evidence, a multi-component training modality appears to be an effective strategy for improving balance, aerobic capacity, and muscle strength in older adults and consequently for maintaining functional capacity during aging. However, the absence of investigations focused on older women, along with the lack of studies that compare this training strategy with others, use elastic bands as training devices, or measure other physical components such as muscle power, make it necessary to perform further research in this field. In addition, future research involving multi-component training programs should include robustly designed RCTs with higher quality than those performed to date.

The maintenance of adequate muscle strength and muscle power is vital for older adults, since physical functioning is related to these two physical qualities (Bassey et al., 1992; Fiatore et al., 1994; Foldvari et al., 2000). Therefore, interventions to improve or maintain strength and power in older adults are requisite for the maintenance of good levels of functional performance. For decades, most studies have focused on improving physical function through the traditional progressive resistance training modality (Gray et al., 2018), focusing on enhancing the muscle strength component, not muscle power. However, recent evidence has revealed the importance of muscle power to physical function (Reid & Fielding, 2012) and suggests that a high-velocity resistance training modality could result in greater physical function benefits than the traditional resistance training strategy, although there is

currently no clear consensus on which provides greater benefits to overall physical function (Brady et al., 2014; Henwood et al., 2008; Reid et al., 2008).

A variety of studies indicate that muscle power is more strongly related than muscle strength to increases in physical function and performance of ADLs (Bassey et al., 1992; Byrne et al., 2016; Evans, 2000; Foldvari et al., 2000; Miszko et al., 2003; Steib et al., 2010; Tschopp et al., 2011). It seems that muscle power explains more of the variance in functional performance than muscle strength (Bean, Kiely, Herman et al., 2002; Bean, Kiely, Leveille et al., 2002, Bean et al., 2003; Carabello et al., 2010; Cuoco et al., 2004; Earles et al., 1997; Foldvari et al., 2000; Forte et al., 2014; Jenkins et al., 2014; Larsen et al., 2009; Marsh et al., 2006; Puthoff & Nielsen, 2007; Samson et al., 2000; Skelton et al., 1994; Stenroth et al., 2015; Suzuki et al., 2001). For instance, in the earliest studies of muscle power in older adults, Bassey et al. (1992) described significant positive linear relationships between knee extensor power and performance in various components of physical function (e.g., stair-climbing, speed of chair rise, and walking speed) in frail older adults (80–99 years). Similarly, Bean, Kiely, Herman et al. (2002) reported that leg extensor power explained 12% to 45% of the variance in different functional tests, approximately 2% to 8% more variance than the maximal knee extensor strength. Foldvari et al. (2000) also found that leg press power explained 40% of the variance in self-reported functional status, while Hruda et al. (2003) reported that changes in knee extension power explained 22% of the variation in TUG test performance and 18% in 6MWT. In general, according to the results reported in the meta-analysis by Byrne et al. (2016), lower limb muscle power explains between one-third and one-half of the variance in functional performance in older adults. The findings of this meta-analysis (44 studies included) also indicate that muscle strength and power are important predictors of physical function in older adults and provide evidence that muscle

power is a marginally better predictor of functional performance than strength (Byrne et al., 2016).

Emerging evidence reveals that the independent effect of the velocity of movement is critical to performance outcome, suggesting that maximal velocity is an equal or better predictor of functional performance than maximal strength (Byrne et al., 2016; Sayers et al., 2005). When maximal velocity (unloaded movement or at different intensities) was compared to maximal isometric and dynamic strength (commonly in the knee extension movement), authors reported that the former had the highest correlation with physical function (Clémenc et al., 2008; Pojednic et al., 2012; Van Roie et al., 2011), explaining substantial variance in 30sec-CS time (from 47% to 59%; Clémenc et al., 2008; Pojednic et al., 2012), stair climb time (from 29% to 90%; Clémenc et al., 2008; Pojednic et al., 2012), and 6MWT score (49%; Clémenc et al., 2008). Because the age-related loss of muscle power may be associated with comparatively greater declines in velocity than in force (Bosco et al., 1980; de Vito et al., 1998), the critical variable for improving functional ability in older adults may not be how strong the muscles are but how quickly we are able to move them.

A possible reason for these findings is that the performance of functional tasks and ADLs in older adults is most often characterized by the combination of repeated cycles of acceleration and deceleration and a variety of proportions of maximum strength produced dynamically across a range of angular velocities, not by slowly controlled contractions (da Rosa Orssatto, Cadore et al., 2019). The muscle activity of agonist and antagonist muscles differs between tasks, with some ADLs involving muscles at high relative efforts while others involve them at low efforts (Beijersbergen et al., 2013). For example, the activation of knee extensor muscles during stair ascent and chair rise was estimated at 78% and 80% of maximum strength, respectively (Hortobagyi et al., 2003). For the same tasks, the peak angular velocities were in the range of 122°/s to 186°/s and 141°/s to 224°/s for knee and hip

extension when sit-to-stand movements were performed slowly and quickly (Gross et al., 1998; Hortobagyi et al., 2003; Schenkman et al., 1998), while the mean and peak angular velocities were at 134 ± 33°/s and 230 ± 47°/s for the knee extensor during stair ascent.

A wide number of studies have analyzed the effect of power strength training on physical function among the elderly (Balachandran et al., 2014; Bean et al., 2004, 2009; Beijersbergen et al., 2017; Beltran Valls et al., 2014; Bottaro et al., 2007; Cadore et al., 2014; Coelho-Junior et al., 2017; Conlon et al., 2016; Correa et al., 2012; de Vreede et al., 2005; de Vos et al., 2005; Drey et al., 2012; Earles et al., 2001; Englund et al., 2017; Fielding et al., 2002; Flández et al., 2020; Gianoudis et al., 2014; Glenn et al., 2015; Henwood & Taaffe, 2006; Henwood et al., 2008; Hruda et al., 2003; Katula et al., 2008; Lohne-Seiler et al., 2013; Lopes et al., 2015; Macaluso et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Nogueira et al., 2009; Onambele et al., 2008; Orr et al., 2006; Pamukoff et al., 2014; Paul et al., 2014; Pereira et al., 2012; Portegijs et al., 2008; Radaelli et al., 2018; Ramírez-Campillo et al., 2014, 2016, 2018; Ramsbottom et al., 2004; Reid et al., 2008, 2015; Richardson, Duncan, Jimenez, Jones et al., 2018; Sayers et al., 2003, 2012, 2016; Signorile et al., 2002; Signorile et al., 2005; Valls et al., 2014; Van Roie et al., 2013; Vasconcelos et al., 2016; Wilhelm et al., 2014). Collectively, these studies suggest that muscle power and physical function can be improved by power strength training across a wide range of combinations in terms of training parameters, including intensity, volume, and duration.

Specifically, the meta-analysis performed by Katsoulis et al. (2018) reported significant improvements in muscle strength assessed by the 30sec-CS test of 23.5%, ranging from 12.7% to 43%. Regarding muscle power, the authors found significant improvements of 7.1% to 8% in the timed stair-climbing tests as well as significant positive changes of 12.8% to 44% in the 5STS test (Katsoulis et al., 2018). In addition, they found significant improvements of 10.2% to 17.3% in balance assessed by the TUG test and significant

adaptations to the SPPB, with changes ranging from 1.75 to 2.7 units (averaging 2.1 units) or 3.3% and 16.3%, respectively (Katsoulis et al., 2018). Finally, the authors found that usual and maximal walking speed improved from 5.9% to 19% while aerobic capacity assessed through the 6MWT improved by 5%; when it was assessed through the 400-m walk, the improvements reached 7.6% (Katsoulis et al., 2018). The magnitude of these changes could be decreased in the range of ~5% to 23% when power training interventions are performed in healthy older adults (Katsoulis et al., 2018).

Most studies that have analyzed high-velocity resistance training included both men and women, though a number of intervention studies have been limited to older women. Interestingly, significantly positive results have been reported in older women in a variety of populations, including healthy, community-dwelling, pre-frail, with pathologies (osteoarthritis), and very old (Reid et al., 2008; Ramírez-Campillo et al., 2016). However, despite positive results from a few studies, additional research is needed to determine the efficacy of high-velocity resistance training on physical function, specifically in older women.

In general, effects on physical function obtained by high-velocity resistance training programs are conditioned by several training parameters, such as frequency, volume, and intensity. In this sense, when training volume and intensity are equated, two and three sessions of power strength training are equally effective for improving physical performance in older women (Ramírez-Campillo et al., 2016). Furthermore, similar neuromuscular adaptations and physical performance can be achieved with muscle power strength training using either 1 or 3 sets per exercise (Radaelli et al., 2019). The optimal intensity for improving physical function in older adults is not clear. Only a small number of studies have investigated the effect of different training intensities, when load is mobilized as fast as possible, on physical function (Macaluso et al., 2003; Orr et al., 2006; Reid, Martin et al.,

2014). The findings of these studies suggest that both muscle power and physical function can be improved by power strength training across a wide range of intensities (20% to 80% of 1RM; Byrne et al., 2016; Katsoulis et al., 2018).

Katsoulis et al. (2018) noted in their meta-analysis, which included 27 studies, that low- (< 50% 1RM), moderate- (between 51% and 69% 1RM), and high-intensity (> 70% 1RM) power training led to clinically significant changes in muscle power and physical function in older adults (men and women). Although significant improvements can be achieved from various intensities, the authors found some differences between the specific physical function components. For instance, high intensity seems to be more effective for gains in chair stand (30sec-CS and 5STS) and stair-climbing tests than moderate or low intensities (Katsoulis et al., 2018). Low intensity seems to be better for balance and postural control as assessed by TUG and walking speed tests (Byrne et al., 2016; Katsoulis et al., 2018), while moderate intensity seems to be most effective for enhancing aerobic capacity as measured by the 6MWT (Katsoulis et al., 2018). This heterogeneous response could be related to the fact that functional activities that require a lower percentage of maximal strength, such as balance or walking, may be more associated with muscle power at lower intensity and higher speed than activities with higher strength requirements, such as stair-climbing, that probably require higher intensities (Katsoulis et al., 2018).

However, the current evidence is not clear in this regard, because some authors reported that muscle power in the leg extensor at 70% of 1RM contributed to higher levels in the variability of stair climb and gait speed results compared to the lower intensity (40%; Herman et al., 2005). Other authors found that the speed of movement rather than external resistance may be a more important determinant of functional adaptation, since similar improvements in functional fitness have been demonstrated when comparing unloaded high-velocity resistance training to loaded training (70% of 1RM; Glenn et al., 2015).

Interestingly, Macaluso et al. (2003) observed equivalent gains in physical function between different training intensities (40% vs 70% 1RM), but they also found a significantly lower rating of perceived exertion during low-load training (40% 1RM) than high-load training (70% 1RM), suggesting that this may be particular relevance for older adults with lower levels of physical function or where exercise may be poorly tolerated.

Along with training intensity, volume, and frequency, results are also conditioned by the duration of the power training intervention. To date, the duration of high-velocity resistance training interventions has ranged from six to 52 weeks (Byrne et al., 2016), with short-term investigations (< 12 weeks) being the most common. The baseline values of muscle power can also affect the final improvements in physical function. Baseline maximal angular velocity of movement has emerged as a significant determinant of changes in functional performance in older adults (Orr et al., 2006; Bean et al., 2009). Participants with lower levels at baseline are able to increase physical function to a greater extent than those with higher levels (Bean et al., 2009; Bean et al., 2010). These data suggest that power and velocity impairments are important targets for reversing age-related loss of physical function and for improving functional performance in older people. Furthermore, adherence rates to power strength training programs could also play an important role in the final results. The average adherence rate reported by Katsoulis et al. (2018) in their meta-analysis was 89%. The high-intensity power strength programs showed the lowest rate (86%), followed by low (89%) and moderate intensity (95%).

Finally, another factor that could impact physical function results is the type of training devices used. High-velocity resistance training can be performed on the same equipment as traditional resistance training. For that reason, most studies among older adults to date used pneumatic resistance machines or free-weight equipment. These kinds of training devices are expensive and not widely available in community settings. The lack of

accessibility to private gyms and expensive machines makes necessary novel approaches to high-velocity resistance training with a focus on improving accessibility to this type of modality for older adults. From a practical perspective, the use of elastic bands as a more practical and accessible means to improve power and physical function in older adults could be an interesting alternative. Few studies have thus far introduced variable resistance through elastic bands as main load equipment or as a complement to machines and free weights (Drey et al., 2012; Hruda et al., 2003; Lohne-Seiler et al., 2013). Hruda et al. (2003) were the first to use elastic bands in power strength training for older adults (men and women, ~85 years) and the only study to date that used elastic bands as the only equipment, not in combination with machines or free weights. After 10 weeks (3 days a week), the authors found significant increases in eccentric (44%) and concentric (60%) average power (measured on an isokinetic dynamometer, 180°/s) and significant improvements in physical function by 31%, 66%, and 33% in the 8-foot up-and-go, chair stand, and walk time tests, respectively (Hruda et al., 2003). It seems that high-velocity resistance training using elastic bands could be at least equally effective for improving physical function in older adults as training performed with machines or free weights. However, further research is needed to elucidate this important question.

To date, the evidence around high-velocity resistance training in older adults shows a high level of heterogeneity. The training programs applied vary notably between studies, with different intensities, volumes, and frequencies applied as well as different training devices and duration of training periods. As noted by Katsoulis et al. (2018), the quality level of the power strength training interventions performed thus far is generally low (measured by PEDro scale) due to the low sample sizes, high dropout rates, and significant differences in baseline values. It is important to highlight this situation, because studies with lower quality ratings may inflate the results in muscle power by ~10% (Katsoulis et al., 2018).

Furthermore, physical activity status at baseline, a basic potential confounder variable, has not commonly been registered when high-velocity resistance training has been implemented in older adults (Katsoulis et al., 2018). However, even in the studies with high quality ratings, training velocity varies widely between participants within the same high-speed training group. Despite instructing participants to move the load "as quickly as possible," the broad ranges of strength, power, functional abilities, and ages of the participants may produce considerable variability in the self-selected "maximum" movement velocity. Even when ensuring that all participants exercise at the same relative percentage of 1RM and RPE, there is limited control of the velocity component of the exercise due to the impossibility of measuring it in a large group of people.

Since the first study conducted by Earles and colleagues (2001) that investigated the effects of high-velocity resistance training in comparison with another training modality (walking) on measures of functional performance in community-dwelling older adults, there have been several studies, mainly in the last decade, that have examined whether power strength or traditional resistance training produces greater functional enhancements in older adults by comparing these two training modalities in the same study (Balachandran et al., 2014, 2017; Bean et al., 2004, 2009; Beltran Valls et al., 2014; Coelho-Júnior et al., 2019; Correa et al., 2012; Bottaro et al., 2007; Drey et al., 2012; Englund et al., 2017; Gray et al., 2018; Henwood & Taaffe, 2006; Henwood et al., 2008; Lopes et al., 2016; Macaluso et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Pamukoff et al., 2014; Ramírez-Campillo et al., 2014; Reid , Martin et al., 2014; Richardson, Duncan, Jimenez, Jones et al., 2018; Sayers et al., 2003, 2012; Tiggeman et al., 2016; Yoon et al., 2017; Zech et al., 2012). Only a few of these studies focused specifically on older women (Correa et al., 2012; Lopes et al., 2016; Ramírez-Campillo et al., 2014; Tiggeman et al., 2016; Yoon et al., 2017).

In general, studies have indicated greater functional enhancements from power strength training compared with traditional resistance training in older individuals (Bean et al., 2009; Miszko et al., 2003; Bottaro et al., 2007; Ramirez-Campillo et al., 2014). However, it should be noted that some studies reported that both types of training modalities improved muscle capacity but did not improve physical function (Fielding et al., 2002; Henwood et al., 2008; Sayers et al., 2003), while others found significant and similar effectiveness in improving functional performance by both training strategies (Bean et al., 2004, Tiggeman et al., 2016). Some studies reported increases in muscle power after using both training modalities but increases in physical function only in the power strength group (Bottaro et al., 2007). Thus, it is not clear in the literature whether high-velocity resistance training increases physical function more than traditional strength training does in older adults.

Some reviews and meta-analyses have attempted to investigate the potential superiority of high-velocity resistance training (fast-intended-velocity resistance training) vs traditional resistance training (moderate-velocity resistance training) for functional performance improvement in older adults (Byrne et al., 2016; da Rosa Orssatto, Moura et al., 2018; da Rosa Orssatto, de la Rocha Freitas et al., 2019; Hazell et al., 2007; Mckinnon et al., 2016; Steib et al., 2010; Tschopp et al., 2011). The meta-analysis by Steib et al. (2010) reported with moderate-level evidence (only three studies included) that power strength training is more effective for enhancing physical performance in older adults than progressive resistance training. However, significant differences between training modalities in favor of power strength training were only found in the ability to rise from a chair (SMD = 1.74, 95% CI = 0.39 to 3.10) and stair-climbing (SMD = 1.27, 95% CI = -0.06 to 2.60), while no differences between training modes on TUG (SMD = 0.03, 95% CI = -0.85 to 0.91) and walking (SMD = -0.62, 95% CI = -1.85 to 0.62) tests were observed (Steib et al., 2010). A year later, the meta-analysis by Tschopp et al. (2011) analyzed data from seven studies and

reported a small effect size (SMD = 0.32, 95% CI = 0.06 to 0.57) and advantage of power strength training over traditional resistance training for functional outcomes. The authors also found greater effects (moderate to large effect) of power training, specifically on balance, compared with conventional strength training (SMD = 0.91, 95% CI = -0.17 to 1.99; Tschopp et al., 2011). In the review by Byrne et al. (2016), 10 of the 13 studies analyzed indicated the superiority of power strength training for both muscle power and functional performance compared to traditional resistance training, suggesting that performing resistance exercises "as quickly as possible" provides a small to moderate advantage over slow velocities for improving physical function. Likewise, da Rosa Orssatto, Cadore et al. (2019) concluded that studies using slower velocities revealed a smaller increase in functional capacity compared with faster velocities (0.56% ± 0.43% and 1.37% ± 1.15% per week, respectively).

Nevertheless, in the most comprehensive meta-analysis to date, da Rosa Orssatto, de la Rocha Freitas et al. (2019) suggest that there is not enough evidence to support the superiority of high-velocity resistance training for improving functional capacity when compared to traditional resistance training, probably due to the lack of high-quality and preregistered studies, high heterogeneity, and small-studies publication bias. In this meta-analysis, which included 15 studies, the results for general functional capacity indicated that the improvements from power strength training may be superior compared to moderate-velocity resistance training in older persons (da Rosa Orssatto, de la Rocha Freitas et al., 2019), but the results presented heterogeneity and small-studies publication bias problems. However, when the authors analyzed the effect of each of the training modalities on the various components of physical activity as measured by several different tests (muscle strength: 30sec-CS; muscle power: 5STS, stair-climbing; balance: TUG, SPPB, short walk tests; aerobic capacity: 6MWT), they found that only in the SPPB were the high-velocity resistance training improvements significantly superior to those obtained by moderate-

velocity resistance training ($p = 0.026$). No significant differences between training modalities in muscle strength (30sec-CS: $p = 0.136$), muscle power (5STS: $p = 0.644$; stair-climbing: $p = 0.243$), balance (TUG: $p = 0.079$; short walk: $p = 0.952$), and aerobic capacity (6MWT: $p = 0.243$) were found (da Rosa Orssatto, de la Rocha Freitas et al., 2019).

Regarding the main characteristics of the studies that have compared both training modalities, training frequency ranged from one to three sessions per week, while the training duration ranged from 6 to 36 weeks, most being short-term studies (≤ 12 weeks). Regarding the training intensity, some studies adopted the same training load in both groups (Bean et al., 2009; Bottaro et al., 2007; Correa et al., 2012; Englund et al., 2017; Marsh et al., 2009; Tiggemann et al., 2016; Zech et al., 2012), while others adopted a higher load in one group or traditional resistance training (Balachandran et al., 2014; Gray et al., 2018; Henwood et al., 2008; Lopes et al., 2016; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Richardson, Duncan, Jimenez, Jones et al., 2018; Yoon et al., 2017). Regarding the training volume, the number of sets per exercise ranged from 2 to 4 and the repetitions per set from 6 to 15. The rest intervals between sets and exercises ranged from 60 to 180 s, while the concentric velocity in the traditional resistance interventions ranged from 2 to 4 s (da Rosa Orssatto, de la Rocha Freitas et al., 2019).

One training characteristic that is similar for almost all studies that compare both training modalities is the training equipment used, with machines and free weights being the most common. To date, only Drey et al. (2012) and Yoon et al. (2017) have analyzed the effectiveness of high-velocity resistance training compared to traditional resistance training using elastic bands as a training device. Drey et al. (2012) combined elastic bands, machines, and body weight resistance, and Yoon et al. (2017) is the only study thus far that has compared both training modalities using only elastic bands. Yoon et al. (2017) found that after 12 weeks, significant increases in physical function (as measured by the SPPB) were

observed in both groups, with better scores registered in the power strength group. However, no significant differences between training modalities were found in any physical function parameters (as measured by the SPPB and the TUG test). The study involved older women with mild cognitive impairments. It seems clear that further research regarding the implementation of power strength training with elastic bands in older adults is needed to ascertain its effects on physical function and in comparison with other training modalities.

The large variability in results obtained for power strength training intervention alone or when it is compared with traditional resistance training can be explained in several ways. First, most studies are of poor quality (they do not achieve the PEDro scale's high-quality cutoff point ≥ 6), because they failed to employ concealed participant allocation, blinding of assessors, intention-to-treat analysis, preregistration, and large sample sizes. Second, there is a large variation in the duration of training programs, although the research is dominated by short-term interventions (< 12 weeks). Third, there is high variability in the training parameters applied, such as volume, frequency, and intensity. Fourth, the health and functional abilities of the participants vary notably among studies, ranging from healthy elderly people to older adults with functional impairments or pre-frail and frail community-dwelling older adults. Fifth, there are disparities in the sex and age of subjects. Sixth, the ceiling effect of many functional tests, especially for healthy individuals, may hide the full effects of the power strength training strategy. Seventh, there is large variability in the functional tests used between studies. Eighth, different methods were used to perform the power strength interventions (e.g., isotonic, isokinetic, using variable resistance such as elastic bands). Finally, different exercises were prescribed, and thus the muscle groups emphasized also differ between studies. All these differences likely contributed to the heterogeneity in the results. Therefore, the area would benefit from larger and higher-quality studies.

Although the mechanisms by which the power strength training modality produces positive changes in physical function in older adults have not yet been elucidated, it seems that when muscles shorten at high velocity, during each contraction, the motor unit recruitment patterns change (Desmedt & Godaux, 1977). Specifically, in high-velocity contractions, the motor unit recruitment thresholds are diminished and the discharge rates are increased as the rates of force and power development increase (Budingen & Freund, 1976; Del Vecchio et al., 2019; Desmedt & Godaux, 1977, 1978; Tanji & Kato, 1973). These changes in the recruitment patterns produce training adaptations such as muscle power and strength improvements, yielding greater functional performance in older adults. However, as with muscle strength, the evidence has demonstrated the curvilinear nature of the relationship between muscle power and functional performance (Bean, Kiely, Herman et al., 2002; Bean et al., 2003; Buchner et al., 1996; Cuoco et al., 2004; Marsh et al., 2006). Therefore, the magnitude of improvement in muscle power is not always proportional to the gains in physical function. This phenomenon supports the concept of functional thresholds for muscle power, whereby a high loss of physical function occurs with declining power below the threshold, and only modest improvements or no changes are produced when power increases above the threshold (Bassey et al., 1992; Buchner et al., 1996; Rantanen & Avela, 1997; Salem et al., 2000). Thus, individuals with lower levels of physical function may experience exponential gains in physical functioning as they improve muscle power, whereas individuals with high levels of physical function may experience fewer benefits as they are already functioning near or over the threshold.

In summary, based on the available data, more high-quality and long-duration studies should be developed to provide evidence about and clarify the effects of high-velocity resistance training on physical function in older adults. In addition, because similar improvements are achieved by a wide range of training intensities, from a practical

perspective, additional research is needed to determine the effects of low- to moderate-intensity power strength training in older adults performed with accessible and suitable training devices, such as elastic bands, to ensure the value of application in real-life scenarios where resources are limited. Further investigation is needed to determine the safety and efficacy of high-velocity elastic resistance training in older women. Due to the inconclusive evidence in comparisons between the ability of traditional resistance training and power training to improve physical performance in older adults, more studies are needed to clarify the benefits of both training modes, as are studies that compare the effects of high-velocity resistance training with other previously validated efficient training modalities for improving physical functioning in older adults, such as the multi-component training modality.

II.X. JUSTIFICATION

Given the major role that exercise has in reversing and preventing the deleterious effects of aging among older adults, and specifically in older women, an investigation into the most appropriate type of exercise program for producing positive adaptations in different systems in older women is of high of relevance.

The identification of the effects of the key training parameters such as training intensity and exercise modality on oxidative stress, bone health, body composition, neuromuscular stress, and physical function in older women to counteract the aging process has not been previously elucidated. Determining the appropriate exercise intensity and training modality for older people and evaluating these interventions' beneficial or adverse effects is of fundamental importance.

Moreover, there is no consensus about the effects that variable resistance such as elastic bands can produce in older adults, and there is a lack of studies that analyze the changes produced by this kind of training device when applied in power strength or multi-component programs for older women. This might contribute to developing evidence of how different elastic-based exercise interventions could facilitate the exercise participation of older adults, comparing the effectiveness, feasibility and safety of resistance training, multi-component, and power strength training programs using elastic resistance.

Furthermore, there is currently a lack of studies that directly compare the impact on older adults of the training modalities analyzed in the present PhD dissertation. The vast majority of existing studies have significant limitations such as a low sample size, a lack of pre-registration, a failure to record the safety and feasibility of the training programs, a lack of information about the sample or exercise protocols, a lack of "gold standard" variables or procedures, and methodological errors when quantifying or prescribing exercise intensity,

especially in those that used elastic resistance. These limitations reduce the studies' quality and external validity. Therefore, conducting high-quality studies such as those detailed in this PhD dissertation is highly relevant in elucidating valid and reliable facts, since previous studies have tended to underestimate or overestimate the effects of elastic-based exercise interventions.

The exercise program's duration is a determinant in the influence of the training effects of the body's responses of older adults. However, short duration interventions (<12 weeks) predominate in the field of exercise, aging, and healthspan studies due to the logistical complications involved in performing longer interventions. Therefore, the studies presented in the present PhD dissertation are of high scientific interest, since they are medium (20 weeks) and long (32 weeks) duration studies.

To summarize, the studies detailed in this PhD dissertation are the first to analyze and compare the effects of training intensity and exercise modality on oxidative stress, bone health, body composition, neuromuscular stress, and physical function in older women, in medium- and long-term exercise interventions using elastic resistance with a high-quality level of evidence.

CHAPTER III
Aims and hypotheses

III.I. PROJECT ONE. EFFECTS OF A 32-WEEK RESISTANCE TRAINING PROGRAM WITH ELASTIC BANDS AT DIFFERENT TRAINING INTENSITIES ON REDOX STATE, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH, AND PHYSICAL FUNCTION IN OLDER WOMEN. A RANDOMIZED CONTROLLED TRIAL.

Taking as a reference the studies analyzed in the previous chapter, it seems necessary to determine what kind of training intensity, whether high or moderate, is more appropriate to achieve positive changes in various biological processes (oxidative stress and bone turnover states), bone health, body composition, and neuromuscular function (muscle strength, balance, aerobic endurance) when a resistance training program using elastic bands is applied in older women. To answer the problem statement, the following objectives have been specified.

III.I.I General aim

The main aim of this PhD research project was to examine and compare the mid- (16 weeks) and long-term effects of a 32-week elastic resistance training program at high and moderate intensity on oxidative stress, bone health (aBMD, bone remodeling and fracture risk), body composition (fat-free mass and fat mass), muscle strength, and physical function in older women. This overall aim was achieved through several specific objectives.

III.I.II Specific objectives

The specific aims of this research were as follows:

1. Specific objective (SO) 1: To investigate the midterm (16 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on oxidative stress biomarkers through assessment of the impact on DNA damage (urinary 8-oxo-dG), lipid peroxidation (8-iso-P, MDA), protein oxidation (protein carbonyls), thiol redox state (GSH, GSSG, GSSG/GSH ratio), and antioxidant enzymes (CAT, GPx and SOD) in older women.

2. SO2: To determine the mid- (16 weeks) and long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on bone remodeling through assessment of the BTMs of bone formation (P1NP, bALP), resorption (β-CTx), and the balance of both processes (bALP/β-CTx ratio) in older women.
3. SO3: To evaluate the long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on bone health through assessment of aBMD and T-score of the lumbar spine (L1–L4 and L2–L4 segments and L1, L2, L3, and L4 individual vertebrae) and the proximal femur (femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip) along with the 25OHD, sodium (Na), potassium (K), and chlorine (Cl) biomarkers in older women.
4. SO4: To determine the long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on fracture risk through assessment of the impact on the 10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture parameters in older women.
5. SO5: To analyze the long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on body composition through assessment of total body mass, total fat mass, total fat-free mass, and total percentage of fat mass in older women.
6. SO6: To investigate the long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on muscle strength of the upper and lower limbs through assessment of the

isokinetic strength of knee and elbow flexion and extension and hip abduction and adduction at 60º/s and 180º/s in older women.

7. SO7: To determine the long-term (32 weeks) effects of training intensity (high vs moderate) in resistance training programs using elastic bands on physical function through assessment of the impact on the endurance strength of upper (30sec-AC) and lower (30sec-CS) limbs, dynamic balance (TUG), and aerobic endurance (6MWT) parameters in older women.
8. SO8: To evaluate and analyze cognitive status (MMSE), the level of BADLs (Barthel index) and IADLs (Lawton and Brody scale), and general socioeconomic, health, and lifestyle data as potential confounding variables.
9. SO9: To identify any differences in the parameters mentioned in SO1 to SO7 at the end of the intervention depending on the training intensity employed.
10. SO10: To determine the effectiveness and safety of high and moderate progressive and supervised resistance training programs performed with elastic bands through assessment of the rates of attendance, compliance, and adverse events reported by older women participants.

III.I.III Hypotheses

The following hypotheses (H) were formulated:

1. H1 (from SO1): A 16-week program of progressive resistance training with elastic bands at high intensity in older women increases oxidative stress by increasing the concentrations of 8-oxo-dG, 8-iso-P, MDA, and protein carbonyls biomarkers, while a moderate intensity routine produces a reduction of the values in the same parameters.

2. H2 (from SO1): Both training intensities produce similar increases in the concentration of thiol redox state and antioxidant enzymes parameters after 16 weeks of progressive resistance training with elastic bands.
3. H3 (from SO2): A 32-week program of progressive resistance training with elastic bands at high intensity improves the bone remodeling circle by increasing the concentrations of P1NP and bALP and by reducing the values of β-CTx at the midpoint (16 weeks) and in the long term (32 weeks), while the moderate intensity produces a positive effect in the same parameters only over the long term.
4. H4 (from SO3): Both training intensities improve the aBMD and T-score of the lumbar spine and proximal femur areas, with no impact in the biochemical markers of 25OHD, Na, K, and Cl after a 32-week program of progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity.
5. H5 (from SO4): Both training intensities reduce the risk of major osteoporotic and hip fracture in the following 10 years after a 32-week program of progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity.
6. H6 (from SO5). Both training intensities improve body composition by decreasing body fat and by increasing muscle mass after a 32-week program of progressive resistance training with elastic bands, with the moderate intensity producing greater effects than the high intensity in all the body composition parameters.
7. H7 (from SO6): Both training intensities improve upper and lower limb muscle strength at low and high velocities after a 32-week program of

progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity at both velocities and in all the muscle groups assessed.

8. H8 (from SO7): Both experimental groups increase their physical function values in terms of muscle strength and endurance of upper and lower limbs, dynamic balance, and aerobic capacity by similar amounts after a 32-week program of progressive resistance training with elastic bands.
9. H9 (from SO8): The potential confounding variables analyzed do not influence the rest of the parameters in any experimental group.
10. H10 (from SO9): At the end (32 weeks) and at the midpoint (16 weeks) of the intervention period, there are differences between the training intensity groups in the parameters analyzed.
11. H11 (from SO10): Both training programs are effective and safe due to their positive effects on all parameters analyzed, the high rates of attendance and compliance of the participants, and the low level of adverse events reported.

III.II. PROJECT TWO. EFFECTS OF MULTI-COMPONENT, POWER STRENGTH AND TRADITIONAL HIGH-INTENSITY RESISTANCE TRAINING WITH ELASTIC RESISTANCE ON REDOX STATE, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH, AND PHYSICAL FUNCTION IN OLDER WOMEN. A 20-WEEK RANDOMIZED CONTROLLED TRIAL.

Although traditional progressive resistance training is perhaps the most widely researched and accepted exercise modality in the elderly population due to its general health benefits, innovative training modalities, such as multi-component and power strength training, have recently been developed and studied to analyze their effects against aging. Given the paucity of studies comparing these new modalities with traditional resistance training, the lack of results in various parameters, the conflicting findings due to the large methodological differences between studies, and their previously discussed limitations, it is difficult to generate exercise recommendations to obtain the best effects in terms of health in older adults through these kinds of training programs.

Thus, it seems necessary to verify what kind of training modality, whether multi-component, power, or traditional high-intensity resistance training, is more appropriate for achieving positive changes in various biological processes (oxidative stress), bone health (aBMD, bone remodeling and fracture risk), cardiovascular risk, body composition, and neuromuscular function (power and endurance muscle strength, proactive and dynamic balance, aerobic endurance) when they are applied using a simple and portable training device such as elastic bands in older women. To answer the problem statement, the following objectives have been specified.

III.II.I General aim

The main aim of this PhD research project was to analyze and compare the effects of multi-component, power strength, and traditional high-intensity resistance training programs using elastic resistance devices on oxidative stress biomarkers, bone health (aBMD, bone remodeling, fracture risk), cardiovascular risk, body composition (fat-free mass and fat mass), muscle strength, and physical function in older women during 20 weeks of training. This overall aim was achieved through several specific objectives.

III.II.II Specific objectives

The specific aims of this PhD thesis are as follows:

1. SO1: To compare the effects of the training modality (multi-component vs power strength training) in an intervention period of 20 weeks using elastic resistance on oxidative stress biomarkers through assessment of the impact on DNA damage (urinary 8-oxo-dG), lipid peroxidation (8-iso-P), thiol redox state (total glutathione, GSH, GSSG, GSSG/GSH, and GSH/GSSG ratios), and antioxidant enzymes (GPx and SOD) in older women.
2. SO2: To determine the effects of the training modality (multi-component vs power strength training) in an intervention period of 20 weeks using elastic resistance on bone remodeling through assessment of BTMs of bone formation (OC) and bone resorption (β-CTx) in older women.
3. SO3: To evaluate the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on bone health through assessment of aBMD and T-score of the lumbar spine (L1–L4 and L2–L4 segments and L1, L2, L3, and L4 individual vertebrae) and proximal femur (femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip) in older women.

4. SO4: To determine the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on fracture risk through assessment of the impact on the 10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture parameters in older women.
5. SO5: To analyze the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on cardiovascular risk through assessment of the waist circumference (WC), hip circumference (HC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) in older women.
6. SO6: To investigate the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on body composition through assessment of the total body mass, total fat mass, total fat-free mass, and total percentage of fat mass in older women.
7. SO7: To determine the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on muscle strength of the upper and lower limbs through assessment of the isokinetic strength of knee and elbow flexion and extension and hip abduction and adduction at 60º/s and 180º/s in older women.
8. SO8: To assess the effects of the training modality (multi-component, power strength, or traditional high-intensity resistance training) in an intervention period of 20 weeks using elastic resistance on physical function through

assessment of the impact on the endurance strength of the upper (30sec-AC) and lower (30sec-CS) limbs, power strength of the lower limbs (5STS and timed stair-climbing tests), proactive (FRT) and dynamic (TUG) balance, and aerobic endurance (6MWT) parameters in older women.

9. SO9: To evaluate and analyze the cognitive (MMSE), nutritional (3-day diet record), anxiety (overall anxiety severity and impairment scale [OASIS]), and depression (overall depression severity and impairment scale [ODSIS]) status; the level of physical activity (Global Physical Activity Questionnaire [GPAQ]), BADLs (Barthel index), and IADLs (Lawton and Brody scale); and the general socioeconomic, health, and lifestyle data as potential confounding variables.
10. SO10: To identify any differences in the parameters mentioned from SO1 to SO8 at the end of the intervention according to the training modality employed.
11. SO11: To determine the efficacy and safety of the supervised and progressive multi-component, power, and traditional high-intensity resistance training programs performed with elastic resistance through assessment of the rates of attendance, compliance, and adverse events reported by the older women participants.

III.II.III Hypotheses

The following hypotheses were formulated:

1. H1 (from SO1): Both the multi-component and power strength training modalities produce similar improvements in the oxidative stress state by decreasing the concentrations of 8-oxo-dG and 8-iso-P and increasing the

activity of the thiol redox state and antioxidant enzymes after an intervention period of 20 weeks using elastic resistance.

2. H2 (from SO2): Both the multi-component and power strength training modalities improve the bone remodeling circle by increasing the concentrations of OC and reducing the values of β-CTx after an intervention period of 20 weeks using elastic resistance.
3. H3 (from SO3): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) improve the aBMD and T-score of the lumbar spine and proximal femur areas after an intervention period of 20 weeks using elastic resistance, with power strength training producing greater effects than multi-component and high-intensity resistance training in the analyzed bone regions.
4. H4 (from SO4): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) reduce the risk of major osteoporotic and hip fracture in the following 10 years after an intervention period of 20 weeks using elastic resistance, with power strength training producing greater effects than multi-component and high-intensity resistance training.
5. H5 (from SO5): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) reduce cardiovascular risk by reducing the WC, HC, WHR, and WHtR after an intervention period of 20 weeks using elastic resistance, with multi-component training producing greater effects than power strength and high-intensity resistance training.

6. H6 (from SO6): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) improve body composition by decreasing body fat and increasing fat-free mass after an intervention period of 20 weeks using elastic resistance, with multi-component training achieving greater effects than power strength and high-intensity resistance training in fat mass and high-intensity resistance training producing better results in fat-free mass than the other training modalities.
7. H7 (from SO7): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) improve the upper and lower limb muscle strength at low and high velocities after an intervention period of 20 weeks using elastic resistance, with power strength training producing greater effects at high velocities than multi-component and high-intensity resistance training in all the muscle groups assessed and high-intensity resistance training achieving greater results than power strength and multi-component training at low velocities in all the muscle groups assessed.
8. H8 (from SO8): All the training modalities studied (multi-component, power, and traditional high-intensity resistance training) increase physical function in terms of muscle strength and endurance of the upper and lower limbs, muscle power strength of the lower limbs, proactive and dynamic balance, and aerobic capacity by similar amounts after an intervention period of 20 weeks using elastic resistance, with the power strength training producing greater effects in power strength than multi-component and high-intensity training programs and the multi-component training achieving greater results in proactive and dynamic balance than the other training modalities.

9. H9 (from SO9): The potential confounding variables analyzed do not influence the rest of the parameters in any experimental group.
10. H10 (from SO10): At the end of the 20-week intervention period, there are differences between the training modalities groups in the parameters analyzed.
11. H11 (from SO11): All the training modalities studied (multi-component, power strength, and traditional high-intensity resistance training) are effective and safe due to their positive effects on all parameters analyzed, the high rate of attendance and compliance of the participants, and the low level of reported adverse events.

CHAPTER IV[17]

Methodology

[17] Partially based on:

1. Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877

2. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

3. Colado, J. C., Pedrosa, F. M., Juesas, A., Gargallo, P., Carrasco, J. J., Flandez, J., Chupel, M. U., Teixeira, A. M., & Naclerio, F. (2018). Concurrent validation of the OMNI-Resistance Exercise Scale of perceived exertion with elastic bands in the elderly. *Experimental Gerontology, 113*, 11-16. https://doi.org/10.1016/j.exger.2017.12.009

In completion of this thesis, two experimental studies were conducted. This chapter presents the methodological aspects of both studies.

IV.I. PROJECT ONE. EFFECTS OF A 32-WEEK RESISTANCE TRAINING PROGRAM WITH ELASTIC BANDS AT DIFFERENT TRAINING INTENSITIES ON REDOX STATE, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH, AND PHYSICAL FUNCTION IN OLDER WOMEN. A RANDOMIZED CONTROLLED TRIAL.

IV.I.I. Study design

This was an eight-month randomized, three-arm prospective parallel design clinical trial. The subjects were randomized into either high-intensity resistance training (HI; n = 39), moderate-intensity resistance training (M; n = 31), or self-management control (C; n = 23) groups by an independent staff member not involved in the study using a computer-generated (Microsoft Excel) random permutation procedure.

The study was part of a larger research program on the effects of different training intensities and training devices on a wide range of physical and physiological parameters. Initially, men were also included, but for the analysis of this PhD dissertation, they were excluded with the intention of focusing more deeply on the effects on the female population of the parameters finally selected.

The study was conducted according to the Helsinki Declaration (1975; revised in 2014), and the experimental protocol was approved by the Human Research Ethics Committee of the University of Valencia (H1395923230221; Appendix G).

IV.I.II. Randomization and blinding

Due to the characteristics of the study, blinding the participants to the treatment was not possible. However, the data collectors and data analysts were independent, and if it was not possible at some point, a random code was created for each participant, making it impossible to identify which group they belonged to.

The randomization was performed after recruitment by an independent staff member not involved in the trial or any screening, testing, training procedures, or contact with the participants, using a computer-generated random permutation procedure. Subjects were not scheduled for outcome measurement according to their order of recruitment or order of treatment allocation. With these procedures, treatment allocation was safely concealed from staff.

IV.I.III. Study population

A. Inclusion and exclusion criteria

Untrained Caucasian older women (aged 60–79 years) volunteered to participate in the study after reading an advertisement containing the study information that was publicly posted between May and September 2014 at several Municipal Activity Centers for Older People (MACOPs) in Valencia, Spain. The inclusion and exclusion criteria were as follows.

Inclusion criteria:

- Age > 60 years
- Physically independent (able to walk 100 m without a walking aid and climb 10 steps without rest)
- On the registration waiting list for physical activity at their respective MACOP
- Sedentary lifestyle (less than one hour of physical activity or exercise a week during the previous six months)
- Medical certificate of suitability or fitness to practice resistance training activities (based on ACSM; Kohrt et al., 2004)

- No plans to leave the area during the intervention
- Cognitive ability to understand and follow the instructions and sign the informed consent form
- Free of any antioxidant supplements for at least six weeks before the start of this study

Exclusion criteria:

- Presence of cardiovascular, musculoskeletal, renal, liver, pulmonary, or neuromuscular and neurological disorders that would prevent the participant from performing the exercises
- Current or prior (past six months) use of hormone replacement therapy
- Body weight changes > 10% in the previous year
- Intake of prescription medications or supplements (e.g., vitamins C, E) that were expected to alter the results of the study (ergogenic, dietary aids, estrogen, beta-blockers, steroid hormones, calcitonin, corticosteroids, glucocorticoids, thiazide diuretics, anticonvulsants, bisphosphonates, raloxifene)
- A history of malignant neoplasms
- Terminal illness with life expectancy of less than one year
- Engagement in regular strength training (more than once a week) during the previous six months

- Participation in another research project (within the last six months) involving dietary, exercise, and/or pharmaceutical intervention
- MMSE lower than 23/30 (Folstein et al., 1975)
- Severe visual or hearing impairment

B. Screening and recruitment process

Recruitment was implemented in Valencia (Spain) by nonprobability convenience sampling through advertisements displayed on notice boards at several MACOPs that had lists of members waiting for physical activity of more than 100 people (Nou Moles, Ruzafa, Benicalap, Benimaclet, Campanar, El Calvari, Marchalenes), posted between May and September 2014.

The screening process had several steps. First, a meeting with the director of the Elderly Section of the Valencia City Council was held to obtain his approval of the entry registration application number 001132014010415 for the authorization of the study (Appendix H). Then, a meeting was held with the managers of each of the MACOPs who agreed to collaborate in the study and who fulfilled the waiting list requirement, specifying the presentation of the project and coordination of activities as well as the dissemination of information and registration of participants.

In each of these centers, a meeting was held with those people who had shown interest in participating voluntarily in the study where they were informed verbally, visually (through a presentation), and in writing of the characteristics of the project. In addition, they were asked to recommend the study to family and friends. A total of 197 individuals indicated interest in participation. Then, a medical history questionnaire was used to screen for exclusion criteria. Study personnel reviewed each subject's responses on the questionnaire to

verify completeness. Finally, all eligible participants were required to obtain approval from their local doctor to clear them of any contraindicated medical conditions for exercise based on ACSM guidelines (Kohrt et al., 2004).

Before being included in the study, all potential participants were comprehensively informed about the study's purpose and procedures as well as the benefits, risks, and discomfort that might result from participation. Each participant provided written informed consent and was free to withdraw from the study at any time (Appendix I). They were also informed that the information they provided and obtained as a result of the examinations would become part of an automated file with the purpose of research and teaching in the areas of health, physical activity, and sport, in compliance with Organic Law 15/1999 of December 13 on the Protection of Personal Data.

IV.I.IV. Experimental procedures

A. General procedure

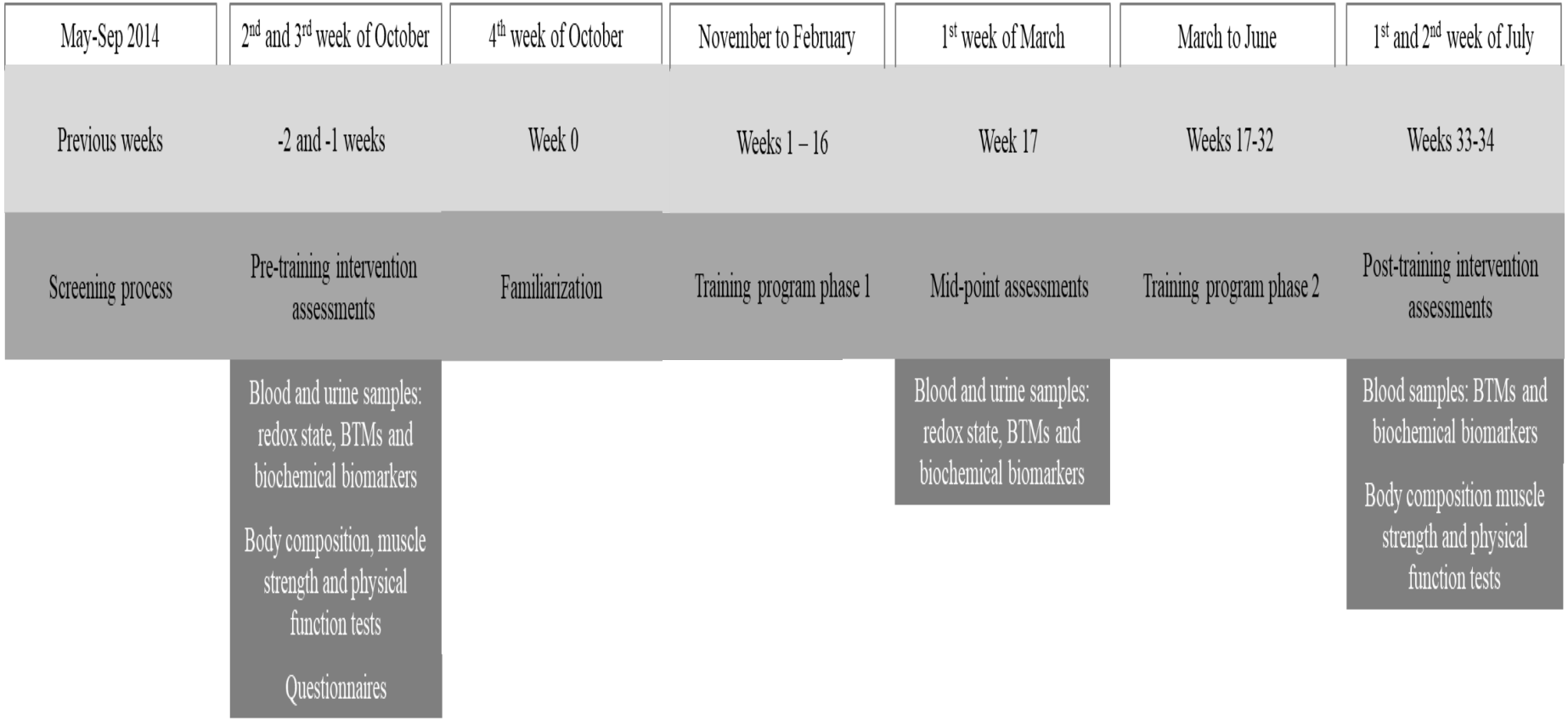
Baseline and postintervention evaluations were carried out two weeks prior (weeks -2 and -1; second and third weeks of October) and after (weeks 33 and 34; first two weeks of July) the intervention. In addition, BTMs, oxidative stress biomarkers, antioxidant enzymes, and thiols were evaluated in one week in the middle of the program (week 17, first week of March; Figure 62). The following primary and secondary dependent variables were assessed in the evaluation periods: oxidative stress (urinary 8-oxo-dG, 8-iso-P, MDA, protein carbonyls, GSH, GSSG, GSSG/GSH ratio, CAT, GPx, and SOD), bone remodeling via BTMs (P1NP, β-CTx, bALP, bALP/β-CTx ratio), bone strength (aBMD and T-score of lumbar spine [L1–L4 and L2–L4 segments and L1, L2, L3, and L4 individual vertebrae] and proximal femur [femoral neck, trochanter, intertrochanter, Ward's triangle and total hip], 25OHD, Na, K, Cl), fracture risk (10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture), body composition (total body mass, total fat mass, total

fat-free mass, and total percentage of fat mass), muscle strength of the upper and lower limbs (peak torque strength via isokinetic strength of knee and elbow flexion and extension and hip abduction and adduction at 60º/s and 180º/s), and physical function (30sec-CS, 30sec-AC, TUG, 6MWT).

In addition, at the beginning of the program, participants were required to complete several questionnaires to control for possible confounding variables like: cognitive function (MMSE), performance of BADLs (Barthel index) and IADLs (Lawton and Brody scale), and sociodemographic and health status data (age, ethnicity, education level, living situation, marital status, employment status, number of comorbidities, prescribed medications). The questionnaires were provided to the participants at the first evaluation session (after physical test measurements) and explained by the research staff, completed by the participants at home, and returned to the research staff during the familiarization sessions or on the second evaluation day (for the control group). Any questions were resolved during the same familiarization sessions or by phone call.

Urine and blood samples were obtained by nurses at the University Hospital Dr. Peset in Valencia, while the other parameters were measured in the Performance Laboratory of the Faculty of Physical Activity and Sport Sciences at the University of Valencia. Biological samples were processed in the Oxidative Pathology Unit of the Department of Biochemistry and Molecular Biology in the Faculty of Medicine at the University of Valencia and in the Clinical Analysis Service at University Hospital Dr. Peset–FISABIO (Fundación para Fomento de Investigación Sanitaria y Biomédica).

Figure 62. *Detailed schematic diagram of the experimental phases in the project one.*



All the assessments were performed by the same researchers (sport scientist, physiotherapist, and nurses) using the same protocols at the same time of the day. These researchers also explained the execution to the participants, did practical demonstrations (if necessary), and collected all the data. All the evaluation staff were previously instructed to ensure consistency in how the tests were performed and how the assessment instruments were calibrated and to ensure that the protocol was standardized.

Regarding the order of the tests, first analyzed were the anthropometric (5 min) and body composition and bone health measurements (20–25 min), followed by isokinetic strength (20 min) and physical function (15–20 min) tests (balance [TUG], dynamic strength [30sec-CS, 30sec-AC], and aerobic capacity [6MWT]). Anthropometric and DXA measures were performed before any strength and physical function measures to minimize any effects of fluid shifts (Romero-Arenas et al., 2013). At the same time, the order of the tests was designed with the intention of minimizing the effects of one test on the next (in terms of neuromuscular and cardiovascular fatigue). For that reason, isokinetic strength assessments were performed before physical function, and within the functional tests, balance tests were executed before strength and aerobic capacity. Performing all the tests took 70–100 min. As the participants were divided into two shifts, the blood collection was performed a day before (shift a) or after (shift b) the rest of the tests, with at least 48–72 hours between the blood extractions and the other tests. The time window between baseline assessment and the start of intervention was two weeks, as was the time between the end of the eight-month training intervention and the post-training assessments.

Participants were asked to wear the same clothing and shoes to the tests before and after the intervention and were instructed to maintain their normal daily routines and dietary intake during the evaluation period. Prior to conducting the primary and secondary dependent variables tests (with the exception of blood analysis), participants fasted for 3–4 hours,

refrained from ingesting stimulants (e.g., caffeine) for 8 hours, and avoided practicing intense exercise for 24 hours but were allowed to hydrate freely. Before the blood analysis, subjects fasted for 12 hours and avoided exercise for at least 12 hours. Further details of the assessments are described below.

B. Collection and processing of blood and urine samples

Prior to performing the extractions, all participants had to sign a voluntary informed consent form drawn up by the ethical committee of the University Hospital Dr. Peset wherein the necessary information about the collection and treatment process of blood samples was provided (Appendix J).

i. Urine collection

Specimens of 10–15 ml of spot urine (first urine in the morning) were collected in polyethylene bottles and transferred to glass tubes. These urine samples were centrifuged at 3,000 rpm for 5 min in a Rotina 380H Hettich centrifuge (Tuttlinger, Germany) to precipitate and remove impurities. Different aliquots were separated and stored at -80°C until use. This collection was performed for 8-oxo-dG and 8-iso-P.

ii. Blood sample collection and storage

After participants fasted for 12 hours and followed the recommendations by the medical team (Appendix K), antecubital venous blood samples were extracted (10–15 ml) into ethylenediaminetetraacetic acid (EDTA) tubes (Reference 367988; Vacutainer, Franklin Lakes, New Jersey) by a qualified nurse from seated participants between 8:00 and 10:00 a.m. (to minimize circadian effects) at the University Hospital Dr. Peset of Valencia. Aseptic techniques and universal precautions were used for blood draws. These samples were kept in a refrigerator at 2°C –4°C until they were processed, which always occurred within 4 hours

of extraction. This collection was performed for oxidative stress, antioxidants, bone turover markers and, chemical biomarkers.

iii. Blood sample separation of plasma and peripheral blood mononuclear cells

Separation was carried out by density-gradient centrifugation with Histopaque (Sigma H-1077) at 1,700 rpm for 30 min (at 12°C). The resulting yellow top layer (plasma) along with the ring of PBMc found between the first and second layers were transferred to Eppendorf tubes, gently resuspended, and stored at 80°C until use. The same procedure was conducted to obtain only the plasma layer, which was also stored at 80°C until use. Prior to their use in the study assays, the samples were sonicated for 3–5 s (Monzo-Beltran et al., 2017). This process was performed for MDA, antioxidants biomarkers, and thiols.

iv. Serum sample separation

Samples of 10 ml of whole blood were drawn from an antecubital vein into dry 10 ml tubes with silicone gel separator and coagulation activator. After retraction of the clot (15–30 min at room temperature), the samples were centrifuged at 3,500 rpm for 5 min at 4°C in a Rotina 380R Hettich centrifuge (Tuttlinger, Germany). The resulting serum supernatant was pipetted and aliquoted. The aliquots were frozen at -80°C until their use. This process was performed for BTMs, protein carbonyls, and chemical biomarkers.

v. Biochemical analysis

The analysis of the biochemical parameters consisted of a complete biochemical-clinical study, which included 25OHD, Na, K, and Cl, which were determined by using an ECLIA (25OHD) and spectrophotometric (Na, K, and Cl) procedures in Cobas 6000 (Roche Diagnostics, Mannheim, Germany) and Architect c16000 (Abbott, Illinois, USA) automatic

analyzers, respectively. The 25OHD was analyzed in plasma, while the Na, K, and Cl in serum (Figure 63).

Figure 63. *Blood extraction.*

C. Oxidative stress, antioxidants, and redox state

i. Urinary 8-oxo-2-deoxyguanosine

The method used to measure DNA oxidation was modified from that described by Espinosa et al. (2007). Specifically, 1 ml of urine was defrosted, and 100 µl of 3 mol/L Tris–EDTA solution (pH 8.6) were added and vortex mixed for 30 s. Then, 1 ml of the solution was applied to a Bond Elute C18(OH)SPE (3 ml) column preprepared with 3 ml methanol and 3 ml distilled water (HPLC grade). The column was washed with 3 ml water followed by 3 ml of 2.5% acetonitrile and 1.5% of methanol in 10 mmol/L borate (pH 7.9). The sample was then eluted with 3 ml of the same buffer and applied to a Bond Elute strong cation exchange column (3 ml) prepared with 3 ml of methanol and 3 ml of borate buffer (pH 7.9). The 8-oxo-dG was then eluted with 2 ml of acetonitrile/methanol buffer in borate and adjusted to pH 6.0 with 1 mol/L HCl. Approximately 4 ml of 50:50 dichloromethane;propan-2-ol were added to the 2 ml of eluent and vortex mixed for 30 s. The samples were then

centrifuged for 10 min at 3,500 rpm, the upper aqueous layer was aspirated off, and 3 ml of organic layer were dried by evaporation in a vacuum chamber (Concentrator plus; Eppendorf AG, 2331 Hamburg) at 50°C. Finally, the samples were reconstituted in 1 ml HPLC running buffer as above but without acetonitrile, and 50 µl were injected into the HPLC column.

Running conditions and EC detection were the same as those described for plasma samples; 8-oxo-dG values were expressed as the ratio of millimole per mole creatinine quantified with the Cayman Creatinine (urine) Colorimetric Assay kit (no. 500701) as described by Borrego et al. (2013). Calibration procedures described by Espinosa et al. (2007) were followed. An HPLC-grade water solution of 8-oxo-dG > 98% (thin-layer chromatography) purchased from Sigma Aldrich Chemical Company, St. Louis, MO (ref. number H5653), was used as a standard sample. Each working day, six different samples with known low and high concentrations of 8-oxo-dG were run twice. Intra-assay CV determined by analyzing duplicates for each sample was 4.69% with 95% CI = 1.78% to 7.6%.

ii. F2-isoprostanes

The levels of 8-iso-P in the urine were quantified following the analytical specifications of the Cayman ELISA assay no. 516351, and the results were expressed as the relationship with the creatinine concentration (nmol/mmol creatinine; Monzo-Beltran et al., 2017). The intra-assay CV was 2.83% with 95% CI = 1.77% to 3.9%.

iii. Malonaldehyde

In the first step of this test, the lipoperoxides were hydrolyzed by boiling in diluted orthophosphoric acid. Subsequently, the adduction products reacting with MDA-thiobarbituric acid (TBA) were eluted and quantified spectrophotometrically. For MDA quantification, 50 µl of PBMc samples were mixed in a sterile Eppendorf tube with 75 µl of H_3PO_4 0.44M and 25 µl of TBA solution and heated at 95°C for 30 min. After adding (on

ice) 150 µl of neutralizing solution (1M of NaOH), the samples were centrifuged at 10,000 rpm for 5 min. The MDA was purified and measured from 100 µl of the resulting supernatant by HPLC-UV using the isocratic elution method with a solution containing 5% acetonitrile and 50 mM potassium phosphate buffer at pH 5.5. Chromatographic assays were 3 min at a flow rate of 1 ml/min (Borrego et al., 2013; Espinosa et al., 2007). The quantification of the compounds was determined at 532 nm. The total protein content was quantified by the Lowry method (Lowry et al., 1951). Values are expressed as nmol/mg protein. The intra-assay CV was 3.21% with 95% CI = 1.9% to 4.51%.

iv. Protein carbonyls

The quantification of carbonylated proteins in biological samples was determined by derivatization with DNP (dinitrophenylhydrazine) measuring it colorimetrically. The ELISA method allows the quantitative measurement of carbonylation from µg of proteins. Commercial Cayman assay kit no. 10005020 was used to analyze the protein carbonyls in serum. Values are expressed as nmol/mg protein. The intra-assay CV was 4.14% with 95% CI = 2.7% to 5.58%.

v. Reduced glutathione, oxidized glutathione, superoxide dismutase, glutathione peroxidase and catalase

All thiol and antioxidant biomarkers were analyzed using the spectrophotometry method following the respective Cayman Chemical (Ann Arbor, USA) assay kit procedures: GSH and GSSH (no. 703002), SOD (no. 706002), GPx (no. 703102), and CAT (no. 707002). Values of GSH and GSSG are expressed as nmol/mg protein, while SOD, GPx, and CAT are expressed as U/mg protein. The SOD analyzed was the total SOD, not the cofactors of Fe-SOD, Cu-SOD, or any other type. Intra-assay CVs were 3.12% (95% CI = 1.84% to 4.4%), 3.94% (95% CI = 2.22% to 5.66%), 2.89% (95% CI = 0.95% to 4.84%), 2.17% (95% CI =

1.51% to 2.83%), 1.12% (95% CI = 0.7% to 1.48%) for GSH, GSSG, SOD, GPx, and CAT, respectively.

vi. Oxidized glutathione / reduced glutathione ratio

The GSSG/GSH ratio was calculated and expressed as a percentage (Monzo- Beltran et al., 2017).

Because the biochemistry data (blood samples) are logistically difficult, invasive, and expensive to collect and analyze, and in accordance with previous studies in which control groups comprising similar populations did not exhibit changes in DNA damage or thiol redox state over a period of time similar to that of the present study (Azizbeigi et al., 2015; Soares et al., 2015), baseline data were used as a single reference for the C group, as has been done in previous studies (Monzo-Beltran et al., 2017). All the biological samples were run in duplicate as per the manufacturer's instructions to ensure reliability of the measurements. The average of the two readings was used for data analysis. If the results differed by more than 15%, the analysis was repeated (CHMP, 2012). Inter-assay CV for assay standards between each 96 well-plate at our laboratory resulted in a CV of less than 5% for all the biomarkers, similar to previous studies (Borrego et al., 2013). The assessment of biomarkers of oxidative stress, antioxidants and thiol status was not possible to carry out at the end of the program due to lack of funding.

D. Bone health

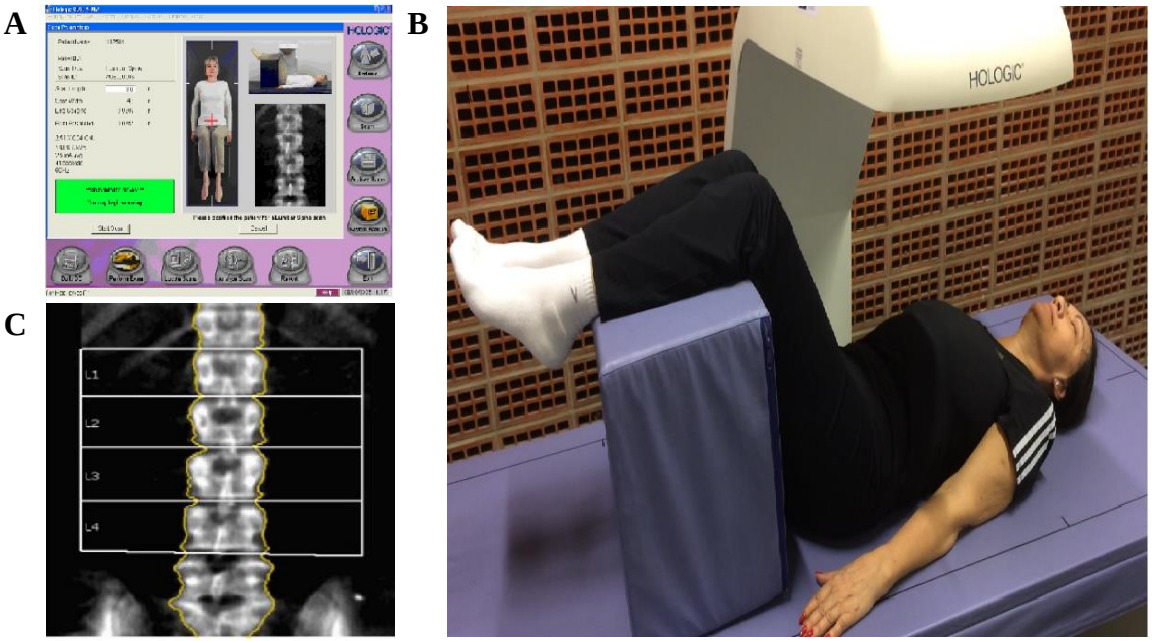
i. Areal bone mineral density and T-score

aBMD and T-score were assessed for the antero-posterior lumbar spine (segments L1–L4 and L2–L4 and single vertebrae L1, L2, L3, and L4) and the proximal femur of the nondominant side (femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip) by DXA (QDR® Hologic Discovery Wi, Hologic Inc., Waltham, MA, USA) equipped with

APEX software (APEX Corp., version 12.4, Waltham, MA, USA). All the scans were standardized according to the manufacturer's recommendations (Hologic user's manual; Hologic, 2006), which included the correct position of the participants, the selection of the global region of interest (RoI) option, and the adjustment of the Toolbox's line mode in accordance with the scanned image.

To evaluate the lumbar spine, participants were placed in a supine, straight, and central position with the legs elevated over a padded box to reduce the lumbar lordosis (Figure 64). The operator ensured that the lumbar spine was within the scan line limits indicated on the scan table and that the scan image was straight and central within the scan field and extended from T12 to L5 so as to image the full L1 to L4 region.

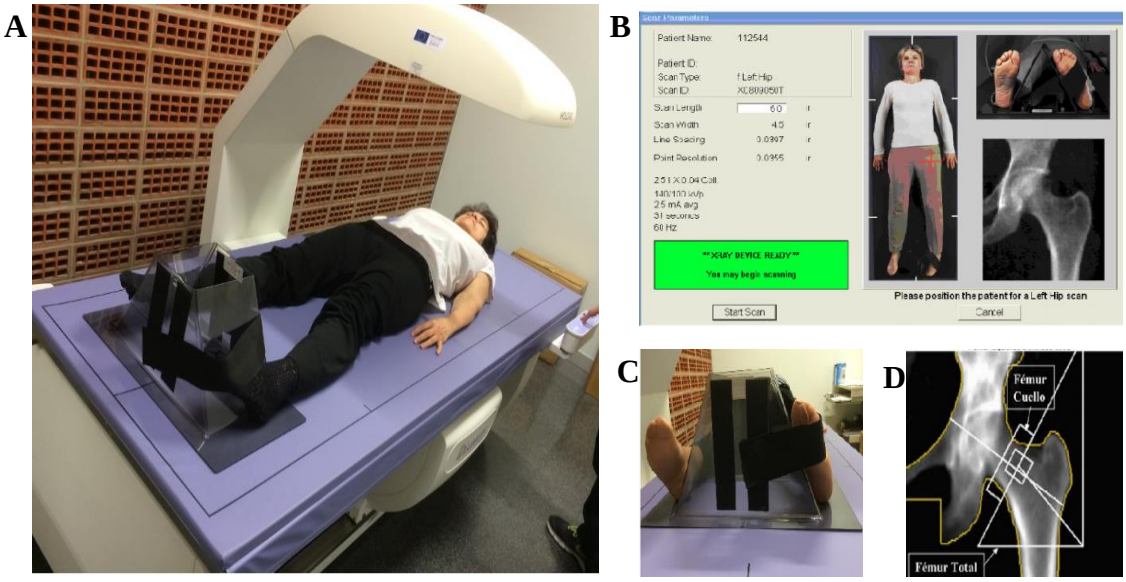
Figure 64. *DXA scan procedure for the assessment of aBMD and T-score in the lumbar spine.*



Note. A. Indications of the procedure software; B. Evaluation position according to detailed procedure; C. Image of the spine (L1-L4) after the scan.

For the proximal femur region, participants adopted a supine, straight, and central position on the scan table with the feet placed on either side of the hip positioner. The participants' arms were placed on their chests, away from the scan field. Participants maintained a slight abduction and an internal rotation of 15°–30° of the nondominant leg to keep the femoral axis straight and the lesser trochanter of the femur not visible (Figure 65).

Figure 65. *DXA scan procedure for the assessment of aBMD and T-score in the proximal femur.*



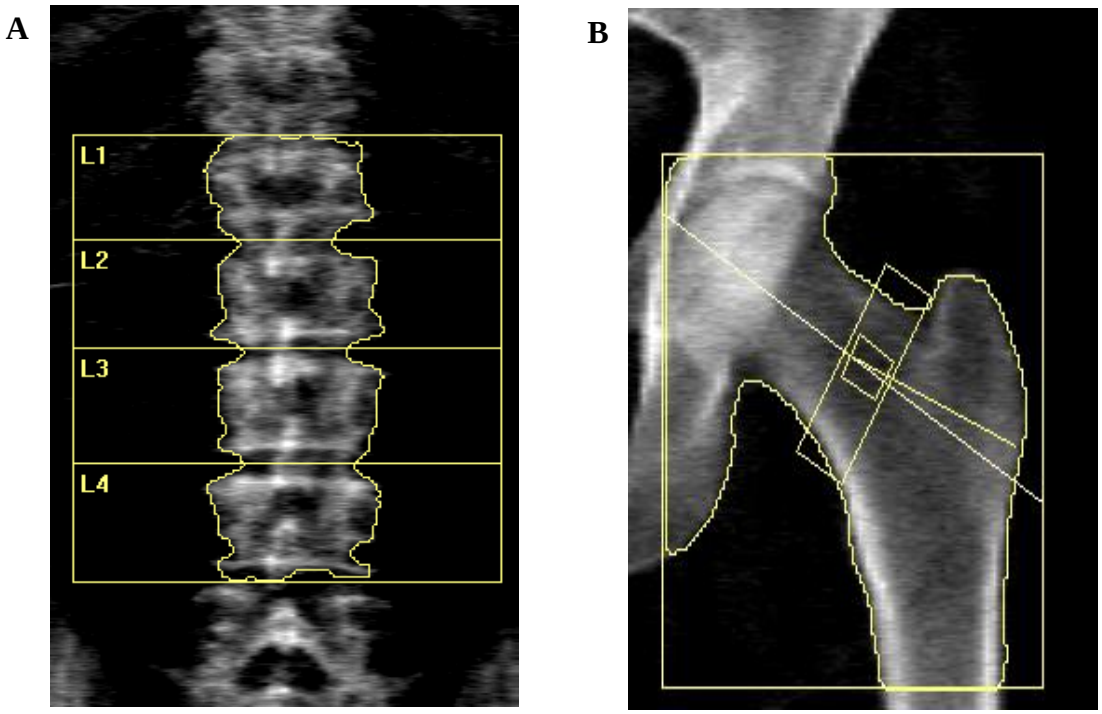
Note. A. Evaluation position according to detailed procedure; B. Indications of the procedure software; C. Clamp to rotate the hip inward; D. Image of the hip after the scan.

All the assessments were performed and analyzed by the same certified technician to minimize interobserver variation (with more than 2,000 scans and analyses performed and an intrareliability < 2%). All the scans were done using the same DXA device. The calibration of total body was carried out daily, and the calibration of the lumbar spine of the densitometer was checked daily through a standard calibration lumbar spine phantom supplied by the manufacturer to account for potential BMD variations due to machine error.

After all scans for all participants were completed, they were analyzed by the investigator. The automatic hip and spine scan analyses were adjusted to ensure that they were properly segmented. For the lumbar spine scan, the RoI included the L1, L2, L3, and L4 vertebrae. The automatic segmentation lines were manually adjusted to ensure that they ran between each vertebra (Figure 66). The global RoI was positioned with the top limit within the T12–L1 intervertebral space and the bottom limit within the L4–L5 intervertebral space, angled to accommodate the shape of the vertebrae. The right and left limits were not altered. The bone map was then identified. Manual adjustments were also made to the automatic analysis by adding or removing necessary bone pixels.

For the proximal femur scan, the RoI included the greater and lesser trochanter, the femoral neck and the coxofemoral joint (Figure 66). The global RoI was positioned with the left border five scan lines from the edge of the greater trochanter, the upper and right borders at least five scan lines away from the edge of the femoral head, and the bottom border 10 scan lines below the lesser trochanter. The bone map was then identified. The midline was placed on the central axis of the hip, the neck box close to the greater trochanter and the trochanteric line below the curve of the greater trochanter, with equal amounts of soft tissue included within the neck box on either side of the femoral neck. The Ward's triangle box was positioned automatically. Manual adjustments were made to the automatic analysis by adjusting the position of the neck box on the proximal femur scan and by adding or removing necessary bone pixels.

Figure 66. *RoIs of lumbar spine and proximal femur.*



Note. Lumbar spine (A) and proximal femur (B) DXA scans with global RoIs.

Values of aBMD and T-scores are expressed in units of g/cm^2 and SD, respectively. The short-term CVs (standard deviation/mean) for repeated measurements of aBMD at the proximal femur in our laboratory are 0.63% (95% CI = 0.36–0.89), 0.96% (95% CI = 0.72–1.21), 0.79% (95% CI = 0.64–0.95), 0.85% (95% CI = 0.49–1.21), and 0.61% (95% CI = 0.39–0.82) for femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip measurements, respectively. The CV-values of the T-score for the same sites are 0.64% (95% CI = 0.09–1.27), 0.43% (95% CI = 0.09–1.81), 0.46% (95% CI = 0.13–0.63), 0.27% (95% CI = 0.12–0.66), and 0.19% (95% CI = 0.03–0.34).

For the lumbar spine, the CVs of the aBMD in our laboratory are 0.79% (95% CIs = 0.61–0.98) and 0.81% (95% CIs = 0.55–1.07) for the lumbar-spine segments of L1–L4 and L2–L4, respectively. For the single vertebrae L1, L2, L3, and L4 the aBMD short-term CVs

are 0.61% (95% CI = 0.33–0.88), 0.78% (95% CI = 0.51–1.05), 0.52% (95% CI = 0.25–0.79), and 0.66% (95% CI = 0.45–0.86). The CV-values of the T-score for the lumbar segments are 0.83% (95% CI = 0.1–1.65) and 0.87% (95% CI = 0.26–1.48), while those for the individual vertebrae are 1.13% (95% CI = 0.24–2.02), 1.85% (95% CI = 0.71–2.98), 1.32% (95% CI = 0.49–2.15), and 0.56% (95% CI = 0.14–1.26).

The test-retest reliability coefficient (ICC) of the device in our laboratory is rated "excellent" for all the parameters (ranged from 0.990 to 0.999), according to the classification proposed by Portney and Watkins (2000), who suggest that ICC values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability.

In addition, intra-rater reliability was also tested, due to the strong influence of the rater in the analysis of the scans. The ICCs for all the variables range from "good" to "excellent" (ICCs between 0.825 and 0.999).

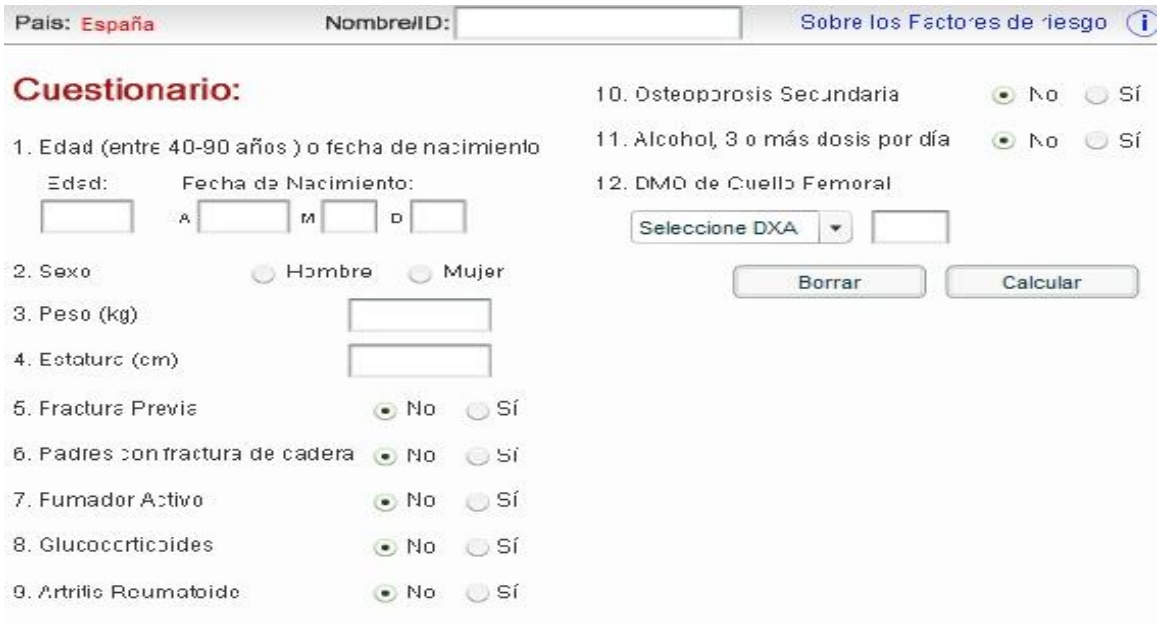
The short-term CVs, test-retest reliability, and intra-rater reliability were estimated from 33 participants (11 from each group) with repeat scans at baseline (measured one week apart), based on the explanations from Koo and Li (2016), who indicate that at least 30 heterogeneous samples are required to analyze the reliability. For the intra-rater reliability, the images collected during this session were analyzed a second time by the same investigator. The same process was used for the rest of the tests performed during the project in which reliability measures were obtained.

ii. A 10-year high risk probability of fracture

A 10-year high-risk probability of fracture was assessed using the FRAX tool (Cosman et al., 2014). The output is the 10-year probability of hip fracture and that of a major

osteoporotic (clinical spine, forearm, hip, or shoulder) fracture. The FRAX® charts provide the fracture probabilities according to the number of risk factors found in an individual. These risk factors were recorded with the FRAX tool inserted into the DXA software. This was done by the same technician who performed the DXA analysis, after an interview with the participant and before the DXA scan. The values of both variables are expressed as percentages (Figure 67).

Figure 67. *FRAX tool at DXA software.*



iii. Bone biomarkers and bone health related parameters

Regarding the BTMs, antecubital venous blood draws were carried out in the morning after 12 hours of fasting and at baseline, both during (week 22) and after the training program. Inter- and post-assessments were carried out after at least 48–72 hours from the last training session to minimize the high variability of some BTMs (Biver, 2012; Seibel, 2005; Szulc et al., 2017; Vescini et al., 2016).

The technicians at the Oxidative Pathology Unit in the Department of Biochemistry and Molecular Biology in the Faculty of Medicine at Valencia University and of the Clinical

Analysis Service at the University Hospital Dr. Peset analyzed the metabolites (P1NP, β-CTx, and bALP) using standardized techniques.

Serum P1NP and β-CTx were measured as markers of bone formation and bone resorption, respectively, using an automated Roche ECLIA system (Cobas 6000, Roche Diagnostics, Mannheim, Germany). Values of P1NP are expressed is µg/L, while those of β-CTx are expressed in pg/mL. The intra-assay CVs for P1NP and β-CTx are 2.66% (95% CI = 1.37–3.94) and 1.62% (95% CI = 0.51–3.74), respectively.

Serum bALP was measured as a marker of bone formation using spectrophotometry, specifically pNPP (p-nitrophenol phosphate) colorimetry, AMP buffer (Architect c16000, Abbott, Illinois, USA). Values are expressed in ng/mL. The intra-assay CV is 3.92%, with a 95% CI of 2.87–4.96. The bALP/β-CTx ratio was calculated and expressed as a percentage.

Plasma 25OHD was assessed through an automated ECLIA system (Cobas 6000, Roche Diagnostics, Mannheim, Germany). Values of 25OHD are expressed in ng/ml. The intra-assay CV is 4.47%, with a 95% CI of 2.65–6.3.

Lastly, Na, K, Cl were also measured, due to their influence on bone health status. They were analyzed in serum via indirect potentiometry (ion-selective electrode; Architect c16000, Abbott, Illinois, USA). Ion-concentration values are expressed in mEq/L. The intra-assay CVs are 3.15% (95% CI = 1.21–4.16), 1.22% (95% CI = 0.58–3.82), and 2.31% (95% CI = 0.83–4.89) for Na, K, and Cl, respectively.

All samples were run in duplicate as per the manufacturer's instructions to ensure reliability of the measurements. The average of both readings was used for data analysis. If the results differed by more than 15%, the analysis was repeated (CHMP, 2012)

E. Anthropometry

i. Height

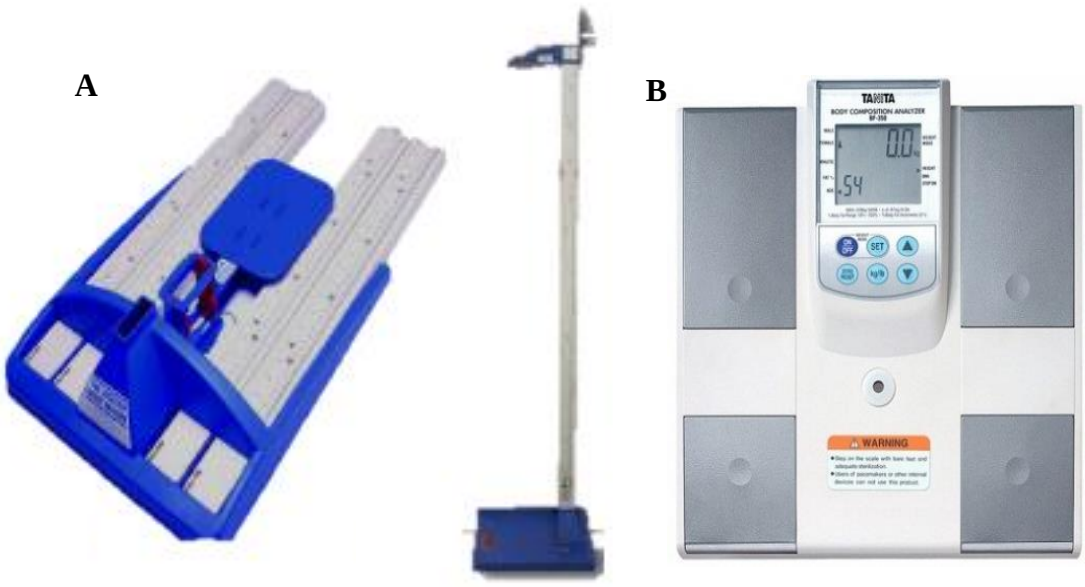
Height was recorded on time to the nearest 0.01 cm using a portable stadiometer (Seca 711, Hamburg, Germany SECA model 217, Seca GmbH & Co. KG, Hamburg, Germany). To ensure precise measurements, first, the subjects had to remove any hair beads that could modify their height, as well as bows or braids located for the correct evaluation (NHANES, 2007). Subsequently, they had to stand barefoot and upright against the stadiometer, with the weight of their body evenly distributed on the ground. The evaluator instructed them to remain with their heels together and toes apart; their buttocks, back, and occipital region had to be in contact with the vertical plane of the height stadiometer. If the body conformation of the older adult did not allow the four contact points – occipital region, back, buttocks and heels – the best possible measurement was obtained according to the protocol. From this position, the subjects took a deep breath at the time of measurement, keeping themselves in the Frankfort plane (the imaginary line that passes through the lower edge of the ocular orbit and through the highest point of the external auditory canal, parallel to the ground and perpendicular to the longitudinal axis of the body). The measurement was then taken with enough pressure to compress the subject's hair, while the older adult held the position after deep inspiration (Figure 68). Values are expressed in meters. The short-term CV for repeated measurements of height is 0.37% (95% CI = 0.23–0.52).

ii. Weight

Weight was recorded once to the nearest 0.01 kg using the Tanita® BF-350 bio-impedance digital scale (Tanita Corp., Tokyo, Japan). Participants were advised to wear light clothing and remove their shoes and any objects in their pockets as well as metal items that could disrupt the electrical current during measurement, and followed the protocol proposed by Dixon et al. (2005). After removing the metal objects, the study coordinator calibrated the

scale to zero and instructed the subjects to step onto the scale. The participants stood barefoot on the bio-impedance scale, placing each foot on the corresponding pairs of electrodes and with their arms extended. Likewise, the coordinator checked that their legs and thighs did not touch and that their arms were not in contact with the body, according to the manufacturer's recommendations. They remained immobile while the analyzer collected the data once the readout on the digital scale became stable (Figure 68). In order to obtain the highest possible reliability and validity in the performance of the test, the participants had to comply with a strict protocol proposed by Dixon et al. (2005). Values are expresses in kilograms. The short-term CV for repeated measurements of weight is 0.96% (95% CI = 0.52–1.41).

Figure 68. *Equipment used to measure height and weight.*



Note. A. Portable stadiometer Seca 711; B. Bio-impedance digital scale Tanita® BF-350.

iii. Body mass index

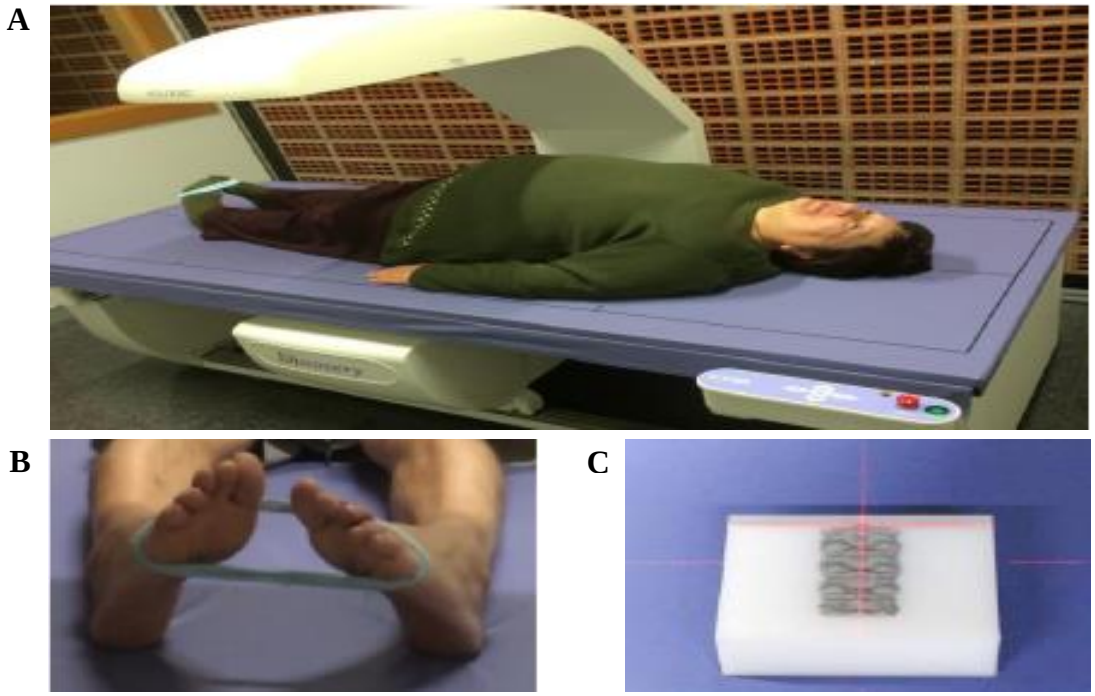
BMI was calculated using the standard formula: body weight (kg)/height^2 (m), and results were classified according to the system used by the WHO (de Onis & Habicht, 1996). The short-term CV for repeated measurements of BMI is 0.77% (95% CI = 0.44–1.63).

F. Body composition

Total body mass, fat mass, fat-free mass, and percentage body fat were assessed for the whole body and for appendicular regions using a DXA (QDR® Hologic Discovery Wi, Hologic Inc., Waltham, Massachusetts, USA) equipped with APEX software (APEX Corp., version 12.4, Waltham, Massachusetts, USA; Figure 73). This test evaluates body composition and density by scanning the entire body for approximately seven minutes. It uses the equivalent of less than 10% of one day's exposure to natural background radiation (0.001 mSv), which corresponds to a lower radiation level than a standard X-ray (0.1 mSv; Sun, Cahill et al., 2013). Quality-control calibration procedures were performed using a spine phantom (Hologic X-CALIBER Model DPA/QDR-1; Hologic, Inc., Waltham, Massachusetts, USA) prior to each testing session according to the manufacturer's instructions. Values are expressed in kilograms for total body mass, fat mass, and total fat-free mass, whereas body fatpercentage is expressed as a percentage.

The participants were positioned in the supine position of the DXA table, with their arms placed close to the sides, hands lying flat and pronated, and legs secured in place using Velcro straps; their hips were maintained at an internal rotation of 25 degrees, according to the equipment manufacturer's instructions (Figure 69). Once correctly positioned, the subjects were instructed to breathe normally during the seven minutes that the assessment lasted, remaining motionless and silent for as long as the beam was running. In addition, they were instructed to press the panic control system, which allowed them to suspend the assessment immediately, if they needed to stop it for any reason.

Figure 69. *DXA scan procedure for the assessment of body composition.*



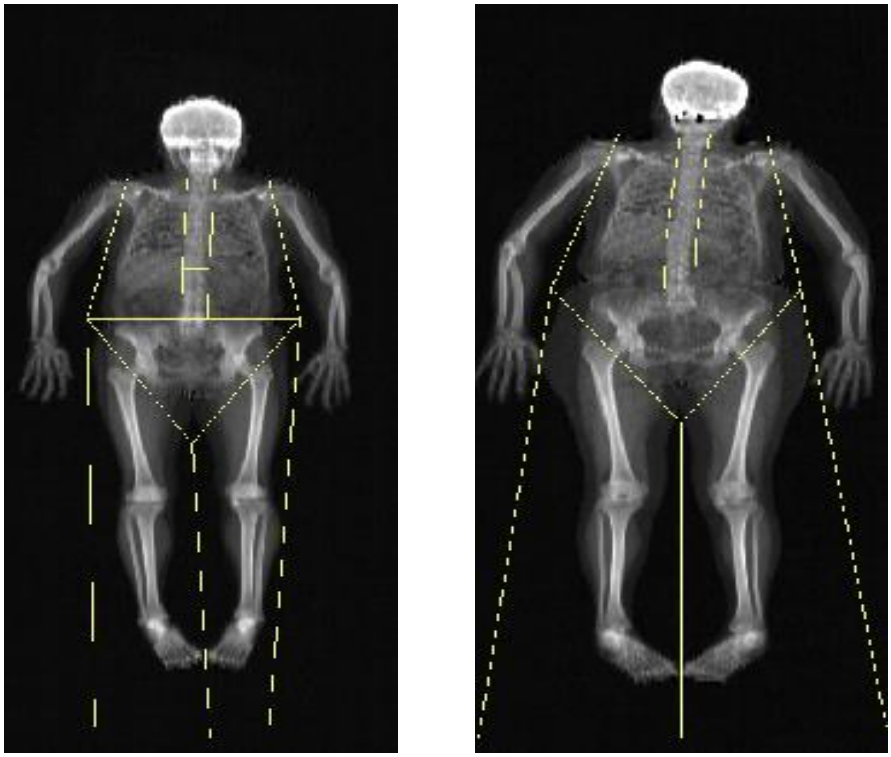
Note. A. Whole body evaluation position according to detailed procedure; B. Hips position at 25 degrees of internal rotation using velcro straps; C. Hologic Model X-CALIBER DPA/QDR-1 spinal column phantom for system calibration.

The X-ray scanner performed a series of transverse scans, moving at 1-cm intervals from the top to the bottom of the whole body. Participants were asked to wear shorts and a T-shirt and to remove any metal or plastic materials they were wearing that could interfere with the DXA examination. The DXA assessment was not performed for participants with implants, because the artifacts could affect the accuracy of the results. They were scanned at the same time of the day for the pre- and post-evaluations. To ensure the reliability of the DXA measurements, all the scans were conducted and manually analyzed by the same certified operator.

The whole-body scans were manually segmented into RoIs; head, trunk, left arm, right arm, left leg, and right leg (Figure 70). Due to high variability in bone structure among

the participants, manual adjustments were made to the automatic analysis by adjusting the position of the limits, following the manufacturer's manual.

Figure 70. *RoIs of whole body for the assessment of body composition.*



Note. Two examples of DXA scan images of the whole body with global RoIs. It can be observed the bone structure variability between subjects.

DXA is a highly reliable and accurate method of determining soft-tissue body composition for the whole body and all the respective regions (Fuller et al., 1992; Horber et al., 1992; Kiebzak et al., 2000; Lohman 1996; Lohman, Tallroth et al., 2009; Mazess et al., 1990). For longitudinal studies in which relatively small changes in body composition need to be detected, whole-body scanning with this instrument have proven to be accurate and reliable (CVs = 0.8–2.8 %; Prior et al., 1997). In addition, it also shows a good correlation compared to MRI and computerized axial tomography (Freda et al., 2009; Fuller et al., 1999; Ramos et al., 2012), with coefficients between 0.81 and 0.97.

Total body mass, total fat mass, total fat-free mass (which contains lean body tissue, total body water, and other non-adipose tissue components), and total percentage of body fat were calculated from the analysis of the whole-body DXA scan. DXA takes into account the upper and lower limbs, trunk, and head to analyze the whole-body composition. Values of total body mass, fat mass, and fat-free mass are expressed in kg, while and the body fatpercentage is a percentage.

The short-term CVs for repeated measurements of total body mass, total fat mass, total fat-free mass, and total percentage of body fat are 1.03% (95% CI = 0.72–1.33), 1.17% (95% CI = 0.54–1.79), 0.80% (95% CI = 0.32–1.27), and 0.74% (95% CI = 0.31–1.11), respectively. The ICC for this device in our laboratory is "excellent" for all the parameters, ranging between 0.955 to 0.997. Furthermore, the intra-rater reliability is also "excellent" for all the variables (ICCs between 0.906 and 997).

G. Neuromuscular strength

All the tests were performed using the Biodex® Multi-Joint System V.4X (Biodex Medical TM, Shirley, NY, USA) isokinetic dynamometer, which is equipped with the Advantage software (Biodex System Advantage, version 3.2). The isokinetic dynamometer was calibrated before each test according to the manufacturer's instructions (Lord et al., 1992).

The dynamic and continuous seated-knee concentric-concentric contraction cycle, elbow flexion-extension, and standing hip abduction-adduction were performed at angular velocities of 180°/s (3.14 rad/s) and 60°/s (1.05 rad/s), because these are considered the optimal velocities for measuring power/functional and maximum strength, respectively (Dvir et al., 2004; Boling et al., 2009; Kakebeeke et al., 2005). Each test consisted of one set of five maximum voluntary contractions on the dominant side, with a recovery period of two

minutes between tests (Brown & Weir, 2001). In each test, the angular velocity of 180°/s was always analyzed first, followed by the 60°/s, with a rest period between them of 60 seconds.

During the concentric tests, the subjects continuously pushed the lever arm of the isokinetic device up and down throughout the whole ROM. In the case of the hip abduction-adduction, the range evaluated was 30° of the ROM (between 0° and 30°), while for the knee flexion-extension, the isokinetic strength was evaluated for 85° of the ROM (between 0 to 5° and 85 to 90° of knee flexion); for the elbow flexion-extension, the range was 60° (between 15° and 75° of knee flexion). The ROM for the knee and elbow exercises was smaller than previously employed with young adults, due to the possible difficulty of the elderly population in fully extending their knee and elbow joints (Lavender & Nosaka, 2006).

Gravity correction, as described in the Biodex test manual, was applied. This was an essential requirement, as it was necessary to take into account the sum of the moments produced in the leg by each of the movements; in the case of a movement in favor of gravity, the moment generated by the weight of the leg was subtracted, and in the case of rotation against gravity, this weight was added (Dvir, 1995; Kannus, 1994). Thus, it was necessary to weigh the lower and upper limb in each of the evaluations.

Subjects did not have prior experience with the isokinetic dynamometer (Kramer, 1990; Steiner et al., 1993), and, after a standardized warm-up [5 min on the treadmill without incline at moderate intensity (ranging from 2.8 to 5.6 km/h; Wass et al., 2005) as well as active stretching and joint-mobility exercises of the lower and upper limbs], they were familiarized with a trial phase of 30-second continuous concentric-concentric cycles (three to five submaximal contractions) at the test velocity that was to be recorded (to acclimatize them to the movement), a 1-minute rest, and an actual test phase of five continuous concentric-concentric cycles, for each muscle group. During the 30-second familiarization, at

least one trial had to be a maximal contraction, as recommended by Snow and Blacklin (1992).

Each test was randomized and performed in the same order and at the same time of the day, both before and after the intervention. While the subjects were performing the tests, and after being instructed to generate maximum force as rapidly as possible, they were given constant and standardized verbal encouragement to produce maximal efforts throughout the five cycles of the actual test phase. All the movements were performed without visual feedback. The same researcher supervised each test, with one reference examiner who monitored for strict protocol compliance. Peak torque (N•m) was recorded for each trial, and only the best reading from the five cycles was used for subsequent analysis. Thus, maximal voluntary concentric isokinetic torque was assessed in Newton-meters, and the peak concentric torque obtained from each test was used for analysis. Values are expressed in N·m.

For each joint evaluated, the test procedures complied with reproducibility criteria (i.e., axes of movement, subject positioning, positioning of proximal joints and attachments and stabilizing straps) adjusting the positions of the dynamometer and the seat for each test movement according to the anthropometry of each subject (the respective joint centers were aligned with the axis of rotation of the dynamometer). The subjects sat upright on the adjustable chair and were tightly secured with shoulder, waist, and thigh straps to minimize extraneous movements (Gleeson & Mercer, 1996; Wilk et al., 1995).

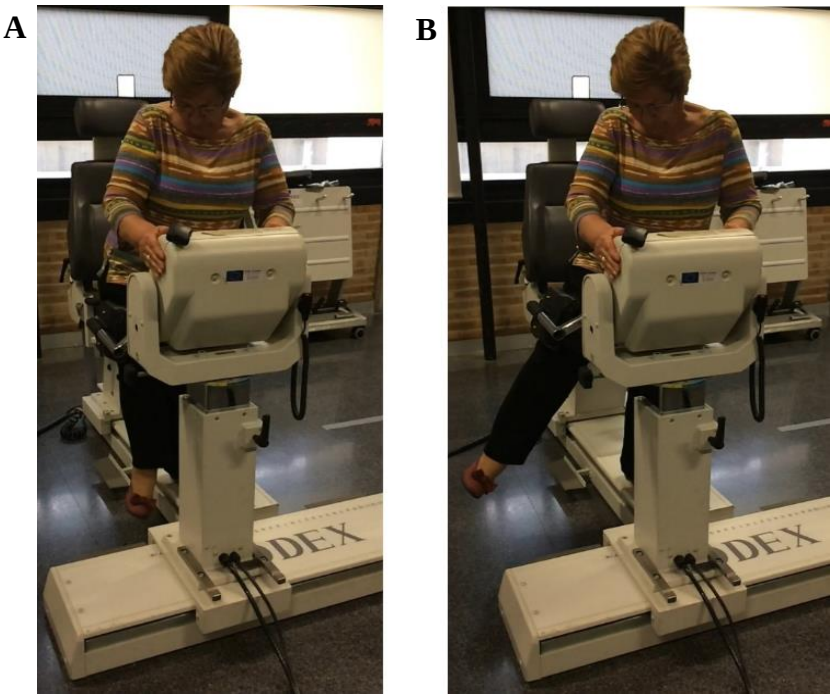
The lever arm (shin pad) was attached immediately proximal to the ankle and the elbow for the knee and elbow flexion/extension tests, and proximal to the knee for hip abduction-adduction. Participants were seated and positioned at a back angle of 85°, with a stabilizing harness fastened against their chest in the knee and elbow tests. A stabilizing belt

was also secured across the participant's left leg. For each test, the subject's knee, elbow, or ankle joint was aligned with the dynamometer's axis of rotation. For each subject, the dynamometer (System 3 Biodex, Shirley NY) settings were held constant across test sessions, and Velcro straps limited any extraneous body movements. The position of each participant in each test was recorded for the baseline evaluations to be repeated in subsequent evaluations; this prevented possible alterations in the final outcomes as a result of the position. The specific protocols of the three tests performed are detailed below.

i. Standing hip abduction-adduction

Subjects were placed in standing position in front of the dynamometer, with the axis of rotation of the hip joint aligned with the rotation axis of the dynamometer in the frontal plane and the hip flexed at approximately 5°. The axis of rotation of the hip joint was defined as the intersection of an imaginary line directed inferiorly from the anterior superior iliac spine down the midline of the thigh and a second imaginary line directed medially from the greater trochanter of the femur toward the medial line of the body (Figure 71). The dynamometer fixation arm was placed on the middle third of the lateral thigh, and a resistance pad was applied at the same level, 2 cm above the upper pole of the patella (O'Dwyer et al., 2011; Sugimoto et al., 2014). The participants lowered their weight onto the supporting leg located on a base, leaving the evaluated leg suspended in the air to avoid contact with the ground (O'Dwyer et al., 2011; Claiborne et al, 2009). To prevent synergistic compensations during the hip abduction-adduction movements, the subjects were instructed to hold on firmly to the top of the dynamometer with both hands and keep their trunk and hips in a neutral position as much as possible (without flexion or extension). The ROM evaluated in this test was 30° (from 0° to 30° of the hip abduction).

Figure 71. *Isokiketic hip abduction-adduction procedure for the assessment of muscle strength.*



Note. Initial (A) and final (B) position of the standing hip abduction-adduction isokinetic assessment.

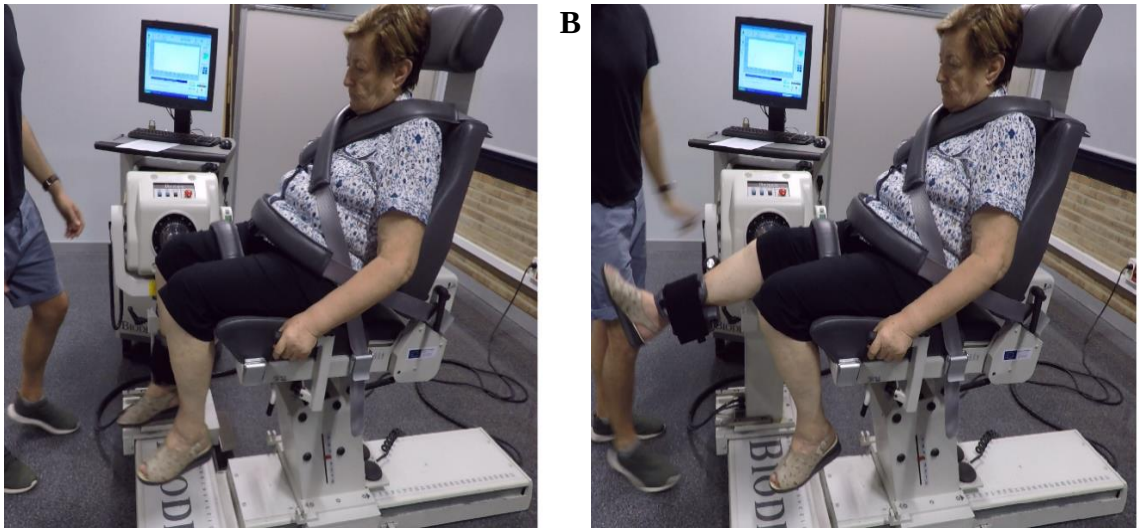
ii. Seated-knee flexion-extension

Participants were seated upright, with their back supported by the backrest of the adjustable chair, with a 110° of hip flexion, they were tightly secured with shoulder, waist, and thigh (of the evaluated leg) straps to minimize extraneous movements. In addition, the subjects held two handholds located on each side of the seat tightly to maintain their position and exert more force in each attempt. The axis of rotation of the knee joint evaluated was aligned with the rotation axis of the dynamometer in the frontal plane, with the knee flexed at 90°. The axis of rotation of the knee joint was defined as the intersection of an imaginary line between the midline of the femur and the tibia, and it was confirmed by the palpation of the external face of the lateral femoral condyle (Figure 72). The lever arm (shin pad) of the dynamometer was attached immediately proximally to the ankle (approximately 2 cm above

the external malleolus). The ROM evaluated in this test was 85° (from 0–5° to 85–90° of knee flexion). This protocol has been widely used previously among the same study population (Jordan et al., 2015; Ozçakar et al., 2003; Otten et al., 2013; Saenz et al., 2010).

Figure 72. *Isokiketic knee flexion-extension procedure for the assessment of muscle strength.*

A **B**



Note. Initial (A) and final (B) position of the seated knee flexion-extension isokinetic assessment.

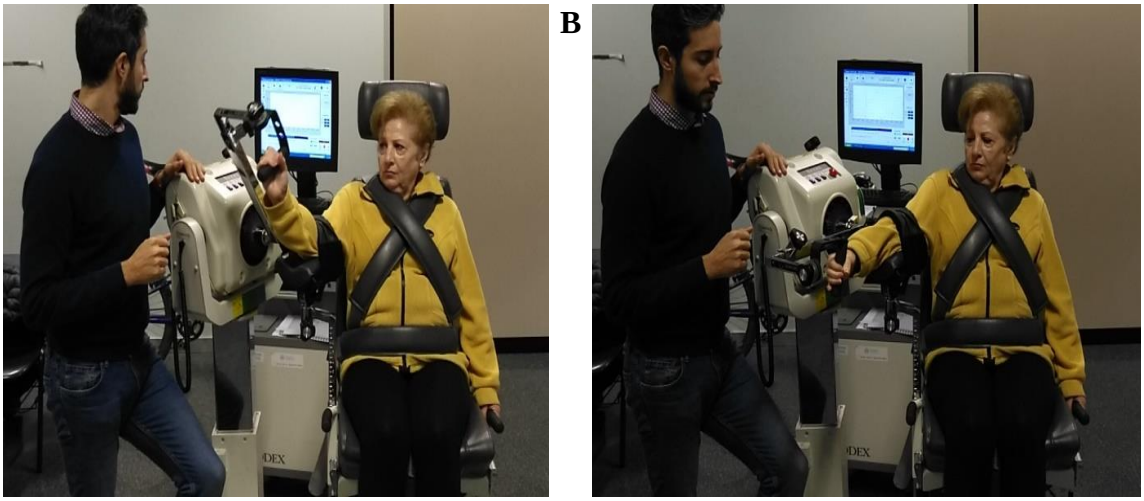
iii. Seated-elbow flexion-extension

Participants were seated upright with their back supported by the backrest of the adjustable chair. Making a 110° hip flexion, they were tightly secured with shoulder and waist straps to minimize any extraneous movements. In addition, the hand of the non-evaluated arm firmly held onto the handle located next to the seat so as to maintain this position and exert more force with each attempt. The participants rested their elbow on the limb-support pad after installed the limb support in chair side receiving tube for side to be tested (with a shoulder abduction of 30° and a shoulder flexion of 60–75°). The axis of rotation of the elbow joint evaluated was aligned with the rotation axis of the dynamometer in the frontal plane. The axis of rotation of the elbow joint was defined as the intersection of an

imaginary line between the midline of the humerus and the ulna, and it was confirmed by the palpation of the external face of the epicondyle (Figure 73). The lever arm (shin pad) of the dynamometer was attached immediately proximally to the humerus (approximately 2 cm above the epicondyle). The forearm and wrist were placed in neutral position throughout the entire test. The ROM evaluated in this test was 60° (from 15° to 75° of elbow flexion).

Figure 73. *Isokiketic elbow flexion-extension procedure for the assessment of muscle strength.*

A **B**



Note. Initial (A) and final (B) position of the seated elbow flexion-extension isokinetic assessment.

The reliability, validity, and reproducibility of the isokinetic-dynamometer strength in older adults have been previously published in a wide range of studies (Feiring et al., 1990; Wilk et al., 1988).

The short-term CVs for repeated measurements of the isokinetic test are 8.77% (95% CI = 1.16–19.2) and 5.08% (95% CI = 3.77–13.94) for standing hip abduction, and 3.71 (95% CI = 0.18–7.24) and 1.32 (95% CI = 0.81–1.84) for standing hip adduction, at 180°/s and 60°/s, respectively. The CVs for seated-knee extension and flexion are 1.9 (95% CI = 1.05–2.74), 2.36 (95% CI = 1.4–3.32), 3.36 (95% CI = 1.32–5.4), and 2.74 (95% CI = 1.56–

3.92) at 180°/s and 60°/s, respectively. For elbow flexion, the CVs are 1.93 (95% CI = 0.91–2.96) and 1.85 (95% CI = 0.64–3.06), whereas the CVs for elbow extension are 3.61 (95% CI = 2.33–4.88) and 3.32 (95% CI = 2.21–4.43), at 180°/s and 60°/s, respectively. In addition, the ICC for this device in our laboratory ranges between "good" (ICC = 0.824) and "excellent" (ICC = 0.998) for all the parameters.

H. Physical function

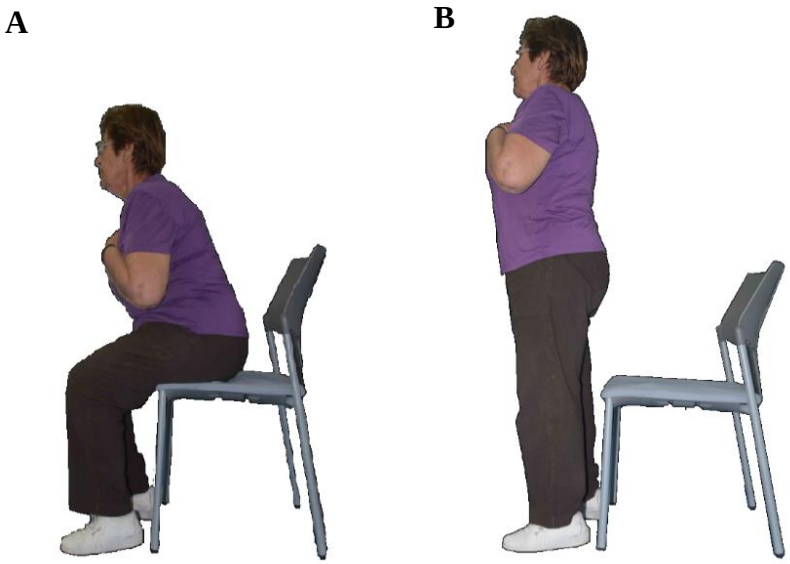
Physical function was evaluated using standardized tests adapted from the SFT battery (Rikli & Jones, 1997, 1999a, 2013a). The endurance strength of the lower limbs was assessed with the 30sec-CS (Rikli & Jones, 2013a). The endurance strength of the upper body was measured by the 30sec-AC (Rikli & Jones, 2013a), while dynamic balance and aerobic capacity were tested with the TUG (Rikli & Jones, 2013a) and the 6MWT (Rikli & Jones, 2013a) test, respectively.

The order of the tests was as follows: balance (TUG), dynamic strength (30sec-CS, 30sec-AC), and lastly aerobic capacity (6MWT), with a rest period of 60 to 180 seconds between tests. All the tests were performed on the same day in the Performance Laboratory of the Faculty of Physical Activity and Sport Sciences at the University of Valencia.

i. Thirty seconds chair stand test

To evaluate lower-extremity muscle strength, the 30sec-CS test from the SFT battery was used (Rikli & Jones, 2013a). Participants began by sitting in the middle of a firm, padded, armless, hard-backed chair, with the seat 46 cm from the floor. They were instructed to keep their back straight, their arms crossed at the wrists and held against their chest, and their feet placed on the floor approximately shoulder-width apart (Figure 74). The back of the chair was supported against a wall for the safety of the subjects.

Figure 74. *Thirty seconds chair stand test.*



Note. Initial (A) and final (B) position of the 30sec-CS assessment.

From this position, the beginning of the timed test was prefaced by the tester with a sign that read "ready, set, go." The participants had to rise to a full standing position and then return to the starting full sitting position as quickly as possible within 30 seconds (Jones et al., 1999). The time was measured to the nearest 0.1 second using a handheld stopwatch (Geonaute, On Start 300; Lila, France). The stopwatch was started after the word "Go," and the researcher silently counted each repetition of the 30 completed seconds. The test was performed once, and the same chair was used for all the subjects. While the subjects were performing the tests, they were given constant and standardized verbal encouragement (e.g., "come on," "let's go") to exert maximal effort during the 30 seconds. They never received feedback about the repetitions performed. To ensure a safe test setting, the chair was placed against a wall. Prior to data collection and following a demonstration by the tester, the participants performed several practice repetitions to familiarize themselves with the technique. Incorrectly performed repetitions were not counted, and the final repetition at the end of the 30-second period was counted only if the subject completed more than 50% of the

upward motion. The test score was the total number of stands completed correctly within 30 seconds. Values are expressed as number of repetitions.

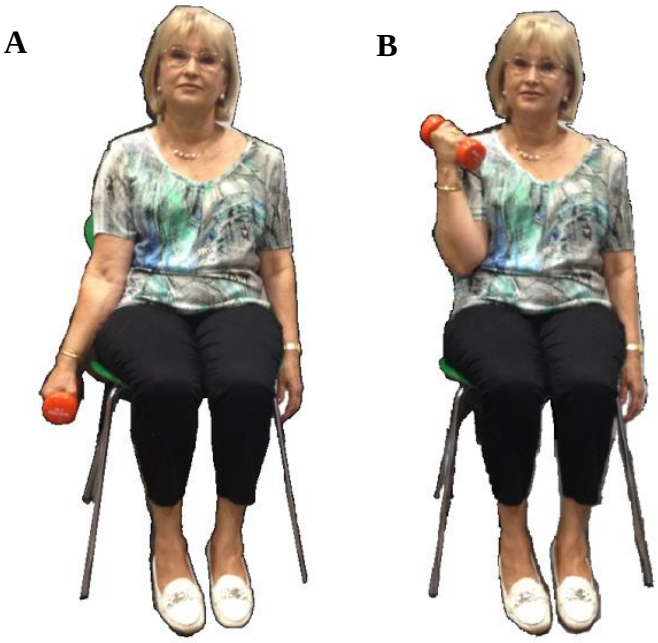
This test has been shown to have good reliability, with a test-retest ICC of 0.84 to 0.92 in a community-dwelling sample of older men and women aged 60 years and over (Jones et al., 1999). The 30sec-CS test includes normative performance standards established according to the participants' age and gender (Rikli & Jones, 1999a, 1999b). This test has also been shown to be a valid measure of lower-body strength in older adults (Hong, 2012; Jones et al., 1999).

The short-term CV for repeated measurements of the 30sec-CS is 1.69% (95% CI = 0.28–3.11). In our laboratory, the test–retest reliability coefficient for this test is "excellent" (ICC = 0.988; 95% CI = 0.975–0.994). Inter-rater reliability was also tested for the physical-function test, as they were carried out by three to five raters. The inter-rater ICC for the 30sec-CS is also "excellent" (ICC = 0.995; 95% CI = 0.991–0.997).

ii. Thirty seconds arm curltest

To evaluate the endurance strength (or upper-extremity muscle strength), the 30-second arm-curl test (elbow flexo-extension movements) from the SFT battery (Rikli & Jones, 2013a) was used. Participants were seated in a straight-backed chair, with feet resting on the ground approximately shoulder-width apart and the dominant part of their body attached to the edge of the chair (Figure 75).

Figure 75. *Thirty seconds arm curl test.*



Note. Initial (A) and final (B) position of the 30sec-AC assessment.

From this position, after holding a 2-kg hand weight with the dominant hand and with elbow extended, the beginning of the timed test was prefaced with a "ready, set, go" sign by the tester. The participant had to perform the largest number of flexo-full elbow extensions they could in 30 seconds, moving only their forearm while keeping the rest of their arm and their trunk fixed. The time was measured to the nearest 0.1 second using a handheld stopwatch (Geonaute, On Start 300; Lila, France). The stopwatch was started after the word "go," and the researcher silently counted each repetition of the 30 completed seconds. The test was performed once, and the same chair was used for all the subjects. While the subjects were performing the tests, they were given constant and standardized verbal encouragement (e.g., "come on," "let's go") to put in maximal effort during the 30 seconds. They never received feedback about the repetitions performed. To ensure a safe test setting, the chair was placed against a wall. Prior to data collection and following a demonstration by the tester, the participants performed several practice repetitions to familiarize themselves with the

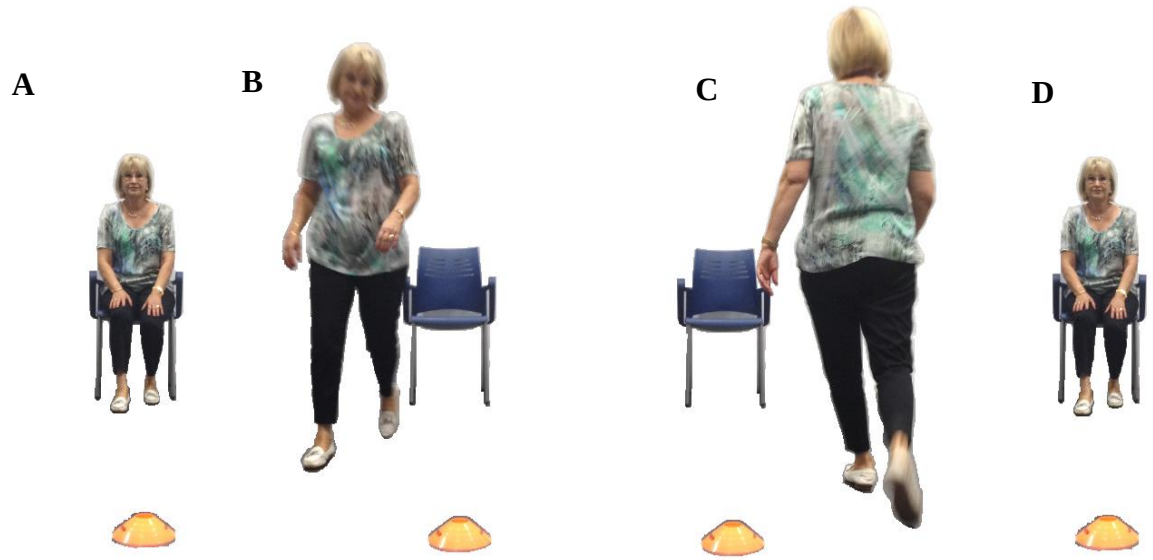
technique. They were not allowed to move their trunk to aid the arm movement. Incorrectly performed repetitions were not counted, and the final repetition at the end of the 30-second period was counted only if the subject completed more than 50% of the upward motion. The test score was the total number of elbow flexion-extensions completed in 30 seconds. Values are expressed as number of repetitions.

The short-term CV for repeated measurements of the 30sec-AC is 2.35% (95% CI = 0.72–3.98). In our laboratory, the test–retest reliability coefficient (ICC = 0.987; 95% CI = 0.974–0.994) and the inter-rater ICC (ICC = 0.994; 95% CI = 0.990–0.997) for the 30sec-CS are both "excellent."

iii. Timed up and go test

To evaluate dynamic balance (Gamble, 2006; Heyward & Gibson, 2014**)**, agility, and functional mobility during three common functional activities – standing up and sitting down in a chair, walking, and turning (Podsiadlo & Richardson, 1991) – the TUG test was taken from the SFT battery (Rikli & Jones, 2013a). The participants were seated in an armless, hard-backed chair with a seat height of 46 cm, placed next to the wall and a cone at a distance of 2.44 meters (8 feet), measured from the back of the cone to the front edge of the chair. The participant had to seat in the middle of the chair, keeping their back straight, their feet resting on the floor, and their hands on their thighs. One foot should be placed slightly forward with respect to the other, and the trunk should be slightly inclined forward. At the "ready, set, go" signal given by the tester, the participants had to get up with or without using their arms and walk as quickly as possible (without running) to the cone, turn it around, and then return to the chair and sit down again (Figure 76).

Figure 76. *Phases of the timed up and go test.*



Note. A. Initial position; B. Go phase; C. Return phase; D: Final position.

The timer was started after the word "go," even if the participant did not start to move. It was stopped when the participant was seated in the chair and making contact with the back of the chair. The test was performed twice with 30 seconds between the attempts, and the examiner recorded the faster trial. The time was measured to the nearest 0.1 second using a handheld stopwatch (Geonaute, On Start 300; Lila, France). The same chair was used for all the subjects. Prior to data collection and following a demonstration by the tester, the participants performed several practice repetitions to familiarize themselves with the technique. While the subjects were performing the tests, they were given constant and standardized verbal encouragement (e.g., “come on,” “let’s go”). They never received feedback about their performance times. The participants carried out the test in their usual footwear. Values measured are expressed in seconds.

This test was shown to be a valid measure for functional mobility and identifying frail members of the older-adult population (Savva et al., 2013). In addition, excellent test-retest,

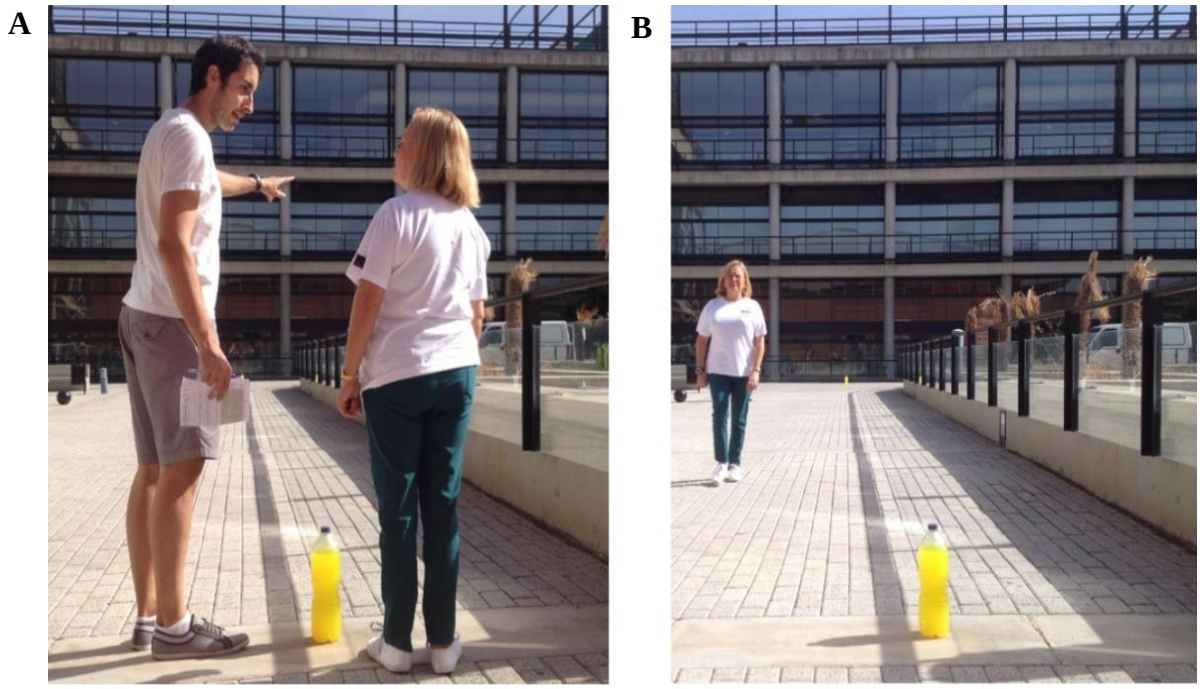
intra-, and inter-reliabilities in older adults have been previously reported (Podsiadlo & Richardson, 1991).

In our laboratory, the short-term CV for repeated measurements of the TUG test is 2.8% (95% CI = 1.25–4.35). The test–retest reliability coefficient for the test is "excellent" (ICC = 0.965; 95% CI = 0.931–0.983), as is the inter-rater ICC (ICC = 0.985; 95% CI = 0.973–0.992)

iv. Six minute walking test

To evaluate aerobic endurance, the 6MWT was taken from the SFT battery (Rikli & Jones, 2013a). This test has proven to be a very useful tool in the objective evaluation of aerobic capacity (Crapo et al., 2002; Enright, 2003). The test was carried out in an open space, on a flat and hard surface located in the Faculty of Physical Activity, Sports Science, and Physiotherapy at the University of Valencia. For the evaluation, a circuit 60 meters long (2 × 30-meter shuttle course) by 4 meters wide was prepared prior to the start of the test. The ends of the lane were delimited and marked by two cones indicating the turning point. Between the cones, marks parallel to the walking course were made with tape on the ground at three-meter intervals to facilitate the counting of the total length covered at the end of the test, improving the accuracy of the count (Figure 77). Participants were instructed to walk alone as quickly as possible (without running) around the 30-meter shuttle course as many times as possible within the time limit.

Figure 77. *Six minute walking test.*



Note. Initial position (A) and during (B) the 6MWT.

Before starting the test, the participants were allowed to slow down and even take a short break before resuming if, at any time during the test, they manifested symptoms of abnormal exhaustion. All the older adults had to perform the test in comfortable clothes and appropriate footwear for walking. The subject was verbally encouraged throughout the test. Only one attempt was performed on the day of the test. The evaluator explained the procedures to the participants before beginning. Once understood, at the “ready, set, go” signal, the participants had to walk as quickly as possible at a sustained pace without trotting or running, following the marked route (30-meter shuttle course) for six minutes. The timer started counting after the word "go," even if the participant did not begin to move immediately. The participants were informed about the elapsed time after three, four, and five minutes to help them regulate their pace. At the end of the six minutes, the timer was stopped, and the participants had to stop for the recording of the distance covered in the last lap, using the closest marking (cone or tape) as a reference. The time was measured to the nearest 0.1

second using a handheld stopwatch (Geonaute, On Start 300; Lila, France), and the test was performed only once. Prior to data collection, a demonstration was given by the tester to make sure that the participants understood what they had to do. While they were performing the test, they were given constant and standardized verbal encouragement (e.g., "come on," "let's go"). They never received feedback about their times. The participants carried out the test in their regular footwear. Values measured are expressed in meters.

The 6MWT is a valid tool for evaluating aerobic endurance among the elderly (Rikli & Jones, 1998; Kervio et al., 2003). The test-retest reliability previously determined by Rikli and Jones is high (ICC = 0.91; Rikli & Jones, 1999a). In our laboratory, the short-term CV for repeated measurements of the 6MWT test is 1.97% (95% CI = 1.14–2.8). In addition, both test-retest (ICC = 0.978; 95% CI = 0.920–0.991) and inter-rater (ICC = 0.990; 95% CI = 0.976–0.996) reliability are "excellent."

I. Questionnaires

i. Cognitive function

Global cognitive function was assessed using the MMSE questionnaire (Folstein et al., 1975). This questionnaire has scores ranging from 0 to 30, and it explores the cognitive areas of orientation, attention, calculation, memory, and language (Appendix L). Higher scores indicate better cognitive function, and scores of 24 or higher (out of 30) indicate normal cognition. Below this, scores can indicate mild (19–23 points), moderate (10–18 points), or severe (≤9 points) cognitive impairment. The questionnaire was provided to the participants at the initial evaluation sessions in the Performance Laboratory of the Faculty of Physical Activity and Health Sciences at the University of Valencia. Following an explanation by the tester, the participants refilled it and returned it to the research personal. In case of doubts, these were resolved.

This test has been previously validated in healthy older adults (Kopecek et al., 2017; Taussig et al., 1996), with a high test-retest reliability (Tombaugh & McIntire, 1992). In our laboratory, the short-term CV for repeated measurements of the MMSE is 1.32% (95% CI = 0.46–2.19). The test-retest reliability coefficient for this test is "excellent" (ICC = 0.982; 95% CI = 0.971–0.993).

ii. Basic activities of daily living

Self-reported information regarding BADLs was collected via the Barthel Index of activities of daily living, a standardized and validated questionnaire for older adults (Mahoney & Barthel, 1965). The Barthel Index assesses the participants' level of independence with respect to the performance of a BADLs, whereby different scores are assigned according to the ability of the examined subject to carry out these activities. The values assigned to each activity depend on the time and any external aids needed to carry out each activity. There are 10 BADLs included in the original index (Appendix M). The activities are valued differently, with an assignment of either 0, 5, 10, or 15 points. The global range may vary from less than 21 (total dependence) to 100 points (total independence). The Spanish version of this test has been previously validated (Cabañero-Martínez et al., 2009; González et al., 2018). The inter-rater reliability has been reported as "moderate" for individual items and "high" for the total score among the elderly population (Sainsbury et al., 2005), with no previous analysis of test-retest reliability. In our laboratory, the short-term CV for repeated measurements of the BADLs is 1.69% (95% CI = 0.28–3.11). The test-retest reliability coefficient for this test is "excellent" (ICC = 0.987; 95% CI = 0.973–0.994).

iii. Instrumental activities of dailiy living

The ability to perform IADLs was assessed via Lawton and Brody's scale for instrumental activities of daily living scale. The scale is composed of eight domains (or items) of function (Appendix N). Each item is assigned a numerical value of either 1 (independent) or 0 (dependent). The summary score ranges from 0 (low-functioning, dependent) to 8 (high-functioning, independent; Lawton & Brody, 1969). The Spanish version of the test has been previously validated for elderly people (Vergara et al., 2012), and both test-retest and inter-rater reliability have been considered "excellent" in previous research on this population (Edwards, 1990). In our laboratory, the short-term CV for repeated measurements of the IADLs is 1.24% (95% CI = 0.32–2.56). The test-retest reliability coefficient for this test ranges from "moderate" to "good" (ICC = 0.779; 95% CI = 0.545–0.891).

iv. Socio-demographic lifestyle questionnaire

At baseline, all the participants filled in a non-validated self-administered lifestyle questionnaire to assess the impact of present and past lifestyle choices and clinical status. In it, they detailed their age, ethnicity, education level, living situation, marital status, employment status, number of comorbidities, current prescribed medications, current and past smoking and alcohol drinking habits, and types of assistive devices (Appendix O). The questionnaire was complete by interview to prevent the misinterpretation and/or skipping of any items (Figure 78).

Figure 78. *Participants of the study filling in some questionnaires.*

J. Compliance

Exercise training compliance was recorded by the attendance at the beginning of each session (Appendix P). Attendance rate for the exercises groups was calculated by dividing the number of exercise sessions the participant attended by the full number of sessions they were expected to perform throughout the study. Adherence was calculated as the percentage completed out of the total intervention-days prescribed (64 sessions = 100%).

K. Data safety monitoring

An adverse event is defined by the Common Terminology Criteria for adverse Events version 5.0 from the U.S. Department of Health and Human Services as "any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure" (US Department of Health and Human Service, 2018).

The trainers recorded any adverse events that occurred during or outside the training sessions (participants were instructed to report any adverse events outside the exercise session to the group instructor) that may or may not be associated with the exercise programs, such as muscle soreness, joint tenderness, increased level of pain, falls, fractures, or joint pain. Modifications to the training program were made on an individual basis as needed based on the occurrence of adverse events. Information on the adverse events was obtained weekly in face-to-face interviews or telephone calls.

The adverse events were recorded based on five grades of severity (US Department of Health and Human Service, 2018): grade 1, mild (mild symptoms with no intervention indicated); grade 2, moderate (marked symptoms with minimal noninvasive intervention indicated, limiting the IADLs); grade 3, severe (important symptoms but not immediately life-threatening, hospitalization and limitation of the BADLs indicated); grade 4, life-threatening (potentially fatal consequences with urgent intervention indicated); and grade 5, death (related to the adverse event). In addition, the events were reported based on four types suggested by the Behavior Change Consortium of the NIH – falls, cardiovascular-related episodes, musculoskeletal-related events, and health care – when reporting the trial results for the physical-training interventions (Ory et al., 2005).

IV.I.V. Exercise protocols

A. General aspects of the training programs

All training sessions were performed in indoor multipurpose rooms located in three MACOPs (Benicalap, Nou Moles, and Ruzafa centers) between November 2014 and June 2015, with two familiarization sessions in the week prior to the start of the intervention. The rooms were equipped with air conditioning and heating systems in order to maintain the temperature at roughly 22°C throughout the duration of the study.

The sessions were directed and supervised throughout by the same qualified and experienced sports scientists and physiotherapy instructors (maximum ratio of participants to trainers is 9:1) to ensure safety and compliance. A research supervisor (specializing in physical activity for older adults) was also present at all the sessions; the supervisor contributed in controlling the training methodology, maintaining the equipment and the room, and ensuring correct performance of the exercises using a list with points to supervise (Appendix Q). Therefore, the study was highly supervised, and the correct development of the project was guaranteed. Each instructor recorded the attendance, grip-width changes, and color of elastic bands used every week.

All the exercise trainers were required to attend a prior theoretical-practical workshop, where they were instructed about how to apply the planned methodology with the elastic bands and perceived exertion on older people, the correct techniques of the exercises (resistance, balance, coordination, and flexibility), and risk prevention during the training sessions (e.g., making sure that the participants have support objects nearby when necessary). In order to achieve greater adherence to the physical-exercise program, the trainers also learned to identify early cues of poor adherence and mastered behavioral-management strategies to enhance compliance. Examples include using music and funny exercises in the breaks between exercises and sets, giving positive feedback, sharing the importance of

feeling secure when performing the exercises, maintaining conversations with the participants, and making phone calls when a participant did not attend a session (Gianoudis et al., 2012; Otero et al 2017). To ensure the correct development of the project, at the end of the workshop, all the instructors received a manual which includes detailed explanations and illustrations of the different training programs that were to be carry out, including the exercises, progressions, safety considerations, as well as attendance sheets. The research team maintained regular contact with the instructors and visited the centers regularly to ensure that the quality of the program was being upheld.

All the supervised programs included two weekly sessions of 55–60 minutes on nonconsecutive days (separated by 48–72 hrs); these always took place at the same time of the day (HI: 11:45–12:45 a.m.; Mondays and Wednesdays) (M: 9:00–10:00 a.m.; Tuesdays and Thursdays) for 32 weeks. Group C did not perform any exercise programs. At the end of the program, subjects who did not miss any session would have completed a total of 62 sessions (64 if counting the two familiarization sessions), distributed as shown in Tables 13 and 14.

Table 13. *Training sessions distribution for HI training.*

Months	Nº weeks	Number of sessions	Days of training sessions
October	0	2 (familiarization)	27,29
November	1-4	8	3,5,10,12,17,19,24,26
December	5-8	8	1,3,8,10,15,17,22,24*,29
January	9-12	8	5,7,12,14,19,21,26,28
February	13-16	8	2,4,9,11,16,18,23,25
March	17-20	7	2,4,9,11,16*,18*,23,25,30
April	21-24	6	1,6*,8*,13*,15,20,22,27,29
May	25-28	8	4,6,11,13,18,20,25,27
June	29-32	9	1,3,8,10,15,17,22,24,29
Total		64 (62+2 familiarización)	

Note. *Festive day or center were closed

Table 14. *Training sessions distribution for M training.*

Months	Nº weeks	Number of sessions	Days of training sessions
October	0	2 (familiarization)	28,30
November	1-4	8	4,6,11,13,18,20,25,27
December	5-8	8	2,4,9,11,16,18,23,30
January	9-12	8	1,8,13,15,20,22,27,29
February	13-16	8	3,5,10,12,17,19,24,26
March	17-20	6	3,5,10,12,17*,19*,24,26,31*
April	21-24	7	2,7*,9*,14,16,21,23,28,30
May	25-28	8	5,7,12,14,19,21,26,28
June	29-32	9	2,4,9,11,16,18,23,25,30
Total		64 (62+2 familiarización)	

Note. *Festive day or centers were closed

Each training session was divided into three components, as recommended by the ACSM (ACSM, 2013, Ehrman, 2010):

1. General warm-up: This included 5–10 minutes of joint-mobility and low-intensity (i.e., 50–60% MHR) aerobic exercises. Following the recommendations of the ACSM (2013), all the sessions began with a general warm-up of 10 minutes, consisting of joint-mobility exercises to facilitate the subsequent movement of the joints. Coordination and active-mobility exercises were then performed to increase the heart rate and body temperature as well as stimulate the muscles and neural systems for subsequent training. Afterwards, active and dynamic stretching of the muscle groups that would be used in the main part of the training was performed, as recommended by Ayala et al. (2012). All this was done to background music (Figure 79).

Figure 79. *General warm-up.*

2. Main part: This comprised 35–40 minutes of resistance exercises, including three specific exercises for upper limbs (upright rowing, incline rowing, and elbow curl) and lower limbs (narrow-stance squats, lunge, and standing hip abduction), along with coordination exercises during the active rests (Figure 80).

Figure 80. *Main part of the training session.*

Note. Lower and upper limbs resistance exercises, coordination exercises and an example of the training gloves used for the sessions.

3. Cool-down: This involved 5–10 minutes of respiratory and flexibility exercises. Once the strength training was finished, the participants completed the last part of the session, where they performed passive recovery exercises accompanied by static stretching in order to reduce the activation of the body (Ayala et al., 2012; Figure 81).

Figure 81. *Part of the cool-down routine.*

Before the beginning of the study, the scientific staff and the instructors checked the reproducibility of the exercises planned for the elders and the progression of the training sessions. Primarily multi-joint exercises were chosen to emphasize both major and minor muscle groups (Garber et al., 2011), with special emphasis on exercises that involve major muscle groups with attachments on or near the hip and spine (in the case of resistance and balance exercises) along with exercises involving intermittent and multidirectional

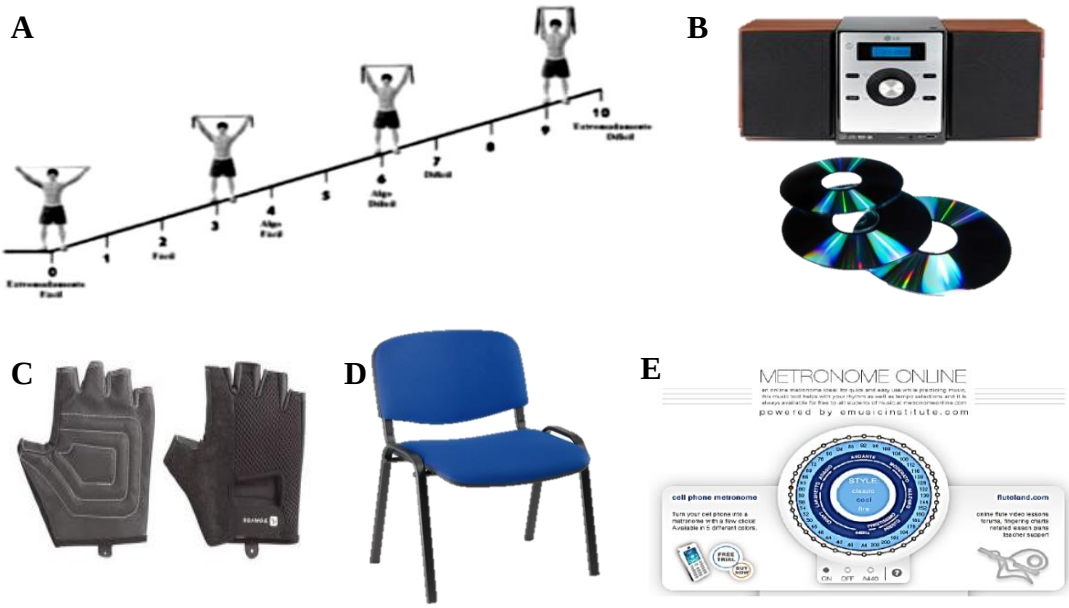
compressive forces (in the case of aerobic and coordination exercises). This is due to the site-specific effect of training on bones (Daly et al., 2018, Pivonka, 2018). In addition, to produce muscular and bone adaptations, large muscle masses were involved to produce a greater caloric expenditure, which could produce greater changes in the body composition of the participants. In order to increase caloric expenditure and improve the cardiovascular system, the recovery periods between sets (micropauses) were active in all the groups. These active rests consisted of programmed choreographies of coordinating movements, and they were also planned to increase adherence to the training sessions. The exercise programs of this study were also based on the Exercise and Physical Activity for Older Adults publication by the ACSM (Chodzko-Zajko et al., 2009), guidelines for treatment in people with osteoporosis (Bonaiuti et al., 2005; Giangregorio et al., 2014), and recommendations for fall prevention (Vieira et al., 2016). They were designed to follow the key training principles of specificity and progressive overload.

Each session was performed in a group, and the participants always executed the exercises in the same order, alternating between the upper and lower limbs to minimize fatigue (Romero-Arenas et al., 2011). Loads were adjusted every week to maintain appropriate training intensities by adapting the color and number of elastic bands along with the grip width. The resistance exercises were performed with Thera-Band® elastic bands (Theraband, Hygenic Corporation, Akron, OH, USA) in five colors: green, blue, black, silver, and gold, in ascending order of difficulty due to the increasing thickness of the band (the resistance of the band increases by 20–30% going from one color to the next when the band is stretched to twice its resting length; Page & Ellenbecker, 2005; Figure 82). All the elastic bands have a length of 1.6 meters.

Figure 82. *Thera-Band® elastic bands used in the study.*

Chairs (used for the exercises and to ensure the safety of the participants), bodybuilding gloves (to avoid the possible discomfort caused by the elastic bands), the OMNI-RES scale (Colado, Garcia-Masso, Triplett et al., 2012; to remind the participants of the intensity at which they should train), a metronome (to control the rhythm of execution of the exercises), and a mini stereo and CDs (to mark the speed of execution of the exercises, as well as to maintain adherence and motivation through the music, which was the same for all the groups) were also used in the study (Figure 83).

Figure 83. *Equipment used in the training sessions.*



Note. A. OMNI-RES perception scale; B. Mini stereo and CD's; C. Globes; D. Chairs; E: Metronome.

The participants were asked to maintain their usual eating and physical-activity habits throughout the duration of the study. Thus, they were unable to participate in other exercise programs during this period. They also accepted being randomly assigned to either the exercise or the no-exercise group.

B. Familiarization

Because none of the participants had previous experience with strength training or the use of elastic bands, they performed two sessions of pre-intervention familiarization to learn (a) the correct techniques of the exercises (the final and initial positions of the body and the ranges of motion, among other things), (b) the suitable execution velocity of the exercises, (c) breath control (to avoid the Valsalva maneuver; Hackett et al., 2013), and (d) how to control the intensity through the combined use of the OMNI-RES perceived exertion scale for the elastic bands (which ranked from 1 to 10), grip width, band color, and number of repetitions (Colado et al., 2018). Control of intensity by this method has been previously validated in young (Colado et al., 2010), middle-aged (Gargallo et al., 2014), and older adults (Colado et al., 2018), and it has been used and supported in previous works (Colado & Triplett, 2008; Fritz et al., 2015; Gargallo et al., 2018, Robertson et al., 2003). The familiarization session took place at the same centers as the main sessions one week before starting the intervention program.

To control and learn the exercise intensity, the participants were asked to take an elastic band that offers a high resistance (i.e., one between green and gold) with a narrow grip and perform one set of 6 or 15 submaximal repetitions of an exercise, depending the intervention group. At the end of the set, such an effort was associated with a quantitative value of 8–9 and a qualitative value of "very hard or heavy" on the OMNI-RES scale. Subsequently, they were asked to perform the same exercise and number of repetitions, but

with a wider grip-width and/or a lower-resistance band, perceiving that exercise as a very light effort and associating it with a quantitative value of 1, or "very easy."

In order to objectify the grip width of the elastic bands, before the beginning of the program, the bands were marked in such a way that the midpoint of the band lengthwise was indicated with the number 25, decreasing the numbering progressively and consecutively towards the ends of the band down to zero. The numerical points were 3 cm apart, as shown in Figure 84. In this way, the highest values were located in the central part of the band and were related to a smaller grip width and therefore greater resistance, while the lowest numbers at the ends were related to a smaller grip width and less resistance.

Figure 84. *Numbered elastic bands to determine grip width.*

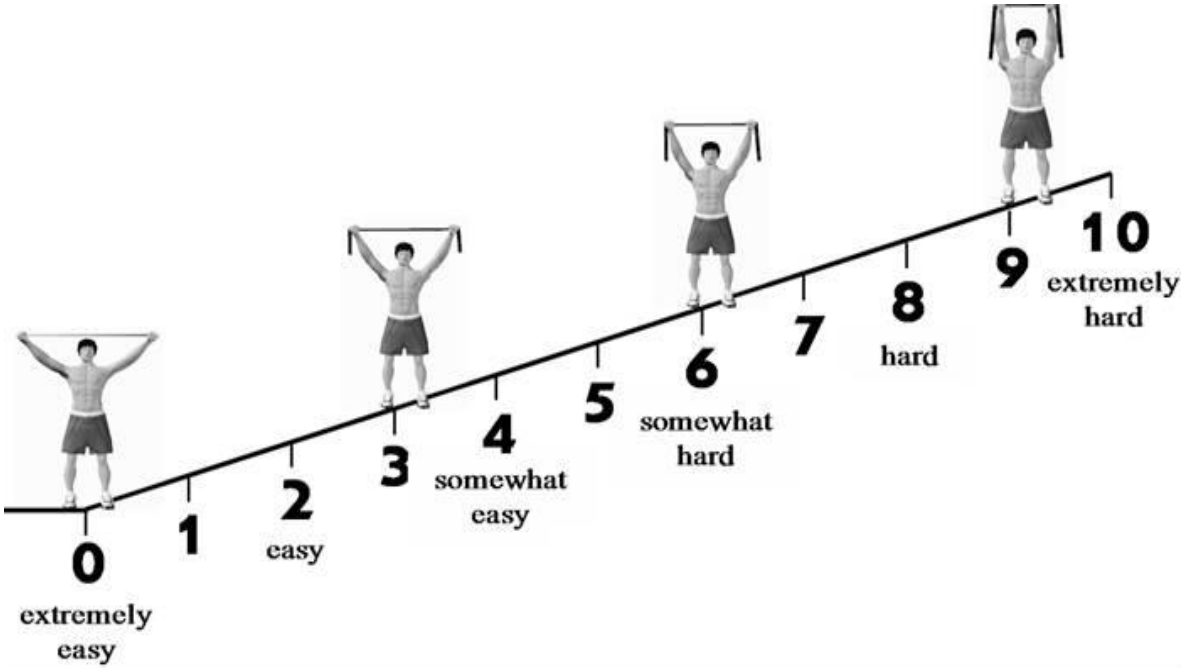
During the first and second familiarization sessions, the participants were asked to perform the exercises at the intensity that was scheduled for the intervention in order to find the correct resistance through the grip width and color for each exercise, thus forming an objective reference of the intensity before starting the program. Each participant did several repetitions to make sure they were done correctly. Normally, three to eight attempts are necessary to find the correct resistance (Ploutz-Snyders & Giamis, 2001). In cases where the participants did not reach or exceeded the necessary repetitions, they were given a rest period of two minutes between each failed attempt. Once achieved, the width of grip and the color of elastic bands for each exercise was recorded. Finally, the speed of execution of the exercises was taught to both training groups though a metronome and the voice of the instructors, who were also stomping in rhythm.

During both familiarization sessions, the participants were also instructed about the correct techniques of the exercises, performing several sets of each one before the start of the training program. During the execution of each exercise, the participants had to perform the movement without losing the tension of the elastic band in the eccentric phase, and they had to complete the concentric phase until the maximum amplitude defined for that exercise was reached. In addition, the women received instructions on how to coordinate their respiratory movements with the execution of both phases (concentric and eccentric).

As a common rule for all the participants of intervention groups, they should always take into account the value of the perceived exertion in order to achieve the appropriate intensity level in each part of the training program. For this reason, the OMNI-RES scale was always visible in the multipurpose rooms where the classes were held (Figure 85). Likewise, the participants were instructed about the guidelines that they had to comply with during the training sessions. These guidelines were: wear comfortable clothes and shoes, do not drink stimulant drinks, and bring a bottle of water to avoid dehydration and a towel to remove

sweat. The participants were instructed to consult any staff (instructor) if they required assistance with their exercise programs.

Figure 85. *OMNI-RES of perceived exertion scale.*



Note. Reproduced from "Concurrent and construct validation of a new scale for rating perceived exertion during elastic resistance training in the elderly" (p. 177), by Colado, Furtado et al., 2020, *Journal of Sports Science & Medicine*, *19*(1).

C. High-intensity resistance training group

The HI group performed six submaximal repetitions equivalent to 85% of 1RM in each set. The perceived exertion level on the OMNI-RES scale (Colado, Garcia-Masso, Triplett et al., 2012) progressed from 6–7 (somewhat hard) in the first 4 weeks to 8–9 (hard) for the remainder of the training program.

Regarding the training volume, which is understood as the product of the number of repetitions completed per exercise series and the number of series performed per session (Hass et al., 2001), three sets per exercise were performed during the first eight weeks, while

this was increased to four sets for the remaining 24 weeks. Although it has been shown that a single set can create adaptations in strength for sedentary people (ACSM, 1998, 2000, 2010) a greater training volume is related to greater improvements in muscle mass and VO_2max (Warburton, et al., 2001). Therefore, we decided to apply the above number of series per exercise.

In order to increase caloric expenditure and improve the cardiovascular system (Barnett, 2006; Dupont et al., 2004, 2007), 120 s of active recovery periods (consisting of slow rhythmic swinging of the extremities, coordinative movements, and cognitive tasks without the use of elastic bands) between sets (micropauses) were carried out during the entire program. The introduction of active pauses with funny exercises was a strategy to improve adherence to the program. In addition, active recovery keeps the heart rate high and stable, which favors the use of fatty acids as an energy source (Haltom, et al., 1999). Moreover, 90 s of passive rest periods between exercises (macropauses) to hydrate or wipe sweat were included during the first 16 weeks and the last eight weeks. During the 17^{th} and 24^{th} weeks, the resting period was reduced to 60 s.

The speed of execution of the exercises was controlled using a metronome marking the cadence (2 seconds each of concentric and eccentric contraction) and maintained throughout the study. The execution speed was controlled by a metronome that marked the cadence, set to 120 beats per minute (bpm). Along with the background music (which was also at 120 bpm), the reinforcement of the monitor counted the times of both phases together with the number of repetitions as follows: 1(number of repetition and concentric phase)-2(concentric phase)-3(eccentric phase)-4(eccentric phase), 2-2-3-4, 3-2-3-4, 4-2-3-4, 5-2-3-4, and so on.

Along with the modifications to the number of sets, the perceived exertion, and the duration of the rest periods, in order to achieve greater progress, the order of the exercises was also changed. Upper- and lower-limb exercises were alternated during the first 24 weeks, and agonist and synergist supersets were performed [with no rest between exercises from the same part of the body (upper or lower)] (Schoenfeld et al., 2015) in the remaining eight weeks. During this period, three instead of four sets of unilateral exercises (standing hip abductions and lunges) were performed due to a lack of time. For the rest of the study, the performance of four sets was maintained.

The training session consisted of 5–10 minutes of general warm-up (joint- mobility and aerobic exercises at low intensity); 35–40 minutes of the main part, which comprised six resistance exercises, three for upper limbs (upright rowing, incline rowing, and elbow curl) and three for lower limbs (narrow stance squat, lunge, and standing hip abduction) along with coordination exercises during the active rests; and 5–10 minutes of the cool-down routine (respiratory and flexibility exercises; Table 15).

For the entire program, all the resistance training exercises were performed with Thera-Band® elastic bands. During the first 24 weeks, the participants performed the exercises in the following order: elbow curl, narrow-stance squat, upright rowing, lunge, incline rowing, and standing hip abduction. With the introduction of the supersets, the order became: standing hip abduction + narrow stance squat, elbow curl + incline rowing, and lunges + upright rowing).

Table 15. *Description of the exercises performed by the experimental groups.*

Upper limb exercises					
Upright rowing		Incline rowing		Elbow curl	
Initial position	Final position	Initial position	Final position	Initial position	Final position
					
In a standing position, legs apart at the hips, arms relaxed next to the trunk in slight internal rotation and hands pronated in a neutral position. Look ahead.	Hands at the level of the xiphoid process, keeping the wrists neutral and elbows elevated, doing an abduction of the shoulders of 60° in the frontal plane and 30° in the scapular plane.	Seated with knees extended and feet hip-width apart. 30° of shoulder flexion and elbow extension. Forearms in internal rotation with pronated wrists in neutral position	45° of shoulder abduction with horizontal abduction and retraction of the scapula. 90° of elbow flexion keeping hands at the level of the xiphoid process.	Standing with feet hip-width apart, elbows extended next to the trunk and forearms externally rotated with wrists supinated in a neutral position.	Standing with feet hip-width apart, full-range elbow flexion keeping wrists neutral.

Table 15. *Continued.*

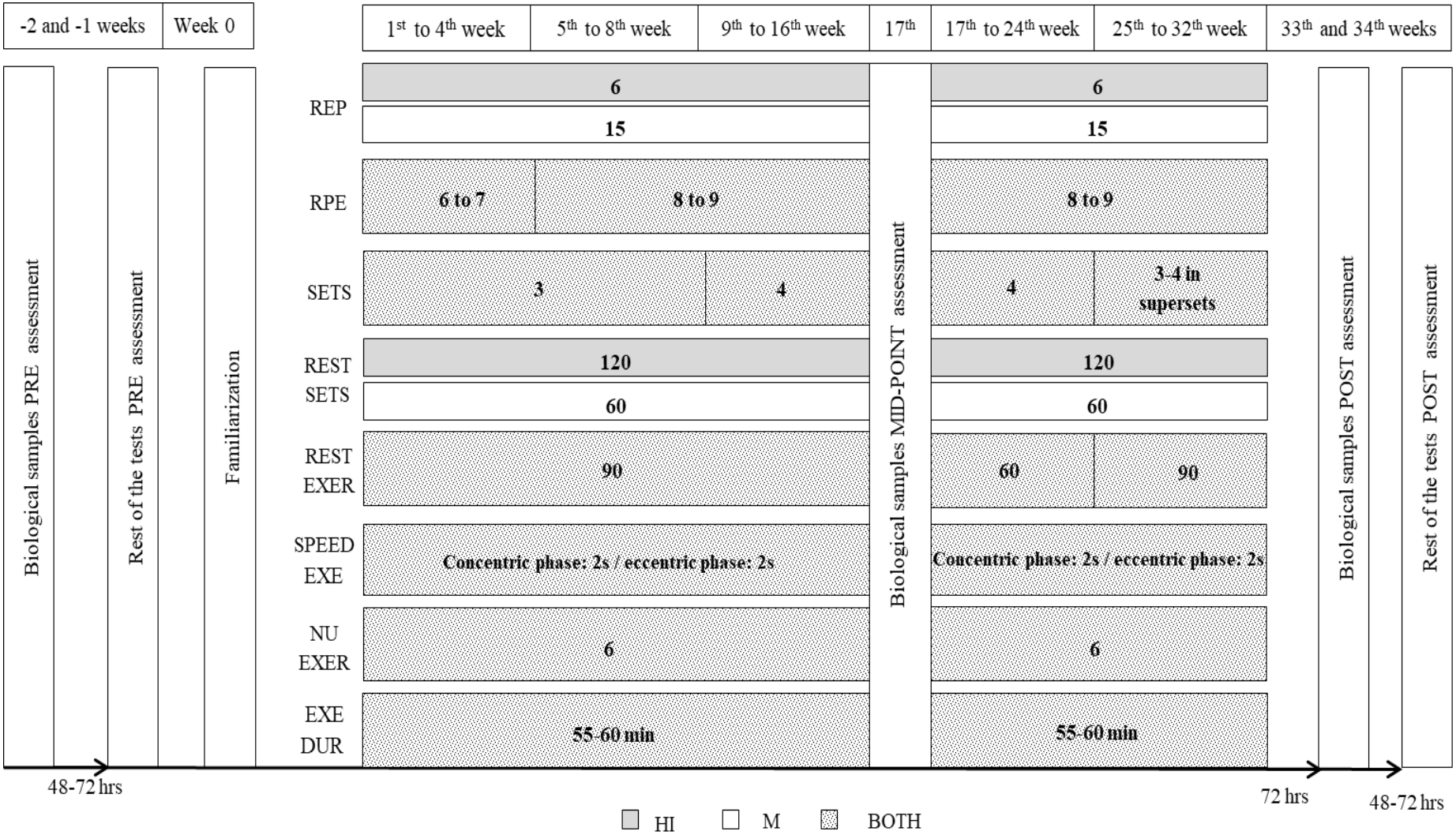
Lower limb exercises					
Narrow stance squat		Lunge		Standing hip abduction	
Initial position	Final position	Initial position	Final position	Initial position	Final position
					
In a standing position, with feet hip-width apart. Look ahead. Elastic bands hold at shoulder height.	90° to 110° of knee flexion. Slightly lean the trunk forward to follow the movement of the legs.	Standing with legs facing each other and hip-width apart, keeping the trunk straight. The forward leg step on the elastic band on the middle. Look ahead and elastic band attached at shoulder height.	The front leg is flexed to 60 to 80° of hip flexion. The contralateral leg provides support by also bending the knee and hip to follow the movement. Pelvis horizontal and trunk straight.	In standing position, feet together with toes pointed forward as well as the eyes. Arms extended next to the trunk and elastic band attached to the hips.	Hip abduction to 40° while the other leg remains extended for support. It is possible to touch a chair to avoid falls.

D. Moderate-intensity resistance training group

The M group performed the same exercise routine as the HI group (the same general warm-up, six resistance exercises, and cool-down), with the difference that this group carried out 15 submaximal repetitions equivalent to 65–70% of 1RM throughout the training period. The training-progression parameters (intensity, load, volume, rest, speed of execution, and order of exercises) were also the same as in the HI group. The only difference was the duration of the rest period between sets, which was 60 seconds for all the training period. The material was also the same across both training groups.

To summarize, the experimental design of the training and assessment characteristics of Project One can be observed in Figure 86.

Figure 86. *Experimental design with a schematic diagram of the training parameters progression during the study along with the timing of the evaluations.*



IV.II. PROJECT TWO. EFFECTS OF MULTI-COMPONENT, POWER STRENGTH AND TRADITIONAL HIGH-INTENSITY RESISTANCE TRAINING WITH ELASTIC RESISTANCE ON REDOX STATE, BONE HEALTH, BODY COMPOSITION, NEUROMUSCULAR STRENGTH, AND PHYSICAL FUNCTION IN OLDER WOMEN. A 20-WEEK RANDOMIZED CONTROLLED TRIAL.

IV.II.I. Study design

This was a randomized five-month, four-armed prospective parallel-design clinical trial with a 1:1 allocation ratio (ClinicalTrials.gov Identifier: NCT03455179; see Appendix R). The subjects were randomly assigned to either the multi-component training (MT; n = 34), power strength training (P; n = 34), traditional high-intensity resistance training (T; n = 34), or self-management control (C; n = 34) group by an independent staff member who was not involved in the study, using a computer-generated random permutation procedure (Microsoft Excel).

The study was part of a larger research program on the effects of different training modalities on musculoskeletal [muscle architecture of rectus femoris and biceps brachii (muscle thickness, pennation angle, cross-sectional area, fascicle length, and echo intensity), muscle quality of upper and lower limbs], neuromuscular [handgrip strength, flexibility (back scratch, chair sit-and-reach test), balance (standing balance, a timed 2.4-meter walk, 4- and 10-meter maximal and normal walking speeds)], metabolic (glycosylated hemoglobin and fasted glucose), lipidic (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides), immunologic (platelet counts, plateletcrit, mean platelet volume, platelet distribution width, leukocytes, neutrophils, lymphocytes, monocytes, eosinophils, and basophils), inflammatory (C-reactive protein), and psychological [quality of life (SF-36 form), sleep quality (the Pittsburgh Sleep Quality Index), exercise perception] parameters among older adults.

Notably, for this PhD dissertation, the older male subjects in the initial sample have been left out in along with certain parameters (those mentioned above) to be able to explore in depth the parameters finally selected in older women, as this population seems to have a higher risk of poor health-related outcomes such as disability, frailty, or sarcopenia, being the most frequently and severely affected (Beard et al., 2016; Leveille et al., 2000). Therefore, these data were eventually excluded from the analysis. In writing this section, we adhered to the guidelines in the Consolidated Standards of Reporting Trials (Schulz, Altman, & Moher, 2010).

The study was conducted according to the Helsinki Declaration (1975; revised in 2014), and the experimental protocol was approved by the Human Research Ethics Committee of the University of Valencia (H1508742840440; Appendix S).

IV.II.II. Randomization and blinding

Due to the characteristics of the study, it was not possible to blind the participants to the treatment. However, the data collectors and analysts were independent; if it was not possible at some point, a random code was created for each participant to enable identification of which group they belonged to.

Using a computer-generated random permutation procedure, randomization was performed after recruitment by an independent staff member not involved in the trial; any screening, testing, or training procedures; or contact with the participants (Microsoft Excel). Subjects were also not scheduled for outcome measurements according to the order of recruitment or that of treatment allocation. Through these procedures, treatment allocation was safely concealed from the staff.

IV.II.III. Study population

A. Inclusion and exclusion criteria

Untrained older Caucasian women (aged 60–79 years) volunteered to participate in the study after reading an advertisement containing the study information that was publicly posted from September to December 2017 at several MACOPs in Valencia, Spain. The inclusion and exclusion criteria are as follows:

Inclusion criteria:

- Age > 60 years
- Physically independent (able to walk 100 meters without a walking aid and climb 10 steps without rest)
- Medical certificate of suitability or fitness to practice resistance-training activities (based on the ACSM; Kohrt et al., 2004)
- No plans to leave the area during the study period
- Cognitive ability to understand and follow the instructions and to sign the informed-consent form
- Free of any antioxidant supplements for at least six weeks before the start of the study
- Willingness to be randomized to either the intervention group and to follow the study protocol

Exclusion criteria:

- Presence of cardiovascular, musculoskeletal, renal, liver, pulmonary, neuromuscular, or neurological disorders that would prevent the participant from performing the exercises
- Uncontrolled endocrine and metabolic disorders
- Acute or chronic inflammatory diseases
- Uncontrolled epilepsy
- Current or prior (past six months) use of hormone replacement therapy
- Having sustained a low-trauma fragility fracture in the past six months
- Body weight changes of >10% in the previous year
- Intake of prescription medications or supplements (i.e., vitamin C or E) expected to alter the results of the study (ergogenic, dietary aids, estrogen, beta-blockers, steroid hormones, calcitonin, corticosteroids, glucocorticoids, thiazide diuretics, anticonvulsants, bisphosphonates, or raloxifene)
- Initiating calcium or vitamin D supplementation in the preceding six months
- A history of malignant neoplasms
- Terminal illness with life expectancy of less than one year
- Engagement in regular strength training (more than once a week) in the previous six months

- Participation in another research project (within the last six months) involving dietary, exercise, and/or pharmaceutical intervention
- Mini-Mental State Examination score lower than 23/30 (Folstein et al., 1975)
- Severe visual or hearing impairment

B. Screening and recruitment process

Recruitment was conducted in Valencia, Spain through non-probability convenience sampling using poster advertisements displayed on notice boards at two MACOPs (Nou Benicalap and Campanar) from September to December 2017. The screening process had three steps. First, information sessions were delivered to potential subjects who showed interest, and they were asked to recommend the study to their families and friends. A total of 181 older women indicated interest in participating. Second, the medical history questionnaire was used to screen for any exclusion criteria. The study personnel reviewed each subject's responses on the questionnaire to verify the completeness of the written responses. Finally, all eligible participants were required to obtain approval from their local doctors to clear them of any contraindicated medical conditions to exercise, based on the ACSM guidelines (Kohrt et al., 2004). Before being included in the study, all potential participants were comprehensively informed about the study purpose and procedures as well as the benefits, risks, and discomfort that might result from participating. Each participant provided written informed consent and was free to withdraw from the study at any time (Appendix T). Likewise, they were informed that the information they provided and obtained as a result of the examinations would become part of an automated file, with the purpose of research and teaching in the areas of health, physical activity, and sport, in compliance with Organic Law 15/1999, of December 13, on the Protection of Personal Data.

IV.II.IV. Experimental procedures

A. General information

Baseline and post-intervention evaluations were carried out two weeks prior to (weeks -3 and -2; the third and fourth weeks of January) and after (weeks 21 and 22; the second and third weeks of July) the intervention and consisted in the assessment of the following primary and secondary variables: oxidative stress (urinary 8-oxo-dG, 8-iso-P, SOD, GPx, total glutathione, GSH, GSSG, GSSG/GSH ratio, and GSH/GSSG ratio), bone remodeling via BTMs (OC, β-CTx), bone strength [the aBMD and T-score of the lumbar spine (segments L1–L4 and L2–L4 as well as individual vertebras L1, L2, L3, and L4) and the proximal femur (femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip)], fracture risk (10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture), anthropometric (height, body weight, WC, HC, WHR, and WHtR), body composition (total body weight, total fat mass, total fat-free mass, and total percentage of fat mass), muscle strength of upper and lower limbs (peak torque strength via isokinetic strength of knee and elbow flexion/extension and hip abduction/adduction at 60º/s and 180º/s), and physical function (5STS, 30sec-CS, 30sec-AC, stair-climbing, SCS, SCP, FRT, TUG, and 6MWT) measurements.

In addition, the participants were required to complete multiple questionnaires at the beginning of the program to control for potential confounding variables, such as nutritional intake (three-day food diary); level of physical (GPAQ) and cognitive function (MMSE); BADLs (Barthel Index) and IADLs (Lawton and Brody scale); level of anxiety (OASIS); level of depression (ODSIS); and socio-demographic and health-status data (age, ethnicity, education level, living situation, marital status, employment status, number of comorbidities, and prescribed medications). The questionnaires were provided to the participants at the first evaluation session (after the physical test measurements), refilled by the participants at home

following an explanation by the research personnel, and returned to the staff during the familiarization sessions or on the second evaluation day (for the control group). In the case of any doubts, they were resolved during the same familiarization sessions.

Urine and blood samples were obtained by the nurses in the two MACOPs (Campanar and Nou Benicalap), while the rest of the parameters were assessed in the Performance Laboratory of the Faculty of Physical Activity and Sport Sciences at the University of Valencia. Biological samples (oxidative stress, antioxidants, and thiol redox state) were processed at the Oxidative Pathology Unit in the Department of Biochemistry and Molecular Biology in the Faculty of Medicine at the University of Valencia, while the BTMs were analyzed by the certified clinical laboratory Analclinic (clinical analysis laboratories in Valencia, Spain).

Both initial and final assessments were performed by the same researchers (sports scientists and physiotherapists) using the same protocols at the same time of the day. The researchers were responsible for explaining the execution of the study to the participants, giving practical demonstrations (if necessary), and collecting all the data. All the evaluation staff were previously instructed to ensure consistency in how the tests were performed, how to calibrate the assessment instruments, and how to standardize the protocol.

With regard to the order of the tests, the anthropometric (10 min) and body-composition/bone health measurements (20–25 min) were analyzed first, followed by isokinetic strength (20 min) and physical function (20–25 min) [in the following order: balance (FRT and TUG); dynamic strength (5STS, 30sec-CS, 30sec-AC, and stair-climbing); and aerobic capacity (6MWT)]. Performing all the test took around 90–120 minutes.

Like in the first project, anthropometric and DXA measures were performed before the strength and physical function measures to minimize any effects of fluid shifts (Romero-

Arenas et al., 2013). At the same time, the order of all the tests was determined with the intention of minimizing the effects of one test on the next (in terms of neuromuscular and cardiovascular fatigue). Therefore, isokinetic strength assessments were performed before physical function, and, within the functional tests, balance tests were carried out before strength/power and aerobic capacity.

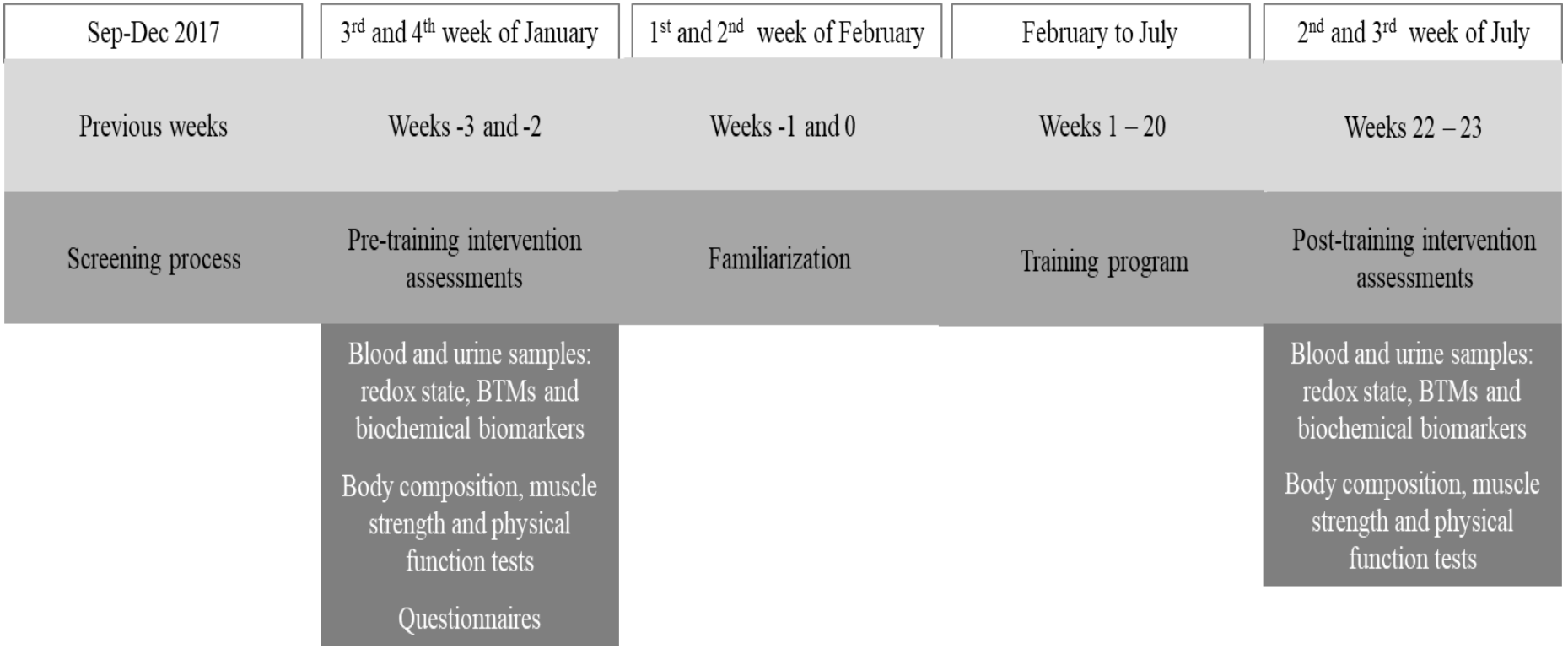
Blood was collected on a different day before the rest of the tests, with at least 48–72 hours in between. The time window between baseline assessment and the start of intervention was aimed to be within two weeks, and the same time window for assessment was due in five months, after the training intervention (Figure 87).

Participants were asked to wear the same clothing and shoes to carry out the test before and after the intervention, and they were instructed to maintain their normal daily routines and dietary intake during the evaluation period. Prior to performing all the primary and secondary dependent-variables test (with the exception of blood analysis), the participants fasted for 3–4 hours, refrained from ingesting stimulants (e.g., caffeine) for eight hours, and avoided practicing intense exercise 24 hours beforehand, but they were allowed to hydrate freely. Before the blood analysis, the subjects had fasted for 12 hours and not exercised for at least 12 hours.

As many of the tests are the same as the first PhD study described earlier (oxidative stress: urinary 8-oxo-dG, 8-iso-P, SOD, GPx, GSH, GSSG, and GSSG/GSH ratio; bone health: aBMD and T-score at the lumbar spine and hip, 10-year probabilities of hip fracture and major osteoporotic fracture, and β-CTx; anthropometry: height, weight, and BMI; body composition: total body mass, fat mass, fat-free mass, and percentage body fat; isokinetic strength: seated knee and elbow flexion-extension and standing hip abduction-adduction at 180°/s and 60°/s; physical function test: 30sec-CS, 30sec-AC, TUG, and 6MWT;

questionnaires: MMSE, Barthel Index, Lawton and Brody scale, and socio-demographic and health-status data; attendance and adverse-events checklist) and to avoid repeating the same content, only further details of the new assessments are described below. At the same time, since the reliability measures (test-retest, intra-rater, and inter-rater) and the short-term CVs of most of the tests performed in the second project were already tested in our laboratory in the first study, and most of the raters in the second study were the same ones from the first (particularly for the DXA and isokinetic devices), the reliability measurements were only assessed in the new tests.

Figure 87. *Detailed schematic diagram of the experimental phases in the project two.*



B. Collection and processing of blood and urine samples

The procedures for urine and blood sample collection and storage were the same as in the first project. In this case, urine samples were collected for the analysis of the oxidative-stress biomarkers of 8-oxo-dG and 8-iso-P, while the blood samples were collected to analyze the antioxidants enzymes of GPx and SOD, along with the thiol state (GSH, GSSG, and total glutathione) and the BTMs (OC and β-CTx) in serum.

C. Oxidative stress, antioxidants, and thiol redox state

Urinary 8-oxo-dG and 8-iso-P, total glutathione, GSH, GSSG, SOD, and GPx were analyzed with the same kits and procedures as in the first project. The only difference is that, in this case, the antioxidant enzymes and thiol status were evaluated in serum, not in PBMc. Values are expressed in nmol/mmol creatinine for urinary 8-oxo-dG and 8-iso-P; µmol/L for total glutathione, GSH, and GSSG; U/ml for SOD; and nmol/min/mil for GPx. The intra-assay CVs are 1.21% (95% CI = 0.65–1.77), 0.78% (95% CI = 0.42–1.13), 1.04% (95% CI = 0.63–1.44), 1.13% (95% CI = 0.61–1.64), 1.01% (95% CI = 0.57–1.44), 2.8% (95% CI = 1.45–4.15), and 0.43% (95% CI = 0.27–0.59) for 8OHdG, 8-iso-P, total glutathione, GSH, GSSG, SOD, and GPx, respectively.

D. Bone health

The aBMD and T-score of the lumbar spine and the hip were assessed using the same equipment and procedures as in the first study. The 10-year probabilities of hip fracture and major osteoporotic fracture were also assessed with the FRAX tool.

With regard to the BTMs, the blood extraction procedure was carried out in the same way as in the first project. However, in the second study, the OC was measured as a marker of bone formation using an automated Liaison® CLIA system (DiaSorin S.p.A, Saluggia, Italy) through a “sandwich” technique. Values are expressed in ng/mL, respectively. The

intra-assay CV is 4.2%, and 95% CI = 1.2–6.61. Serum β-CTx was again measured as a marker of bone resorption following the same procedures. Values are expressed in ng/mL. The intra-assay CV is 3.9%, with a 95% CI of 1.4–5.74.

E. Anthropometry

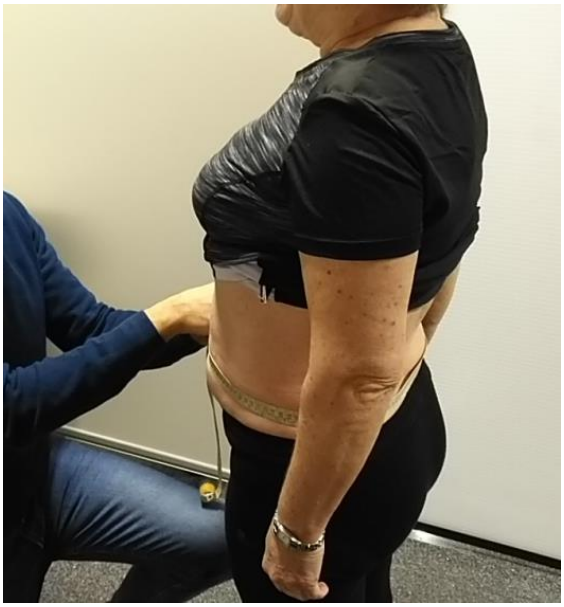
Heights and weights were measured with the same materials and procedures as in the first study.

i. Waist circumference

The WC was assessed in centimeters using an inelastic tape, which provides a constant 100-g tension. The tape was placed on bare skin, without compressing the subcutaneous adipose tissue, at the midpoint between the lowest palpable rib margin and the top of the iliac crest in the anatomical position (ACSM, 2014; NHANES, 2007). The measurement was recorded at the end of a normal expiration while subjects stood erect with arms hanging loosely at the sides and feet together (Figure 88). Two measurements were made, and the mean value was taken. If the difference between the two measurements exceeded 1 cm, the measurements were repeated (WHO, 2011b). The WC is an indicator of abdominal visceral adipose tissue and therefore of cardiovascular-disease risk (AHA, 2013; Harris et al., 1999; Pouliot et al., 1994; Zamboni et al., 1998). An increase of 1 cm in WC is associated with a 2% increase in risk of future cardiovascular diseases (De Koning et al., 2007).

The short-term CV for repeated measurements of the WC is 0.98% (95% CI = 0.77–1.2). In our laboratory, the test–retest reliability coefficient for this test is “excellent” (ICC = 0.994; 95% CI = 0.987–0.997). In addition, intra-rater reliability was also tested, due to the strong influence of the tester on the outcome procedure. The intra-rater reliability is “excellent” (ICC = 0.992; 95% CI = 0.985–0.996).

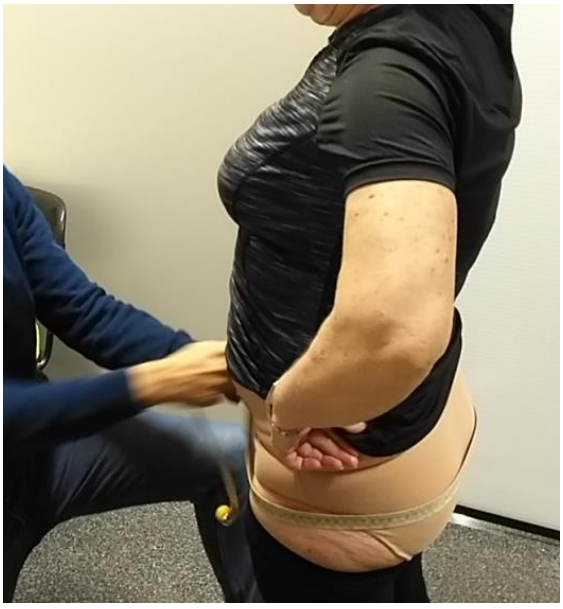
Figure 88. *Waist circumference assessment.*



ii. Hip circumference

The HC was measured in centimeters around the widest portion of the buttocks, with the tape parallel to the floor, using a stretch-resistant tape that provides a constant 100-g tension (Figure 89). Both waist and hip diameters were obtained following the WHO guidelines (WHO, 2011b).

Figure 89. *Hip circumference assessment.*



The short-term CV for repeated measurements of the HC is 0.72% (95% CI = 0.52–0.92). In our laboratory, the test–retest reliability coefficient for this test is "excellent" (ICC = 0.994; 95% CI = 0.988–0.997). Intra-rater reliability was tested for the same reason as that for WC, and it is also "excellent" (ICC = 0.991; 95% CI = 0.982–0.996).

iii. Waist-to-hip ratio

The ratio of WC to HC was calculated, as it is strongly associated with cardiovascular-disease events (Kannel et al., 1991), metabolic risk factors (Depres & Lemieux, 2006), and death (De Koning et al., 2007;Seidell et al., 1994). An increase of 0.01 units in WHR is associated with a 5% increase in risk of cardiovascular diseases (De Koning et al., 2007).

iv. Waist-to-heigth ratio

The ratio of WC to height was calculated as a proxy for central (visceral) adipose tissue (Ashwell et al., 1996; Ashwell & Gibson, 2014; Roriz et al., 2014), being a marker of "early health risk" (Ashwell & Gibson, 2016).

F. Body composition

Total body mass, fat mass, lean mass, and percentage body fat were assessed following the same procedures and with the same equipment as in the first study.

G. Muscle strength

The same muscle groups were assessed with the same equipment and procedures to evaluate muscle strength.

H. Physical function

Physical function was evaluated using standardized tests adapted from the SFT battery (Rikli & Jones, 1997, 2001, 2013a) and the SPPB (Guralnik et al., 1994) among other

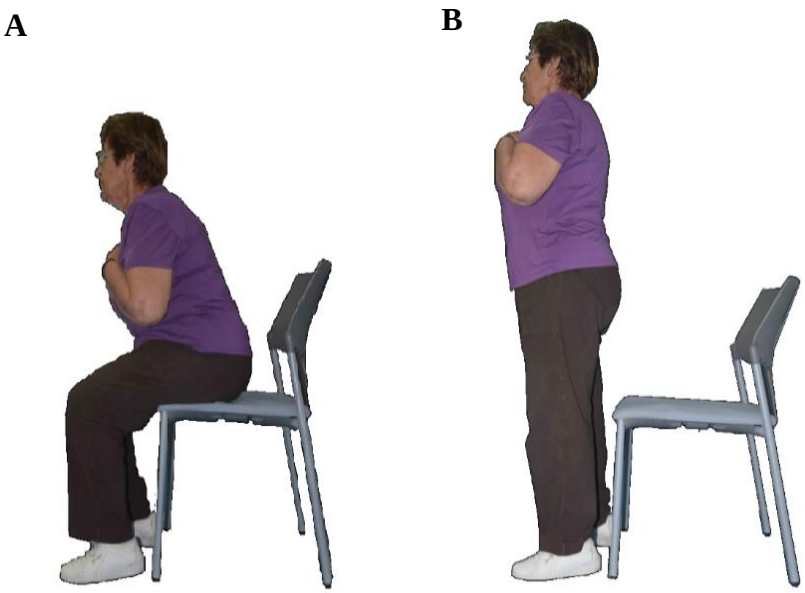
sources, taking into account previously published protocols (Fritz et al., 2018; Gargallo et al., 2018). The power and the endurance strength (or muscular endurance) of the lower limb were assessed with the 5STS (Guralnik et al., 1994), 30sec-CS (Rikli & Jones, 2013a), and timed stair-climb test (Bennell et al., 2011). Upper-body endurance strength was measured using the 30sec-AC (Rikli & Jones, 2013a). Finally, proactive, dynamic balance and aerobic endurance were tested with the FRT (Duncan et al., 1990), TUG (Rikli & Jones, 2013a), and 6MWT (Rikli & Jones, 2013a), respectively.

The order of the tests is as follows: balance (FRT and TUG), dynamic strength (5STS, 30sec-CS, 30sec-AC, and timed stair-climbing), and aerobic capacity (6MWT), with a rest period of 60 to 180 seconds between tests. All the tests were performed on the same day in the Performance Laboratory of the Faculty of Physical Activity and Sport Sciences at the University of Valencia. The 30sec-CS, 30sec-AC, TUG, and 6MWT were performed in the same way as in the first study.

i. Five sit-to-stand test

Lower-limb functional power was evaluated using the 5STS test from the SPPB (Guralnik et al., 1994). The participants began by sitting in the middle of a firm, padded, armless, hard-backed chair, with the seat 46 cm from the floor, and they were instructed to keep their back straight, their arms crossed at the wrists and held against their chest, and their feet on the floor approximately shoulder-width apart (Figure 90). The back of the chair was supported against a wall for their safety.

Figure 90. *Five sit-to-stand test.*



Note. Initial (A) and final (B) position of the 5STS.

From this position, the beginning of the timed test was prefaced with a "ready, set, go" signal from the tester. The participants had to rise to a full standing position and then return to the starting full sitting position as quickly as possible five times. The stopwatch was started after the word "go," and the researcher silently counted each of the five completed sit-to-stand cycles. The stopwatch was stopped when the subject returned to the seated position for the fifth time. Prior to data collection and following a demonstration by the tester, the participants performed several practice repetitions to familiarize themselves with the technique. The test was performed twice, with a 1-minute break between each attempt. The better result from the two trials was recorded for analysis. The time for completion was measured to the nearest 0.1 second using a handheld stopwatch (Geonaute, On Start 300;Lila, France), and the same chair was used for all the subjects. While the subjects were performing the tests, they were given constant and standardized verbal encouragement throughout the five repetitions. They never received feedback about the repetitions performed. This protocol

is similar to those described in the literature as being reliable and correlated with fall and balance (Bohannon, 1995). Values are expressed in seconds. This test has been previously validated in healthy older females (Goldberg et al., 2012), and it has demonstrated "excellent" test-retest (Goldberg et al., 2012) and inter-rater reliability (Wallman et al., 2013) in the elderly population.

The short-term CV for repeated measurements of the 5STS test is 2.02% (95% CI = 1.1–2.94). In our laboratory, the test–retest reliability coefficient for this test is "excellent" (ICC = 0.985; 95% CI = 0.969–0.993). Inter-rater reliability was also tested for the physical function test, as they have been carried out by three to four raters. The inter-rater ICC for the 5STS is "excellent" (ICC = 0.993; 95% CI = 0.987–0.996).

ii. Timed stair-climbing test

The functional muscle power of the lower limbs was assessed by the timed stair-climb test (Bean et al., 2007; Bennell et al., 2011). After the tester gave the start signal of "ready, set, go," the participants ascended two flights of stairs (11 steps per flight, with an 18-cm rise per step) as quickly and safely as possible without using the handrails or any other aid (the handrail and the tester were available for balance support only if needed; Skelton et al., 1995; see Figure 91). After 11 steps, the participants made a right-hand wrap-around turn and then completed the remaining 11 steps. The time to complete this task was recorded to the nearest hundredth of a second using a (Geonaute, On Start 300;Lila, France). Participants were required to step on all of the steps, and taking two steps at a time was not permitted. Constant and standardized verbal encouragement was given to elicit maximal efforts from the participants, but they never received feedback about the time results of the trials. The test was performed two times, with a rest period of three minutes between attempts. The faster of the two trials was recorded for data analysis. Prior to data collection and following a

demonstration by the tester, the participants performed one practice repetition to familiarize themselves with the task. Values are expressed in seconds.

Figure 91. *Timed stair-climbing test.*

Note. Development of the timed stair-climbing test.

In addition, to standardize the outcome measure, each time result was divided by the number of steps to calculate the participant's SCS in steps per second. This protocol is similar to that used previously by other investigators, who found it to have an acceptable test-retest reliability (ICC = 0.84–0.86; Tiedemann et al., 2007), and it was also validated for older adults (Malmberg et al., 2002).

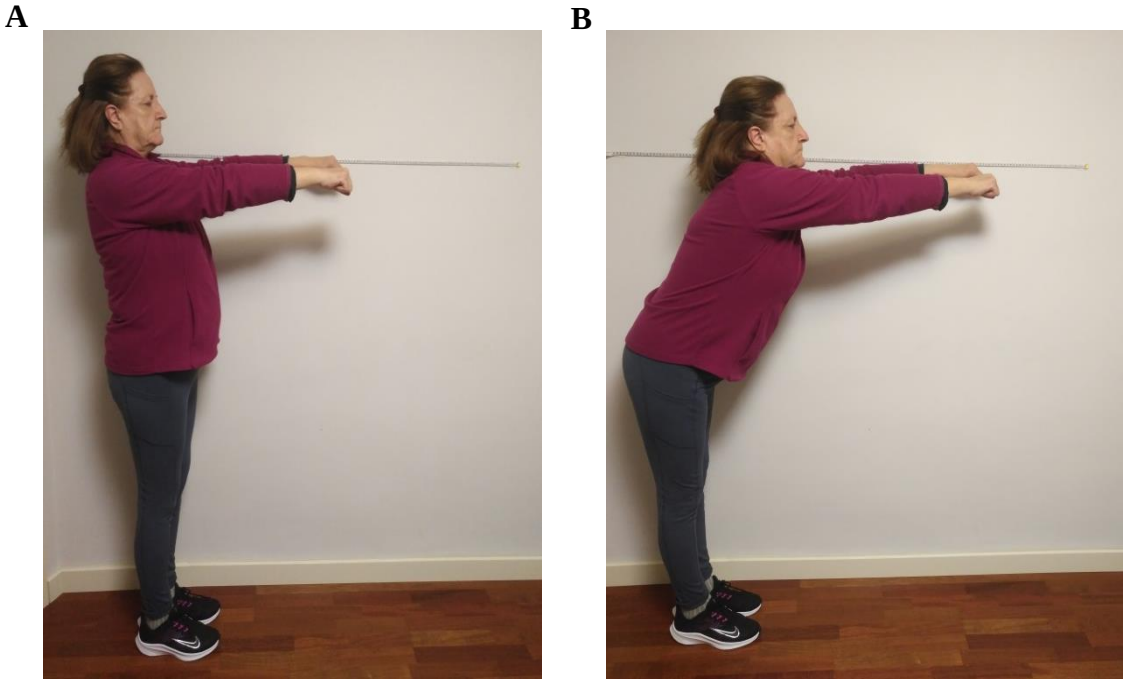
The SCP output was also calculated using the formula described by Lazowski et al. (1999) and other authors (Henwood & Taaffe, 2006), which is as follows: power = weight (kg) × acceleration due to gravity (9.8 m/s^{-1}) × step height (0.18 m) × number of steps (22) / time (s). Results are expressed in watts (W).

The short-term CV for repeated measurements of the timed stair-climb test is 2.87% (95% CI = 1.63–4.12). In our laboratory, the test–retest reliability coefficient for this test is "excellent" (ICC = 0.968; 95% CI = 0.935–0.984). The inter-rater ICC for the test is also "excellent" (ICC = 0.997; 95% CI = 0.995–0.999).

iii. Functional reach test

To evaluate proactive balance, the FRT was performed (Duncan et al., 1990). The FRT measures the participant's ability to reach forward while maintaining a fixed base of support in the standing position. Each subject was asked to stand in a normal, relaxed stance perpendicular to a wall, and a height-adjustable tape measure was secured to the wall at the height of the subject's acromion. The subjects must stand next to the wall, and, without touching it, they must raise their arms closest to the wall until 90 degrees (parallel to the floor), with closed or clenched fists. In this position, the placement of the third metacarpal along the wall tape was recorded. Subsequently, the subjects then reached as far forward as they could without losing their balance, taking a step, or lift their heels off the ground, and the placement of the end of the third metacarpal in this final position was again recorded by the evaluator (Figure 92).

Figure 92. *Functional reach test.*



Note. Initial (A) and final (B) position of the FRT.

Rotating the body to reach a greater distance was not allowed. The functional range in centimeters was calculated as the difference in distance between the final and the initial position of the same third metacarpal. Each subject completed three trials as described by Duncan et al. (1990), with the average of the two better trials used for subsequent analyses. There was no rest between attempts. It was important to tell the subject not to rotate their body to reach a greater distance. Prior to data collection and following a demonstration by the tester, the participants performed several practice repetitions to familiarize themselves with the technique. While the subjects were performing the tests, they were given constant, standardized verbal encouragement. They never received feedback about the results performed. The participants carried out the test in their regular shoes. Values are expressed in centimeters. This test has been shown to be a valid tool for measuring proactive balance in healthy older adults (Duncan et al., 1990; Newton, 2001), with good test-retest (ICC = 0.92)

and inter-rater reliability (ICC = 0.98; Duncan et al., 1990), and it is a sensitive measure that is strongly connected to physical frailty in the elderly population (Weiner et al., 1992)

The short-term CV for repeated measurements of the FRT is 1.49% (95% CI = 0.68–2.31). In our laboratory, the test–retest reliability coefficient for this test is "excellent" (ICC = 0.994; 95% CI = 0.988–0.997), and the inter-rater ICC is also "excellent" (ICC = 0.997; 95% CI = 0.995–0.999).

I. Nutritional intake

Nutritional status was assessed by a diet record over three consecutive days (two weekdays and one Saturday; Thompson & Byers, 1994). At the end of the baseline physical-test evaluations, two nutritionists from the University Clinic of Nutrition, Physical Activity and Physiotherapy provided detailed verbal, written, and picture instructions (using the table of food components) to aid the participants in completing their food diaries and ensure standardization of the dietary records (Appendix U). They were supplied with food scales and measuring cups to help measure food and determine the correct portion sizes.

The participants had to record the type, amount, and time of consumption of all foods and fluids consumed over a 24-hour period during these three days. All multivitamins, minerals, and other supplements were also recorded. They were encouraged to provide as much detail as possible, including the brand names of known foods and the exact cooking methods. The **s**ubjects filled out the self-administered three-day dietary food logs to quantify nutrient intake over time and returned them for the first two weeks of the study.

The questionnaires were checked for completeness by the nutritionist staff at each respective testing appointment, so that any ambiguous or missing information can be clarified. Dietary information from the questionnaires was entered and analyzed using the commercially available nutrient-analysis software program DIAL 3.5.0.3 (ALCE

INGENIERIA, Madrid, Spain). Total energy intake (Kcal/day), macronutrients (carbohydrates [CHO], proteins, and fats; expressed in g/day), micronutrients as minerals (calcium, ferrous, iodine, magnesium, zinc, selenium, sodium, potassium, phosphorous, and fluoride; expressed in mg/dl), and vitamins (B1, B2, B3, B5, B6, B9, B12, C, A, H, D, and E; expressed in mg/d and µg/d) were all quantified.

The subjects did not receive dietary advice, and they were instructed to maintain their initial nutritional habits until the end of the study so as not to affect the outcome measures. To verify compliance with these instructions, dietary and activity habits were assessed at the beginning and the end of the training program.

It has been demonstrated that a three-day dietary record is a valid tool for estimating dietary intakes in older adults without cognitive impairments (Luhrmann et al., 1999), with a "moderate" to "high" reliability for almost all nutrients (Tremblay et al., 1983).

J. Level of physical activity

Prior to the intervention, the participants' self-reported levels of physical activity were assessed with the GPAQ (Armstrong & Bull, 2006). This test from the WHO (WHO, 2010b) evaluates the duration and the intensity (moderate and vigorousphysical activity) of the physical activity performed in the domains of (1) work (such as paid or unpaid work, study or training, household chores, harvesting food/crops, fishing or hunting for food, and seeking employment), (2) during travel or transportation to and from places (e.g., getting to work, the shops, the market, and places of worship), and (3) during recreational or leisure activities in a regular week (Appendix V). The GPAQ also includes a question about the total time in a typical week spent in sedentary behavior, defined as sitting or reclining while awake with very low energy expenditure (Tremblay et al., 2017). In total, the test comprises 16 questions.

The domains required participants to report the number of days per week in which the activity was performed, followed by the number of hours and minutes per day**.**

Total physical activity (the sum of vigorous and moderate activity) in minutes was calculated for the work and recreational domains. In addition, the total vigorous physical activity per week in minutes was calculated using the sum of vigorous physical activity at work and recreation (excluding transportation), whereas the duration of moderate physical activity per week in minutes was calculated with the sum of moderate physical activity for work, recreation, and transportation according to the GPAQ analysis guidelines (WHO, 2010b). The total self-reported physical activity was calculated as the sum of the total vigorous and moderate physical activities across all three domains.

Moreover, the estimates of total and domain-specific physical activity in MET-minutes/week – that is, units of relative energy expenditure – were also analyzed. Time spent on moderate-intensity activities and travel to a place for at least 10 consecutive minutes was multiplied by a MET value of 4, while time spent on vigorous-intensity activities was multiplied by a MET value of 8. Sedentary time was multiplied by 1.5. The daily average physical activity of the three domains, along with the sedentary behavior, was also calculated. To analyze whether the population follows the WHO's health recommendations on physical activity (≥150 minutes of moderate-intensity physical activity or ≥ 75 minutes of vigorous intensity physical activity, or an equivalent combination of moderate and vigorous-intensity physical activity reaching at least 600 MET-minutes; Chu et al., 2015; Win et al., 2015), the number and percentage of participants who follow each and all the recommendations were also determined.

The questionnaire was provided to the participants at the initial evaluation sessions in the Performance Laboratory of the Faculty of Physical Activity and Sport Sciences at the

University of Valencia. Following the tester's explanation, the participants filled in the questionnaire and returned it to the research personal two weeks later. In the case of doubts, they were resolved.

No studies have specifically examined the reliability and validity of the GPAQ in the elderly population (Keating et al., 2019). However, many studies that have previously established high validity and reliability of the GPAQ in different countries have included participants whose ages were above 60 years old (Bull et al., 2009; Chu et al., 2015, 2018; Herrmann et al., 2013; Hoos et al., 2012; Miguel et al., 2019; Trinh et al., 2009). In addition, the GPAQ has been found to be equivalent to the International Physical Activity Questionnaire (IPAQ; Lingesh et al., 2016; Misra et al., 2014).

K. Questionnaires

The MMSE, Barthel Index, and Lawton and Brody scale, along with socio-demographic and health-status data, were also registered in the same way as in the first project. In addition, the number of medications used for each participant was recorded at the beginning of the study, along with the anxiety and depression states.

i. Anxiety state

The anxiety state was recorded at the beginning of the study using the OASIS (Campbell-Sills et al., 2009; Appendix W). The OASIS is a five-item self-report scale that assesses the severity, impairment (social and work), and behavioral avoidance caused by anxiety symptoms. Items are coded on a 5-point scale (0–4). The sum of the scores is used to obtain the total score, which can be a maximum of 20. Previous studies have shown good test-retest reliability, internal consistency ($\alpha = 0.80$), as well as discriminant and convergent validity (Campbell-Sills et al., 2009; Norman et al., 2006; Norman et al., 2011). Moreover,

the Spanish version has shown similar internal consistency (α = 0.86), validity, and sensibility as the original (González-Robles et al.,2018).

ii. Depression state

The depression state was recorded at the beginning of the study using the ODSIS (Bentley et al., 2014; Appendix Y). The ODSIS is a brief self-report scale with five items that assess the severity and functional impairment associated with depressive symptoms. Items are coded on a 5-point scale (0–4). The sum of the scores is used to obtain the total score, which can be a maximum of 20. To complement this information, a sixth question about lifetime suicidal ideation was included. Previous studies have shown that the ODSIS has excellent internal consistency when applied to different samples (α = 0.91, 0.92, and 0.94 in student, community, and outpatient samples, respectively; Ito et al., 2015). Furthermore, its convergent or discriminant validity has also been determined to be good (Ito et al., 2015). In addition, the Spanish version of the ODSIS has recently been validated as an adequate tool to assess the depression-related severity (Mira et al., 2019).

L. Compliance and data safety monitoring

Attendance and adverse events were recorded by following the same procedures as in the first study.

IV.II.V. Exercise protocols

A. general aspects of the training programs

All training sessions were performed in multipurpose rooms located indoors in two MACOPs in Valencia (Campanar and Nou Benicalap centers) between February and July 2018, with four familiarization sessions in the two weeks prior to the start of the intervention. The rooms were equipped with air conditioning and heating systems in order to maintain the temperature at roughly 22°C throughout the duration of the study.

The sessions were consistently directed and supervised by the same qualified and experienced sports scientist and physiotherapist instructors (maximum ratio of participants to trainers was 9:1) to ensure safety and compliance. A research supervisor (specializing in physical activity for older adults) was also present at all the sessions. The supervisor contributed to controlling the training methodology, maintaining the equipment and the room, along with ensuring the correct performance of the exercises through a list with points to supervise (Appendix Q). Therefore, the study was highly supervised, and the correct development of the project was guaranteed. Each instructor recorded the attendance, grip-width changes, and the color of the elastic bands used every week.

Like in the first study, all exercise trainers were required to attend a prior theoretical-practical workshop, where they were instructed on applying the planned methodology with the elastic bands and perceived exertion in older people, ensuring the correct technique of the exercises (resistance, balance, aerobic, coordination, and flexibility), and avoiding risks in the training sessions (for example, by making sure the participants have support objects nearby when necessary). In order to increase adherence to the physical exercise program, the trainers also learned how to identify early cues of poor adherence and behavioral management strategies to enhance compliance with exercise, such as using music and funny exercises in the breaks between exercises and sets, giving positive feedback, sharing the importance of feeling secure when performed the exercises, maintaining conversations with the participants, and making phone calls when a participant did not attend a session (Gianoudis et al., 2012; Otero et al., 2017). To ensure the correct development of the project, at the end of the workshop, all the instructors received a manual, which includes detailed explanations and illustrations of the different training programs to be carried out, including the exercises, progressions, safety considerations, as well as attendance sheets. The research team

maintained regular contact with the instructors and visited the centers periodically to ensure that the trainers were upholding the quality of the program.

All the supervised programs include two weekly sessions of 60 to 80 minutes on nonconsecutive days (separated by a period of 48–72 hours) at the same time of the day (MT: 11:30–13:00 a.m., Tuesdays and Thursdays; P: 9–10:30 a.m.; and T: 10:30–12:00 a.m., both Tuesdays and Fridays) for 20 weeks. The control group did not participate in any exercise programs. At the end of the program, subjects who did not miss any sessions would have completed a total of 37–38 sessions (41–42 if counting the four familiarization sessions), distributed as shown in Tables 16 and 17.

Table 16. *Training session distribution for MT training.*

Months	Number of weeks	Number of sessions	Days of training sessions
January and February	-1,0	4 (familiarization)	30,1,6,8
February	1-3	5	13,15,20,22,27
March	4-7	8	1,6,8,13,15,20,22,27,29*
April	8-10	6	3*5*,10,12,17,19,24,26
May	11-15	9	1*,3,8,10,15,17,22,24,29,31
June	16-19	8	5,7,12,14,19,21,26,28
July	20	2	3,5
Total		42 (38+4 familiarización)	

Note. *Festive day or centers were closed

Table 17. *Training session distribution for P and T training.*

Months	Number of weeks	Number of sessions	Days of training sessions
January and February	-1,0	4 (familiarization)	30,2,6,9
February	1-3	5	13,16,20,23,27
March	4-7	7	3,6,9,13,16*,20,23,27,30*
April	8-10	6	3*6*,10,13,17,20,24,27
May	11-15	8	1*,4,8,11,15,18,22,25,29
June	16-19	9	1,5,8,12,15,19,22,26,29
July	20	2	3,6
Total		41 (37+4 familiarización)	

Note. *Festive day or centers were closed

Every training session was divided into three components, as recommended by the ACSM (ACSM, 2013, Ehrman, 2010):

1. General warm-up: 5–10 minutes of joint mobility and low intensity (50–60% MHR) aerobic exercises, same as in the first study.

2. Main part: 60 minutes of resistance exercises in the P and T programs, including two specific exercises for upper limbs (bicep curl and horizontal chest press), two for lower limbs (lunge and hip abduction), and two involving the muscle groups of the upper and lower limbs (squat plus vertical rowing and squat plus military shoulder press); or 60 min of balance, strength, and aerobic training in the MT program.

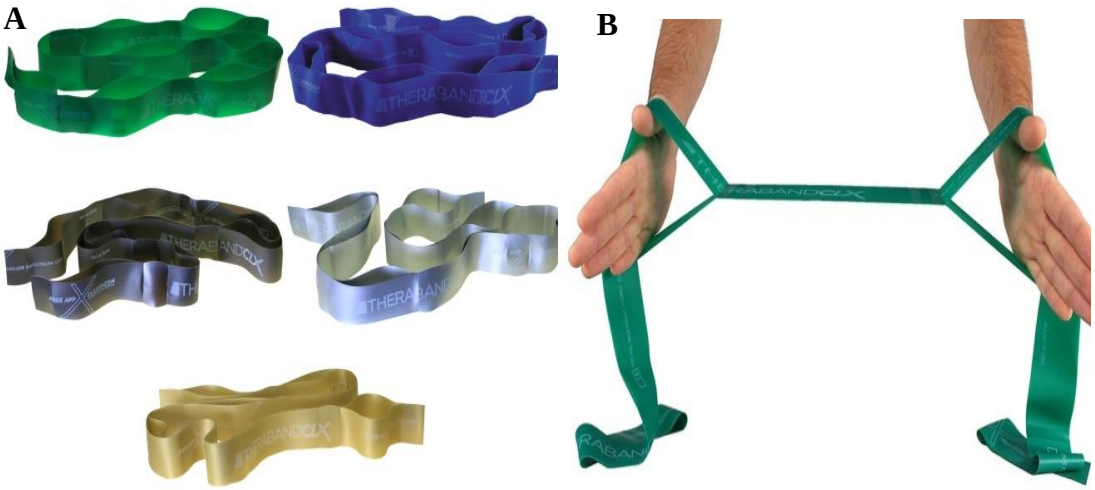
3. Cool-down: 5–10 minutes of respiratory and flexibility exercises, same as in the first study.

Like in the first project, before the study, the scientific staff and the instructors checked the reproducibility of the exercises planned for the elders as well as the progress of the training sessions. Multi-joint exercises were primarily chosen to emphasize both major and minor muscle groups (Garber et al., 2011), with special emphasis on exercises that involve major muscle groups with attachments on or near the hip and the spine (in the case of resistance and balance exercises) due to the site specific-effect of the training on bones (Daly, Dalla Via et al., 2019, Pivonka, 2018), along with exercises with intermittent and multidirectional compressive forces (in the case of aerobic and coordination exercises). In addition, for the purpose of producing muscular and bone adaptations, large muscle masses was involved to cause a greater caloric expenditure, which could produce greater changes in the body composition of the participants. In order to increase caloric expenditure and improve the cardiovascular system, the recovery periods between sets (micropauses) were active in all the groups. These active rests consisted of programmed choreographies of coordinating

movements, and they were also planned to improve adherence to the training sessions. The exercise programs in this study were based on the Exercise and Physical Activity for Older Adults guide from the ACSM (Chodzko-Zajko et al., 2009), guidelines for treatment in people with osteoporosis (Bonaiuti et al., 2005; Giangregorio et al., 2014), and recommendations for fall prevention (Vieira et al., 2016). They were designed to follow the key training principles of specificity and progressive overload.

Each session was performed in a group, and each participant always executed the exercises in the same order, alternating between upper and lower limbs to minimize fatigue (Romero-Arenas et al., 2011). The loads were adjusted every week to maintain the appropriate training intensities by adapting the color and number of elastic bands along with the grip width. The resistance exercises were performed with CLX Loops elastic bands (TheraBand®; Hygenic Corporation, Akron, OH, USA; Figure 93), which come in five colors: green, blue, black, silver, and gold, in ascending order of hardness due to the increase in the thickness of the band (the resistance of the band increases by 25–40% going from one color to the next when the band is stretched to twice its resting length). These kinds of elastic bands are versatile and simple, as their consecutive loops provide multiple grip and anchoring options. All the elastic bands had a length of 10 loops. The same equipment was used as in the first study (chairs, bodybuilding gloves, OMNI-RES scale, metronome, mini stereo, and CDs).

Figure 93. *TheraBand® CLX Loops elastic bands used in the study.*



Note. A. Different TheraBand® CLX Loops elastic bands; B. Loops of elastic band.

Participants were asked to maintain their usual eating and physical-activity habits throughout the study. Thus, they were unable to participate in other exercise programs during the duration of the study. They also agreed to be randomly assigned to either the exercise or the no-exercise group.

B. Familiarization

Because none of the participants had previous experience with strength training or the use of elastic bands, the subjects performed four sessions of pre-intervention familiarization to learn (a) the correct techniques of the exercises (e.g., final and initial positions of the body, ranges of motion), (b) the suitable execution velocity of the exercises, (c) breath control (to avoid the Valsalva maneuver; Hackett et al., 2013), and (d) intensity control through the combined use of the OMNI-RES scale for the elastic bands (which ranked from 1 to 10), grip width, band color, and number of repetitions (Colado et al., 2018). Control of intensity by this method has been previously validated in young (Colado et al., 2010), middle-aged (Gargallo et al., 2014), and older adults (Colado et al., 2018), and it has been used and supported in

previous works (Colado & Triplett, 2008; Fritz et al., 2015; Gargallo et al., 2018, Robertson et al., 2003). The familiarization session took place at the same centers as the main sessions one week before starting the intervention program.

To control and learn the exercise intensity, the participants were asked to take an elastic band with a high resistance (between green and gold) in a narrow grip and to perform one set of 6, 10, or 15 submaximal repetitions of an exercise (depending the intervention group). At the end of the set, such an effort was associated with a quantitative value of 8–9 and a qualitative value of "very hard or heavy" on the OMNI-RES scale. Subsequently, they were asked to perform the same exercise and number of repetitions, but with a wider grip width and/or a lower resistance band, perceiving the exercise as a very light effort and associating it with a quantitative value of 1, or "very easy."

On consecutive familiarization days, the participants were asked to perform the exercises at the intensity scheduled for the intervention to find the correct resistance through the grip width (loop 1, 2, or 3) and the corresponding color for each exercise, thus providing an objective reference of the intensity before starting the program. Each participant did several repetitions to make sure they were done correctly. Normally, to find the correct resistance, three to eight attempts are necessary (Ploutz-Snyders & Giamis, 2001). If the necessary number of repetitions was not reached or exceeded, a rest period of two minutes was given in between each failed attempt. Once completed, the grip width and elastic-band color for each of the exercises was recorded. Finally, the execution speed of the exercises was taught to both training groups using a metronome and the voice of the instructors, who were also stomping in rhythm.

The participants were also instructed about the correct technique of the exercises, performing several sets for each one before starting the training program. In fact, during the

second and third sessions, they performed two sets for each exercise, and three sets were performed during the final familiarization session.

In addition, the participants also learned during this familiarization period that they had to perform the movements without losing the tension of elastic band in the eccentric phase. They also had to complete the concentric phase until the maximum amplitude defined for that exercise was reached. In addition, the women received instructions on how to coordinate their respiratory movements with the execution of both phases (concentric and eccentric).

In the P group, the participants had to learn that they should avoid exceeding an RPE value of 3–4 with the first repetition of each set, as well as a value 6 in the last repetition of the same set, to ensure the maintenance of a high execution speed (Bautista, Chirosa, Chirosa et al., 2014; Naclerio et al., 2011; Sayers et al., 2016). If the necessary number of repetitions was not reached or exceeded, a rest period of two minutes between each failed attempt was allowed.

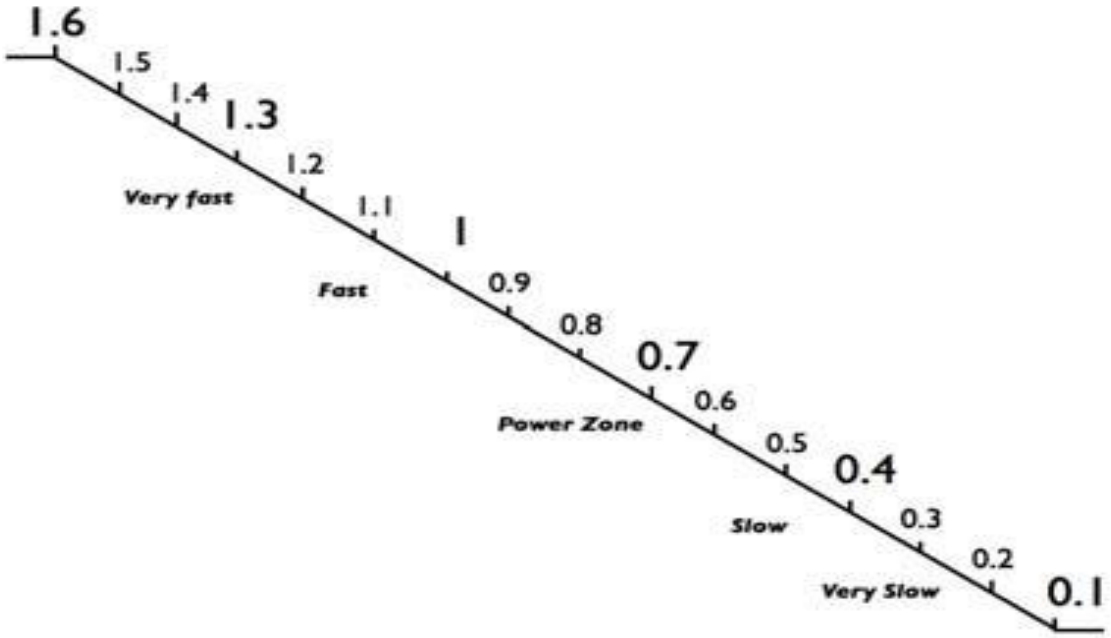
As a common rule for all the participants of the intervention groups, they should always take into account the value of the RPE to achieve the appropriate intensity level in each part of the training program. Therefore, the OMNI-RES scale was always visible in the multipurpose rooms where the classes were held. Likewise, the participants were instructed on guidelines that they had to comply with during the training sessions. The guidelines were: wear comfortable clothes and shoes, do not take stimulant drinks, and bring a bottle of water to avoid dehydration and a towel to remove sweat. All participants were instructed to consult any staff member (instructor) if they require assistance with their exercise program.

C. Power strength training

The P group performed 12 (in the first two weeks to consolidate the technique) and 10 (for the rest of the program) submaximal repetitions in each set with a perceived exertion of 3–4 (very low) on the OMNI-RES scale (Colado, Garcia-Masso, Triplett et al., 2012; Colado et al., 2018) in the first repetition, which is equivalent to 40–60% 1RM (low load or intensity). They never exceeded a value of 6 at the end of the 10 repetitions (Bautista, Chirosa, Chirosa et al., 2014; Naclerio et al., 2011). Thus, a high-velocity displacement of the load was guaranteed, which is essential to achieving physical-function improvements (it is necessary a velocity greater than 0.88 m/s; Sayers et al., 2016). For this proposal, the participants had to perceive that the displacement of the load was done "quickly" in the first repetition, since this perception is associated with a velocity displacement greater than 1 m/s for loads of 30–60% (Bautista, Chirosa, Tamayo et al., 2014) in both upper- and lower-limb exercises (Bautista, Chirosa, Chirosa et al., 2014). The participants also had a qualitative perceived-exertion scale as a reference in the room to remember this key aspect (Figure 94).

The training session consisted of a general warm-up (joint-mobility and aerobic exercises at low intensity); six resistance exercises, including two upper-limb exercises (elbow curl and horizontal chest press), two lower-limb exercises (lunge and standing hip abduction), and two exercises combining both upper and lower limbs at the same time (squat plus upright rowing and squat plus shoulder press); and finally the cool-down routine (respiratory and flexibility exercises; Table 18). All the exercises were performed throughout the program with elastic bands of the CLX type (TheraBand®, Hygenic Corporation, Akron, OH, USA) in the following order: squats plus vertical rowing, bicep curl, lunge, horizontal chest press, squat plus vertical shoulder press, and standing hip abduction.

Figure 94. *Quantitative and qualitative scale of perception of velocity.*



Note. Velocity (m/s represented at the top of the line and perception at the bottom. Reproduced from "Development and validity of a scale of perception of velocity in resistance exercise" (p. 543), by Bautista, Chirosa, Chirosa et al., 2014, *Journal of Sports Science & Medicine, 13*(3).

The number of sets per exercise progressed from three in the first eight weeks to four in the remaining twelve weeks, with 90 seconds of active recovery between sets (rhythmic swinging of the extremities, coordinative movements, along with cognitive tasks without the use of elastic bands) and 60 seconds of rest between exercises for hydration or sweat wiping. The introduction of low-intensity active pauses with funny exercises was a strategy to improve adherence to the program, in addition to increasing caloric expenditure and improving the cardiovascular system.

The participants executed the concentric phase as quickly as possible, with a break of one second at the end of this phase, and they performed the eccentric phase in two to three seconds. The execution speed was controlled by a metronome that marked the cadence, set to

120 bpm, along with the background music (also at 120bpm) and the reinforcement of the monitor that counted the times of both phases together with the number of repetitions: 1(number of repetition, rapid)-2(phase, pause)-3(phase)-4(phase), 2-2-3-4, 3-2-3-4, 4-2-3-4, 5-2-3-4, and so on.

Table 18. *Description of the exercises performed by the P and T groups.*

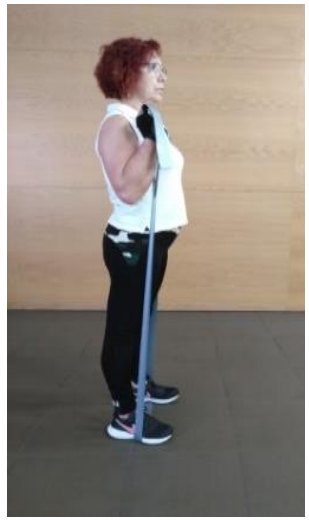
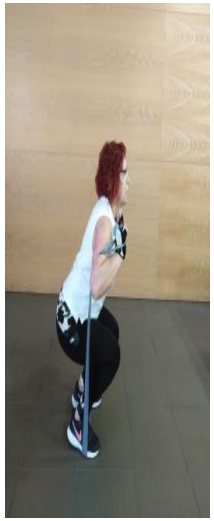
Squat + upright rowing		Horizontal chest press		Biceps curl	
Initial/middle position	Final position	Initial position	Final position	Initial position	Final position
	 				
In a standing position, legs apart at the hips, arms relaxed next to the trunk in slight internal rotation and hands pronated in a neutral position. Look ahead. 90 to 110° of knee flexion. Slightly lean the trunk forward to follow the movement of the legs.	Hands at the level of the xiphoid process, keeping the wrists neutral and elbows elevated, doing an abduction of the shoulders of 60° in the frontal plane and 30° in the scapular plane.	Standing with feet hip-width apart, the elastic band behind the back at chest height. Hands at chest, elbows close to the trunk, forearms and wrists in neutral position.	Standing with feet hip-width apart, elastic band is pressed forward and at the same time with both hands at the level of the xiphoid process doing a full-range elbow extension with internal rotation of forearms and keeping wrists neutral.	Standing with feet hip-width apart, elbows extended next to the trunk and forearms externally rotated with wrists supinated in a neutral position.	Standing with feet hip-width apart, full-range elbow flexion keeping wrists neutral.

Table 18. *Continued.*

Squat + shoulder press			Lunge		Standing hip abduction	
Initial/middle position		Final position	Initial position	Final position	Initial position	Final position
						
In a standing position, with both feet on the center on the band, hip-width apart. Look ahead. Elastic bands hold at shoulder height. 90 to 110° of knee flexion. Slightly lean the trunk forward to follow the movement of the legs.		In a standing position, with feet hip-width apart. Elastic band is pushed up above shoulders with full-range elbow extension, internal rotation of forearms and wrists neutral.	Standing with legs facing each other and hip-width apart, keeping the trunk straight. The forward leg step on the elastic band on the middle. Look ahead and elastic band attached at shoulder height.	The front leg is flexed to 60 to 80° of hip flexion. The contralateral leg provides support by also bending the knee and hip to follow the movement. Pelvis horizontal and trunk straight.	In standing position, feet together with toes pointed forward as well as the eyes. Arms extended next to the trunk and elastic band attached to the hips.	Hip abduction to 40° while the other leg remains extended for support. It is possible to touch a chair to avoid falls.

D. Traditional high-intensity resistance training

The T group performed the same routine as the P group (same general warm-up, six resistance exercises, and cool-down), with the difference that the speed of execution was 2 seconds for both the concentric and the eccentric phase. The rhythm was controlled by the same methods as the P sessions. The participants carried out six submaximal repetitions equivalent to 85% of the 1RM per exercise (high-intensity training sessions). The perceived exertion level on the OMNI-RES scale (Colado, Garcia-Masso, Triplett et al., 2012; Colado et al., 2018) progressed from 6–7 (somewhat hard) in the first 4 weeks to 8–9 (hard) in the remaining 16 weeks. The number of sets per exercise progressed from three in the first eight weeks to four in the remaining 12 weeks, with 120 seconds of active recovery between sets and 90 seconds of rest between exercises (same recovery exercises as the P group). Like the P group, all strength exercises throughout the program were performed with CLX elastic bands (TheraBand®, Hygenic Corporation, Akron, OH, USA) and in the same order.

E. Multi-component training

The MT training sessions were composed of the same general warm-up and cool-down exercises as the P and T programs, lasting for the same amount of time, and with the main part integrated by balance, strength/coordination, and aerobic/coordination blocks lasting between 15–20 minutes each. Participants performed balance exercises, followed by resistance/coordination, aerobic/coordination, and flexibility exercises in each session.

The balance-training component (15–20 min) incorporated a variety of exercise that can be classified into three categories: (1) standing static balance (e.g., single-leg and tandem foot stand), (2) proactive balance (e.g., displacements in different directions with one leg, transferring the weight from one leg to the other, involving lateral and antero-posterior weight shifts), and (3) dynamic balance (e.g., walking in a straight line or line walking, heel-toe walking, changes in distance and direction of the walking displacement, heel-and-toe

walking, walking backwards and sideways, heel-to-toe forward and back). The three types were performed consistently in each session, and some of the dynamic-balance exercises were sometimes included in the warm-up and the aerobic block. The difficulty of the exercises was progressing in the training program to produce new challenges to the proprioceptive, neuromuscular, and vestibular systems by suppressing the visual component (closing the eyes), reducing the base of support, decreasing support points, changing the center of mass (placing the arms alongside the body without movement, crossing the hands to the shoulders), and increasing the execution time (from 30 seconds to 1 minute) or number of sets/repetitions (DiStefano et al., 2009; Lesinki et al., 2015a; Lesinki et al., 2015b; Oddsson et al., 2007; Sherringtom et al., 2011). The participants had a chair next to them to feel more safer and to use in case of a big imbalance. The following balance exercises were carried out:

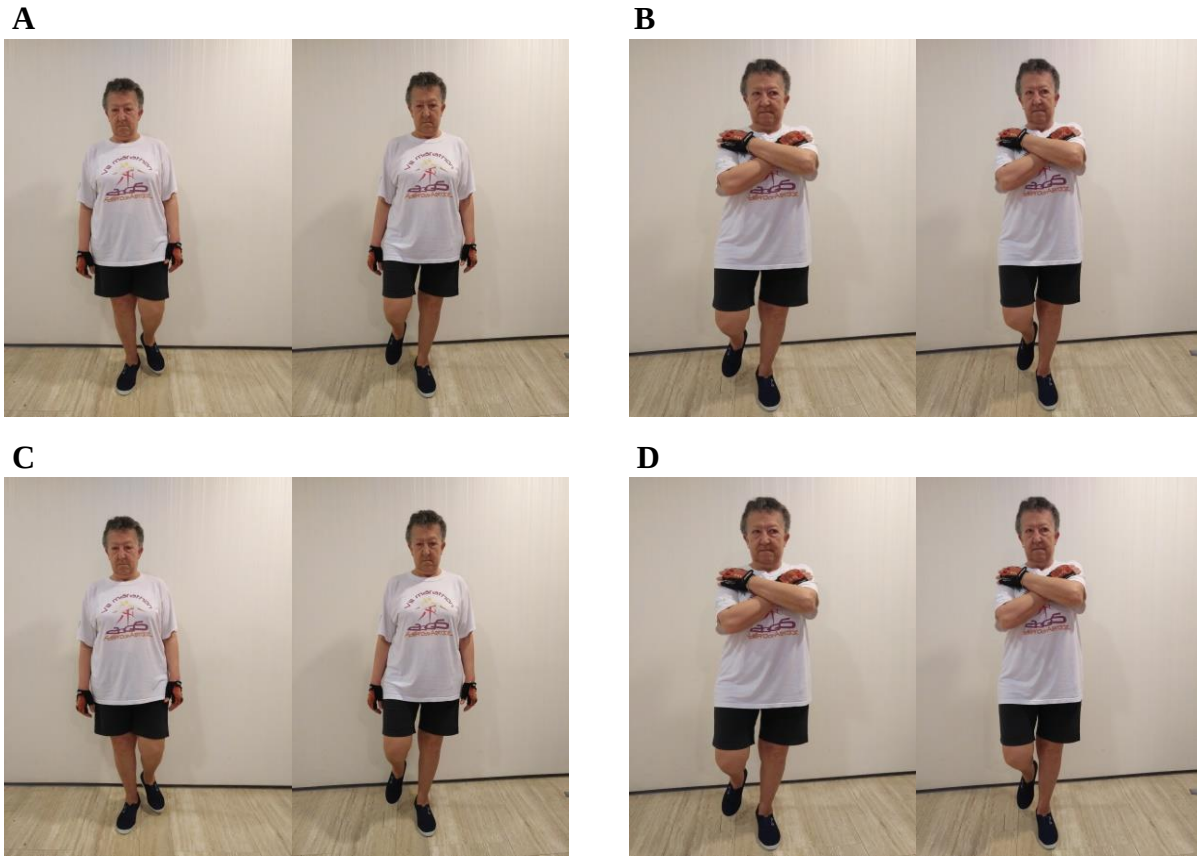
1) Static balance:

Type 1: Single leg standing exercises. Progressions were as follows. Weeks 1–4: 4 × 30-second single-leg stands, with open eyes and arms alongside the body without movement; Weeks 5–8: 4 × 30-second single-leg stands, with open eyes and hands crossed to the shoulders; Weeks 9–12: 4 × 1-minute single-leg stands, with open eyes and arms alongside the body without movement; Weeks 13–16: 4 × 1-minute single-leg stands, with open eyes and hands crossed to the shoulders; Weeks 17–20: 4 × 30-second single-leg stands, with closed eyes and arms alongside the body without movement (Figure 95).

- Single-leg stand with dominant leg, open eyes, and arms alongside the body without movement.
- Single-leg stand with non-dominant leg, open eyes, and arms alongside the body without movement.

- Single-leg stand with dominant leg, open eyes, and hands crossed to the shoulders.
- Single-leg stand with non-dominant leg, open eyes, and hands crossed to the shoulders.
- Single-leg stand with dominant leg, closed eyes, and arms alongside the body without movement.
- Single-leg stand with non-dominant leg, closed eyes, and arms alongside the body without movement.
- Single-leg stand with dominant leg, closed eyes, and hands crossed to the shoulders (only for those with a good sense of balance, for whom the previous exercise was not challenging enough).
- Single-leg stand with non-dominant leg, eyes closed and hands crossed to the shoulders (only for those with a good sense of balance, for whom the previous exercise was not challenging enough).

Figure 95. *Single leg static balance exercises.*



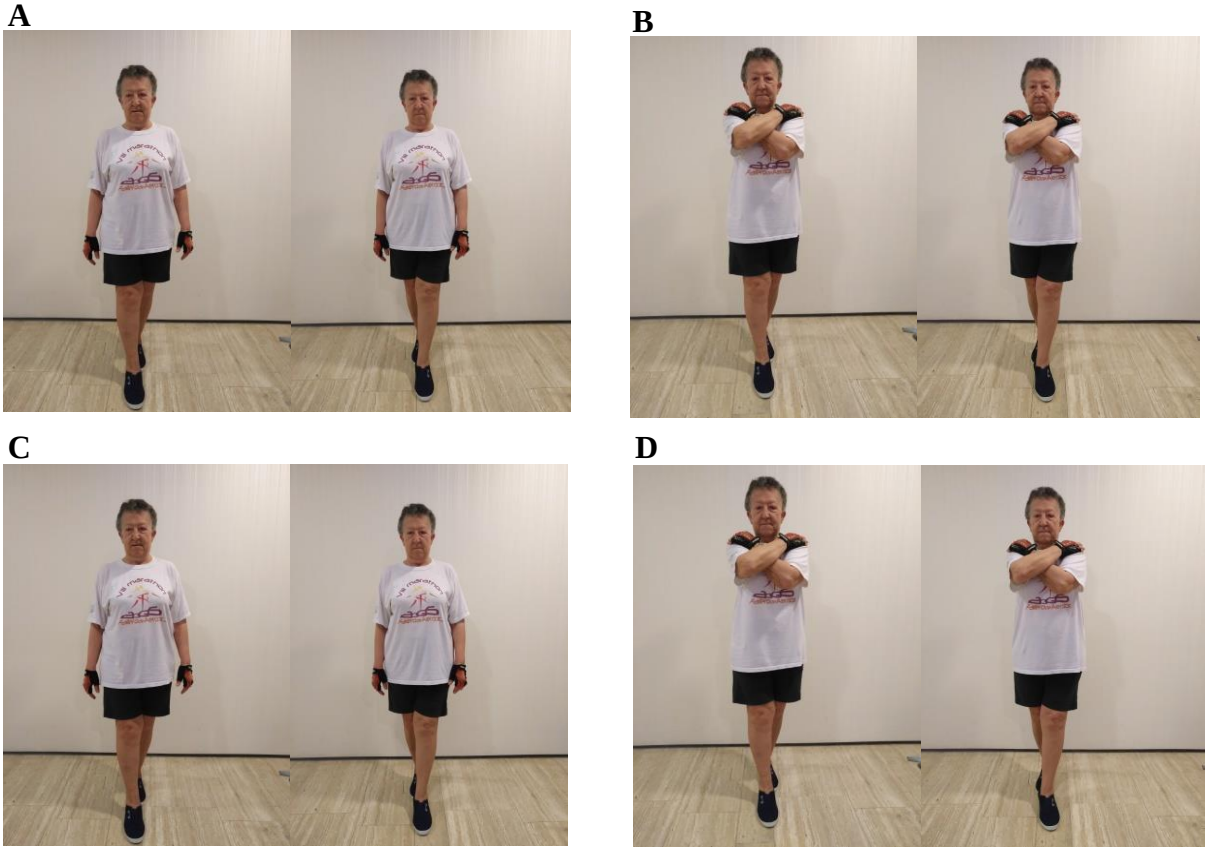
Note. A. Single leg stand with dominant and non-dominant leg, eyes opened and arms alongside the body; B. Single leg stand with dominant and non-dominant leg, eyes opened and hands crossed to the shoulders; C. Single leg stand with dominant and non-dominant leg, eyes closed and arms alongside the body; D. Single leg stand with dominant and non-dominant leg, eyes closed and hands crossed to the shoulders.

Type 2: tandem-stand exercises. Progressions were as follows. Weeks 1–4: 4 × 30-second tandem stands, with open eyes and arms alongside the body without movement; Weeks 5–8: 4 × 30-second tandem stands, with open eyes and hands crossed to the shoulders; Weeks 9–12: 4 × 1 tandem stands, with open eyes and arms alongside the body without movement; Weeks 13–16: 4 × 1-minute tandem stands, with open eyes and hands crossed to

the shoulders; Weeks 17–20: 4 × 30-second tandem stands, with closed eyes and arms alongside the body without movement (Figure 96).

- Tandem stand with dominant leg forward, open eyes, and arms alongside the body without movement.
- Tandem stand with non-dominant leg in front, open eyes, and arms alongside the body without movement.
- Tandem stand with dominant leg in front, open eyes, and hands crossed to the shoulders.
- Tandem stand with non-dominant leg in front, open eyes, and hands crossed to the shoulders.
- Tandem stand with dominant leg in front, closed eyes, and arms alongside the body without movement.
- Tandem stand with non-dominant leg in front, closed eyes, and arms alongside the body without movement.
- Tandem stand with dominant leg in front, closed eyes, and hands crossed to the shoulders (only for those with a good sense of balance, for whom the previous exercise was not challenging enough).
- Tandem stand with non-dominant leg in front, closed eyes, and hands crossed to the shoulders (only for those with a good sense of balance, for whom the previous exercise was not challenging enough).

Figure 96. *Tandem balance exercises.*



Note. A. Tandem stand with dominant or non-dominant leg forward, eyes opened and arms alongside the body; B. Tandem stand with dominant or non-dominant leg forward, eyes opened and hands crossed to the shoulders; C. Tandem stand with dominant or non-dominant leg forward, eyes closed and arms alongside the body; D. Tandem stand with dominant or non-dominant leg forward, eyes closed and hands crossed to the shoulders.

2) Proactive balance: Progressions were as follows. Weeks 1–10: Two trials each for displacement with each leg, with open eyes and free arms; Weeks 11–20: Three trials each for displacement with each leg, with open eyes and free arms (Figure 97).

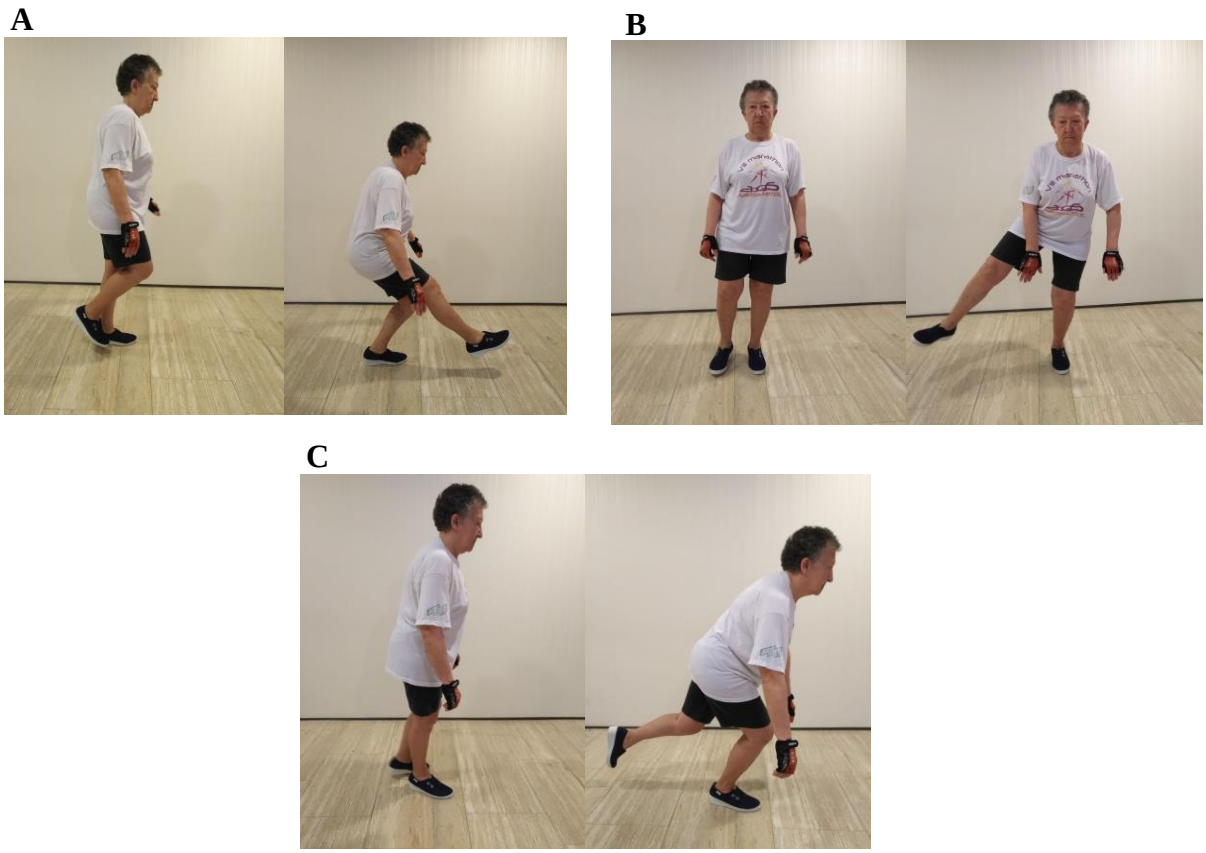
- Single-leg stand with the dominant leg, open eyes, free arms, and anterior displacement of the unsupported leg.

- Single-leg stand with the non-dominant leg, open eyes, free arms, and anterior displacement of the unsupported leg.
- Single-leg stand with the dominant leg, open eyes, free arms, and lateral displacement of the unsupported leg.
- Single-leg stand with the non-dominant leg, open eyes, free arms, and lateral displacement of the unsupported leg.
- Single-leg stand with the dominant leg, open eyes, free arms, and posterior displacement of the unsupported leg.
- Single-leg stand with the non-dominant leg, open eyes, free arms, and posterior displacement of the unsupported leg.

3) Dynamic balance: Progressions were as follows. Weeks 1–4: One trial for each exercise with open eyes and free arms; Weeks 5–8: One trial for each exercise with eyes open and hands crossed to the shoulders; Weeks 9–12: Two trials for each exercise with open eyes and free arms; Weeks 13–16: Two trials for each exercise with eyes open and hands crossed to the shoulders; Weeks 17–20: Three trials each for displacement with each leg, eyes open and arms free.

- Walking in a straight line or line walking
- Heel-toe walking forward and back
- Walking backwards and sideways
- Changing direction of the walking displacement

Figure 97. *Proactive balance exercises.*



Note. A. Single leg standing with the dominant or non-dominant leg, eyes opened, free arms and anterior displacement of the unsupported leg; B. Single leg standing with the dominant or non-dominant leg, eyes opened, free arms and lateral displacement of the unsupported leg; C. Single leg standing with the dominant or non-dominant leg, eyes opened, free arms and posterior displacement of the unsupported leg.

In the resistance-training block (20–25 min), the participants carried out 15 submaximal repetitions (moderate intensity) with a perceived exertion level on the OMNI-RES scale of 6–7 (somewhat hard) in the first four weeks and 8–9 (hard) in the remaining 16 weeks of two resistance exercises (squat plus upright rowing and lunge, always in this order), performed with CLX elastic bands (TheraBand®, Hygenic Corporation, Akron, OH, USA). The execution speed was 2 seconds for concentric phase and 2 seconds for eccentric phase.

The number of sets per exercise was increased from three in the first eight weeks to four in the remaining 12 weeks, with 90 seconds of active recovery between sets and 60 seconds of rest between exercises.

Given the demonstrated importance of reproducing the various challenges encountered in daily life to prevent fall risk, as well as the relevance of the impact ground forces to improving bone health, in the aerobic part (15–20 min) of the session, exercises were proposed that required moving through space along with stationary weight-bearing movements. For the stationary impact aerobic exercises, the participants performed weight-bearing activities with a small, moderate, or high impact, such as stomping, stepping, marching in place, skipping, heel drops (raising the body weight onto the toes and then letting it drop to the floor, keeping the knees locked and hips extended), knee bends, lightly hopping in place, jumps involving opening and closing legs and arms at the same time, and activities with similar ground-reaction forces (Bergmann et al., 1993; Nilsson & Thorstensson, 1989)

In addition, this block included aerobic exercises with displacements (in different combinations, directions, and paces) such as: forward, backward, lateral, and multidirectional walking; jogging; dancing; step choreographies; introducing changes of direction in exercises (such as accelerating and decelerating back and forth, and sideways walking with stops and turns); changing the speed of the execution (e.g., walking as quickly as possible without running); and walking with larger steps and coordinated arms movements. At least 100 impacts per session were always exceeded. The intensity of this part progressed from 65% to 85% of the MHR over the training weeks, as monitored by the Polar Team Pro System (Polar Team Pro Sensor, Polar Electro, Kempele, Finland) in five random participants, which monitors the heart rate of different people at the same time. In addition, the Borg rating of perceived exertion scale (Borg, 1998) was used for the rest of the participants, ranking between 11 and 15 (fairly light to hard) on the 0–20 ranking scale (Carvalho et al., 2010).

The coordination exercises were performed during the rest periods of the resistance and aerobic blocks, and they consisted of psychomotor (reaction-time) exercises, dance movements, and obstacle exercises. Specific cognitive challenges were also integrated into this block (coordination) to engage the executive function and to specifically stimulate cognitive flexibility and inhibition of habitual responses. For instance, the participants performed task sequences while reversing or "scattering" an instructed order, or they learned different stimulus–response associations and then switched between these according to external cues. The difficulty of these exercises increased progressively so as to generate adaptations. Finally, the flexibility block (a 10-minute cool-down routine) involved respiratory and static stretching exercises for the trunk and the upper and lower limbs. The participants performed one repetition of each stretch for 20 seconds. They were informed that they had to notice a slight tension during every stretch (Figure 98). To summarize, the experimental design with the training and assessment characteristics of the project two can be observed in the Figure 99.

Figure 98. *Part of the flexibility routine.*

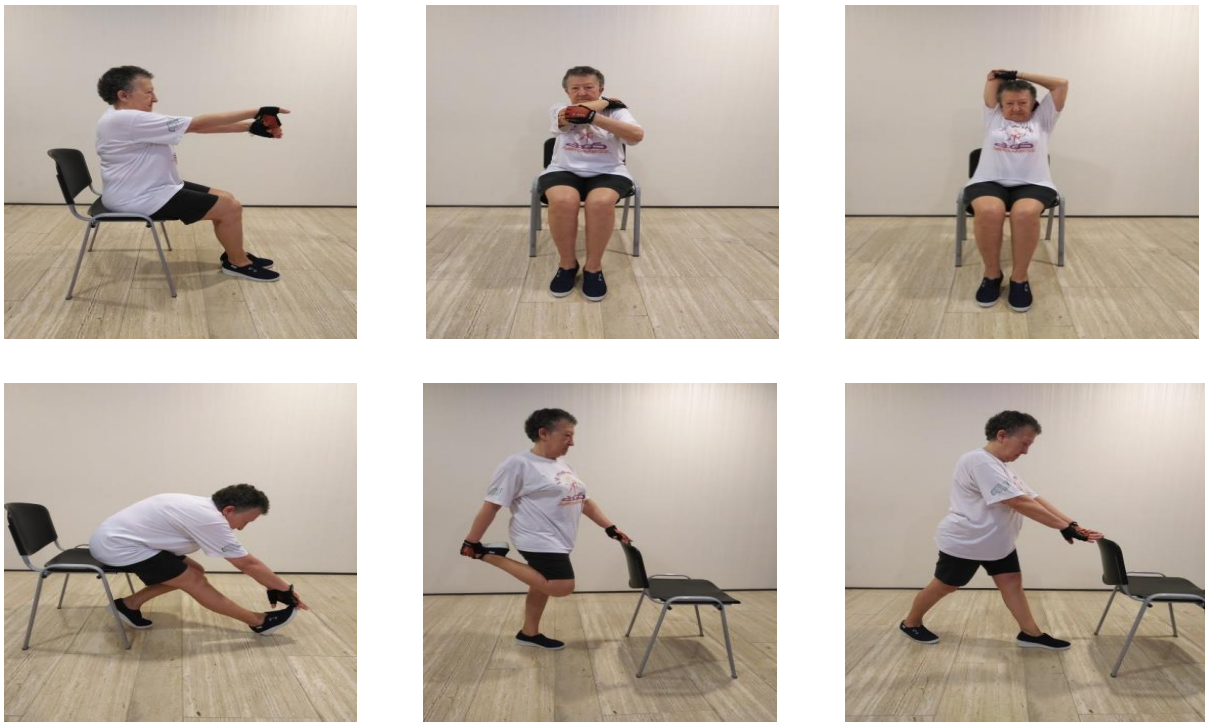
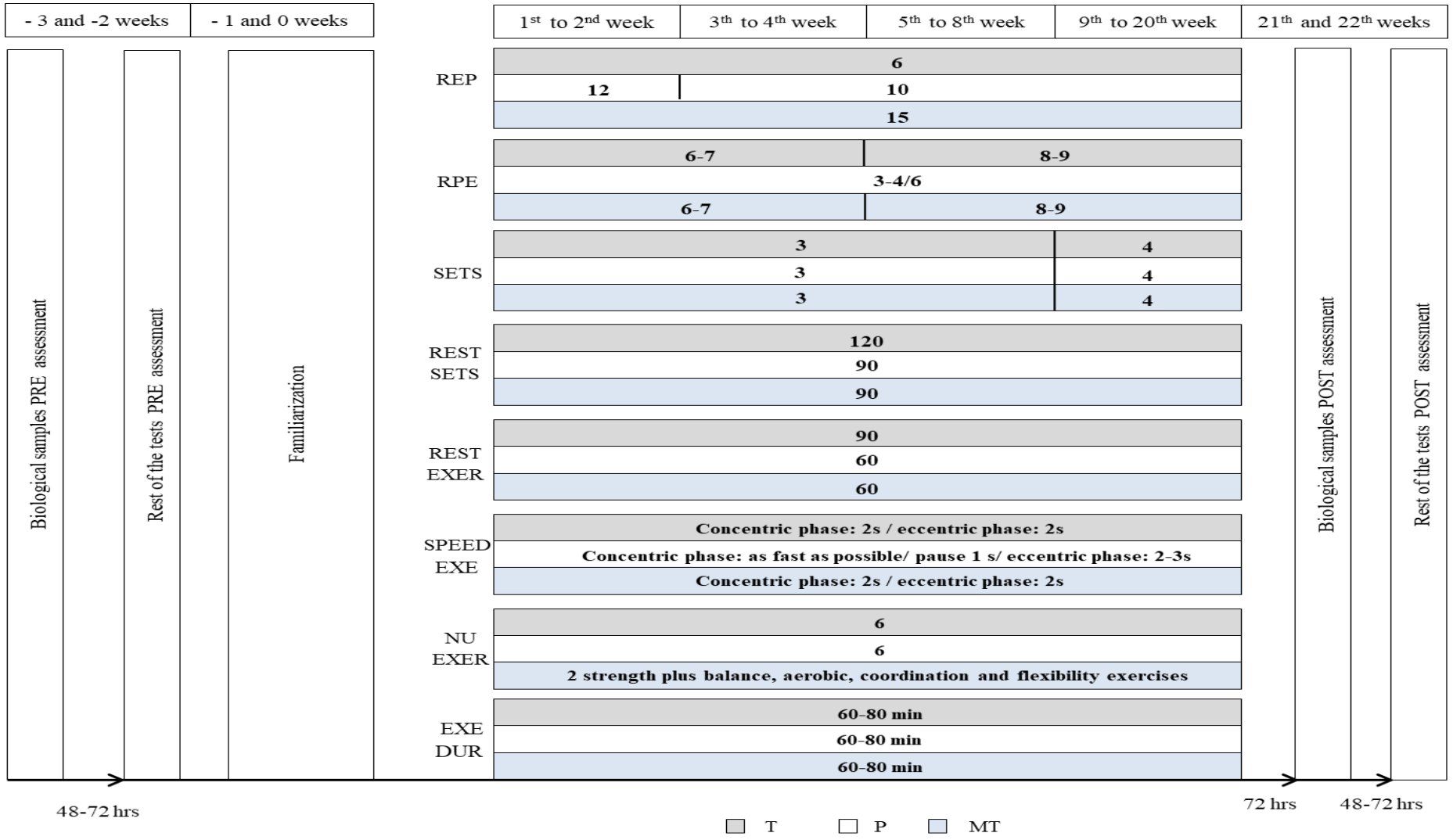


Figure 99. *Experimental design with a schematic diagram of the training parameters progression during the study along with the timing of the evaluations.*



IV.II.VI. Statistical analysis of both projects

Following the Consolidated Standards of Reporting Trials (CONSORT) guidelines on the reporting of RCTs (Hollis & Campbell, 1999; Moher et al., 2001), the results were first analyzed in accordance with the principle of the intention-to-treat analysis (ITT), whereby the baseline measurement for each individual who withdrew from the study was carried forward to the post-intervention phase (Gupta, 2011). With this approach, overoptimistic estimates of the efficacy of an intervention as a result of removing non-compliers and dropouts are avoided, as it admits noncompliance and protocol deviations. The ITT analysis provides an unbiased estimate of the efficacy of the intervention.

According to previous research and guidelines (Day, 2018), in addition to the ITT analyses, efficacy or per-protocol analyses (PPAs) of the training programs were also carried out as a secondary support of the ITT approach for all the variables and all the individuals who completed the trial regardless of their compliance with the training sessions. To facilitate the reading and analysis of the results, and because there was no major differences between the analyses, only the ITT results are provided in the Chapter V (Results and Discussion), along with the differences between the two types of analyses when applicable. Meanwhile, the PPA results are presented in the Chapter XII (Supplementary Material).

Data distribution was tested with the Kolmogorov–Smirnov test and a box-plot analysis, while the homogeneity of the variance was tested through the Levene test. Variables that were not normally distributed were transformed using the natural logarithm (log10). Outliers were determined using exploratory data analysis, which identifies real/severe and potential/non-severe outliers. If severe outliers (greater than three SDs from the mean) were detected, trimming (when there was strong reason to believe that it was a mistake) and winsorization (replacing the score with the means plus two times the SD) processes were

carried out (Field, 2009; Hoaling & Iglewicz, 1987). Potential outliers (greater than 1.5 SDs from the mean) were not statistically treated.

A one-way analysis of variance (ANOVA) was performed to assess differences between the groups at baseline. A two-way ANOVA for repeated measures with experimental groups (first project: HI, M, C; second project: MT, P, T, C) and timeframe (first project: pre- and post-test or pre- and inter-test; second project: pre- and post-test) as factors, followed by Bonferroni corrections, was used to examine time, group, and interaction effects through within- and between-group comparisons.

In addition, although there were no statistical differences between the groups at baseline for most of the dependent variables, a two-way analysis of covariance (ANCOVA) for repeated measures was used on all outcome variables to correct for initial group differences at the conclusion of the study, using baseline values as covariates and adjusting for age. Pre-test values were used as covariates to improve precision and control for possible imbalances during the randomization process and between baseline values (Senn, 2013; Van Breukelen, 2006; Van Breukelen & VanDijk, 2007; Vickers & Altman, 2001). This is the preferred approach for analyzing randomized trials with baseline and follow-up measurements, because it corrects for baseline values (Vickers and Altman 2001) and eliminates any possible influences of initial score variances on training outcomes. When the F-ratio was significant, the 95% confidence interval was used to determine whether a significant difference existed between the adjusted ANCOVA means pre- and post-training or pre- and inter-training as well as the post-training differences among groups, and Bonferroni's test was used for post-hoc comparisons.

The Cohen's d effect size (ES) was calculated according to the methodological procedures defined by Cohen (2013) for the between-groups analysis of the post-training

measurements and for the pre- and post-training measurements of all the groups. An ES of less than 0.2 is considered a "trivial" effect, between 0.20–0.49 a "small" effect, between 0.50–0.79 a "moderate" affect, and in excess of 0.80 a "large" effect (Cohen, 1988). Effect sizes indicate the effectiveness of a treatment and help to assess whether a statistically significant difference is of practical concern. Within-group ESs were calculated as the post-training mean minus the pre-training mean divided by the pooled SD of the pre-training data (Cohen, 1988), while between-group ESs were determined as follows: ES = ME – MC/SDC, where ME is the post-training-period mean of the experimental group, MC is the post-training-period mean of the control group, and SDC is the post-training SD of the control group (Martins et al., 2015). A partial eta squared (η^2) was also calculated to determine the magnitude of the ESs, and it can be interpreted as "small" (0.08), "medium" (0.18), or "large" (0.41; Morris & Fritz, 2013).

The delta percentage (Δ%) was calculated with the standard formula: change (%) = [(posttest score − pretest score)/pretest score] × 100. A 95% confidence level (significance level $p < 0.05$) is accepted as statistically significant.

The ICC estimates (test-retest, intra-rater, and inter-rater reliabilities) and their 95% CIs were calculating based on single-rating, absolute-agreement, and two-way mixed-effects model for the test-retest and intra-rater reliabilities, and they are based on the mean-rating ($k = 3$), absolute-agreement, and two-way mixed-effects model for the inter-rater reliability (Ko & Li, 2015). The short-term CV and intra-assay variation were calculated by dividing the SD of the observations or measurements by the seat mean and multiplying by 100. The average of the individual CVs is denoted as the intra-assay or short-term CV.

The statistical analyses were performed using commercial software (SPSS, Version 25.0; SPSS Inc., Chicago, IL). All data are reported as the means + the SD. Confidence

intervals were used to indicate the clinical importance of the results and represent the range within which the true magnitude of the effect lies (Petrie & Sabin, 2007; Wright, 2003). A wide interval indicates that the estimate is imprecise, whereas a narrow one indicates a precise estimate. Statistical significance was set at $p \leq 0.05$. Trends were reported when *p*-values were greater than 0.05 and less than 0.120. To calculate the required sample size for both studies, an a priori power analysis was performed with the G*Power program (v. 3.1.5.1). The results of both studies are reported in accordance with CONSORT (CONSORT statement, 2017).

CHAPTER V[18]

Results and discussion

[18] Partially based on:

1. Gargallo, P., Colado, J. C., Juesas, A., Hernando-Espinilla, A., Estañ-Capell, N., Monzó-Beltran, L., García-Pérez, P., Cauli, O., & Sáez, G. T. (2018). The effect of moderate-versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing, 20*(2), 205-217. https://doi.org/10.1177/1099800417753877

2. Flández, J., Gene-Morales, J., Modena, N., Martin, F., Colado, J. C., & Gargallo, P. (2020). Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women. *Journal of Human, Sport and Exercise, 15*(4), S000-S010. http://dx.doi.org/10.14198/jhse.2020.15.Proc4.30

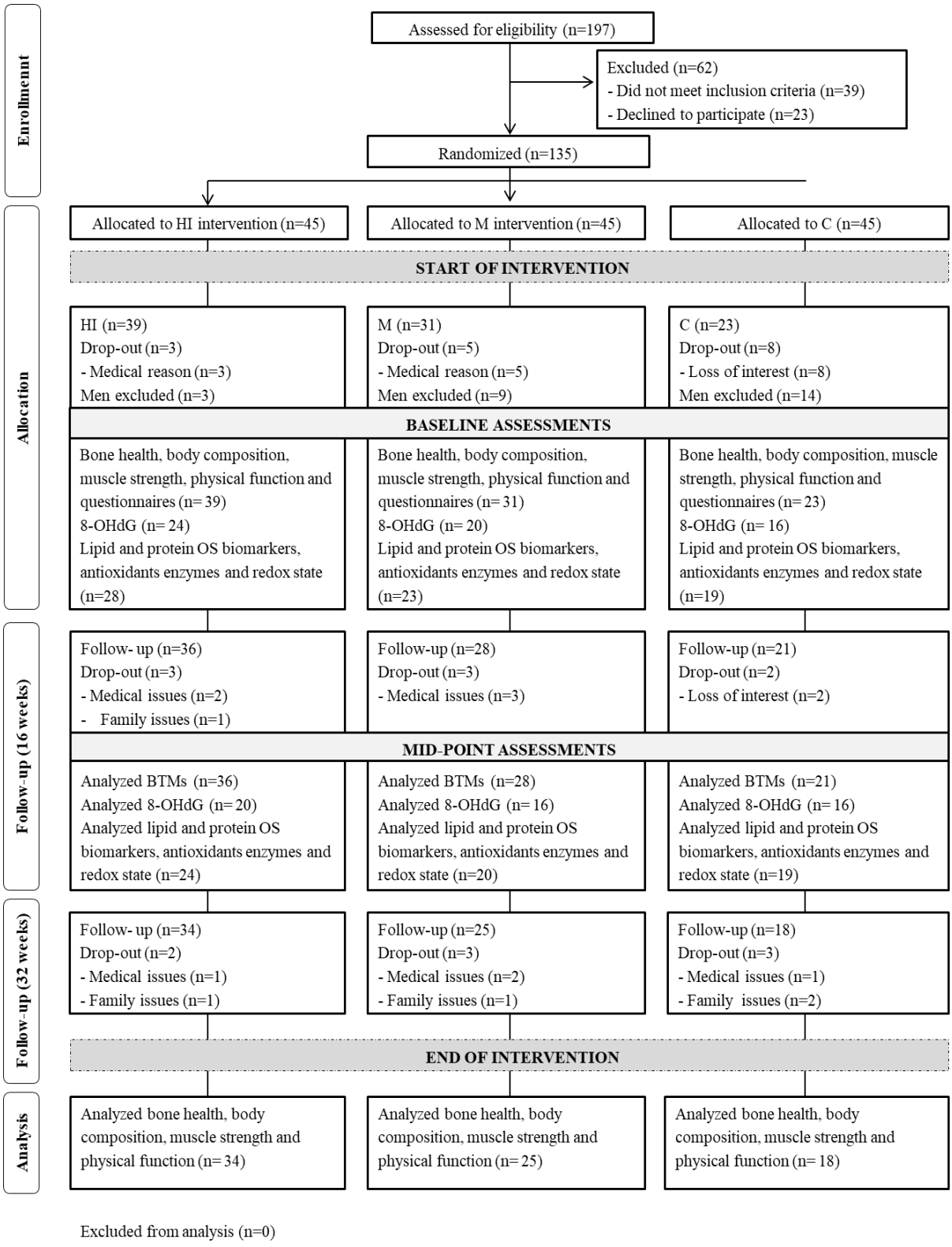
V.I. PARTICIPANT FLOW AND SAMPLE CHARACTERISTICS

V.I.I. Project one

Details of the participant flow throughout the study are displayed in Figure 100. As mentioned in the Chapter IV, men were also included in the study, but for the analysis of this PhD dissertation, they were excluded with the intention of focusing more deeply on the effects of the female population at the parameters finally selected. In addition, because the very low number of men in the HI group (n = 3) could have affected the detection of differences between groups with the level of confidence and statistical power in the present study, and the results could be strongly influenced by chance, we decided to exclude men from the analyses presented here. Furthermore, the unequal sample sizes between groups in the case of men (HI: n = 3; M: n = 9; and C: n = 14) would dramatically decrease statistical power and increase Type I error rates (Rusticus & Lovato, 2014), which was our other reason for excluding them.

Additionally, due to the high cost of oxidative stress biomarkers (particularly 8-oxo-dG) and the lack of funding, it was not possible to analyze the oxidative stress biomarkers in the entire sample at 16 and 32 weeks. Lipid and protein oxidative stress biomarkers, antioxidant enzymes, and redox states were analyzed in a higher proportion of subjects than 8-oxo-dG, due to their lower cost. The samples were equally distributed among the groups according to the proportion of women who were initially assigned to each group (HI > M > C), with the intention of also making the sample size as similar as possible between the three groups with respect to the initial ratios. The assessment of oxidative stress biomarkers was only possible up to Week 16, due to a lack of funding for assessments at the end of the training period. In the case of BTMs, due to their low cost, it was possible to analyze the entire study population in the middle and at end of the training period.

Figure 100. *Flowchart of participation.*



Note. HI: high-intensity grou; M: moderate-intensity group; C: control group; OS: oxidative stress; BTMs: bone turnover markers; 8-oxo-dG: 8-oxo-2' –deoxyguanosine.

From the local community, a total of 197 subjects (160 women) responded to the recruitment notices. Of the 160 women, 51 were excluded. Nineteen declined to participate upon receiving a detailed description of the commitments of the study, and 32 did not meet the eligibility requirements for the following reasons: Parkinson's disease (n = 3), multiple sclerosis (n = 2), ongoing treatment with specific medications [diuretic (n = 4), hormone replacement therapy (n = 5), and corticosteroids (n = 6)], age below 60 years (n = 2), MMSE below 23 (n = 1), engagement in regular strength training (n = 2), plans to leave the area during the intervention for a long period (n = 1), and inability to commit due to scheduling conflicts and time constraints (n = 6). There was a good recruitment rate for participants (109/160 = around 70%). Of the 109 women (135 total participants including men) eventually randomized into the three groups (HI = 42; M = 36; C = 31), 93 started the intervention (HI = 39; M = 31; C = 23), and 77 finished the eight-month study (HI = 34; M = 25; C = 18). Further details about dropout and exclusion are provided in Section V.II.I. An outline of the participant flowchart from recruitment to final analysis is displayed in Figure 100.The baseline participant characteristics (demographic indicators and other descriptive parameters) of the subjects by group and of the entire sample are detailed in Table 19. There were no significant differences ($p > 0.05$) between the groups at baseline in terms of sample characteristics. In addition, there were significant differences between the groups at baseline in 8-oxo-dG (HI vs M; M vs C), 10-year probability of a major osteoporotic fracture (HI vs M; M vs C), 10-year probability of a hip fracture (HI vs M), isokinetic hip abduction strength at 180°/s (HI vs M; HI vs C) and 60°/s (HI vs M; HI vs C), isokinetic knee flexion (HI vs C) and extension (HI vs M; HI vs C) strength at 180°/s, isokinetic elbow flexion strength at 60°/s (HI vs M), elbow extension at 180°/s (HI vs M; HI vs C) and 60°/s (HI vs M), 30sec-CS (HI vs C; M vs C), 30sec-AC (HI vs C), and in 6MWT (M vs C). For the rest of the parameters, no significant differences between the groups were found at baseline.

Table 19. *Baseline characteristics.*

	HI (*n* = 39)	M (*n* = 31)	C (*n* = 23)	All (*n* = 93)
Demographics				
Age				
Total, mean ± SD [95%CI]	71.10 ± 5.44 [69.34–72.87]	68.56 ± 6.03 [66.39–70.74]	69.83 ± 7.65 [66.52–73.14]	69.93 ± 6.27 [68.64–71.21]
<69, n (%)	15 (38.4)	20 (64.5)	11 (47.8)	46 (49.4)
>70, n (%)	24 (61.5)	11 (35.4)	12 (52.1)	47 (50.5)
Ethnicity or race, n (%)				
Caucasian	30 (76.9)	25 (80.6)	17 (73.9)	72 (77.4)
Non-hispanic	3 (7.6)	-	-	3 (3.2)
Latino	3 (7.6)	2 (6.4)	5 (21.7)	10 (10.7)
Asian	1 (2.5)	-	-	1 (1)
Indian	-	-	1 (4.3)	1 (1)
African/caribbean	-	2 (6.4)	-	2 (2.1)
Education level, n (%)				
No education	-	4 (12.9)	5 (21.7)	9 (9.6)
<High school (primary)	8 (20.5)	6 (19.3)	5 (21.7)	19 (20.4)
High School (secondary)	14 (35.8)	10 (32.2)	8 (34.7)	32 (34.4)
Vocational	9 (23)	5 (16.1)	4(17.3)	18 (19.3)
University<4 yr (tertiary) (pre-U/diploma)	7 (17.9)	6 (19.3)	1 (4.3)	14 (15)
University ≥ 4yr (tertiary) (degree and above)	1 (2.5)	-	-	1 (1)
Living situation, n (%)				
Alone	9 (23)	6 (19.3)	4 (17.3)	19 (20.4)
With partner	26 (66.6)	23 (74.1)	16 (69.5)	65 (69.8)
With family (children and others)	4 (10.2)	2 (6.4)	3 (13)	9 (9.6)
Marital status, n (%)				
Single (never married)	1 (2.5)	3 (9.6)	1 (4.3)	5 (5.3)
Married	29 (74.3)	22 (70.9)	13 (56.5)	64 (68.8)
Separated	1 (2.5)	1 (1)	2 (8.6)	4 (4.3)
Divorced	2 (5.1)	1 (1)	2 (8.6)	5 (5.3)
Widowed	6 (15.3)	4 (4.3)	5 (21.7)	15 (16.1)
Employment status, n (%)				
Employed	6 (15.3)	4 (12.9)	3 (13)	13 (13.9)
Retired	10 (25.6)	3 (9.6)	4 (17.3)	17 (18.2)
Full time student /voluntary work / unemployed	3 (7.6)	4 (12.9)	2 (8.6)	9 (9.6)
At home doing housework /caring for family	20 (51.2)	19 (61.2)	12 (52.1)	51 (54.8)
Unemployed due to sickness /disability	-	1 (3.2)	2 (8.6)	3 (3.2)

Table 19. *Continued.*

	HI (*n* = 39)	M (*n* = 31)	C (*n* = 23)	All (*n* = 93)
Anthropometry				
Height (cm), mean ± SD [95%CI)]	152.82 ± 4.59 [151.33–154.31]	153.36 ± 6.09 [151.16–155.55]	152.30 ± 5.06 [150.12–154.49]	152.88 ± 5.21 [151.81–153.95]
Body mass (kg), mean ± SD [95%CI)]	64.89 ± 10.08 [61.72–68.07]	67.35 ± 10.68 [63.79–70.91]	66.50 ± 8.75 [62.37–70.64]	66.05 ± 9.90 [64.02–68.08]
% body fat (%), mean ± SD [95%CI)]	42.83 ± 4.48 [41.40–44.27]	44.47 ± 4.38 [42.86 –46.08]	43.76 ± 4.71 [41.90–45.63]	43.59 ± 4.49 [42.67–44.51]
BMI (Kg/m^2), mean ± SD [95%CI)]	28.19 ± 3.99 [26.90–29.29]	29.08 ± 4.78 [27.35–30.80]	29.03 ± 4.01 [27.29–30.76]	28.70 ± 4.25 [27.83–29.57]
BMI classification[a], n (%)				
Obese (BMI: ≥30)	15 (38.4)	11 (35.4)	11 (47.8)	37 (39.7)
Overweight (BMI: 25-29.9)	15 (38.4)	15 (48.3)	10 (43.4)	40 (43)
Normal weight (BMI: 18.5-24.99)	9 (23.0)	5 (16.1)	3 (13)	17 (18.2)
Underweight (BMI: ≤ 18.49)	-	-	-	-
Percentage body mass classification[b], n (%)				
Obese (%: ≥ 43)	22 (56.4)	20 (64.5)	15 (65.2)	57 (61.2)
Overweight (%: 38-42.9)	14 (35.8)	7 (22.5)	6 (26)	27 (29)
Normal weight (%: 25-37.9)	3 (7.6)	4 (12.9)	2 (8.6)	9 (9.6)
Underweight (%: ≤ 24.9)	-	-	-	-
aBMD classification[c], n (%)				
Osteoporosis	7 (17.9)	9 (29)	7 (30.4)	23 (24.7)
Osteopenia	23 (58.9)	16 (51.6)	10 (43.4)	49 (52.6)
Normal	9 (23)	6 (19.3)	6 (26)	21 (22.5)
Others body composition disorders, n (%)				
Sarcopenic[d]	10 (25.6)	9 (29)	3 (13)	22 (23.6)
No sarcopenic	29 (74.3)	22 (70.9)	20 (86.9)	71 (76.3)
Sarcopenic obesity[e]	20 (51.2)	16 (51.6)	9 (39.1)	45 (48.3)
No sarcopenic obesity	19 (48.7)	15 (48.3)	14 (60.8)	48 (51.6)
Sarcopenic obesity[f]	12 (30.7)	9 (29)	4 (17.3)	25 (26.8)
No sarcopenic obesity	27 (69.2)	22 (70.9)	19 (82.6)	67 (72)
Osteopenic/osteoporotic[g] obesity	30 (76.9)	25 (80.6)	19 (82.6)	74 (79.5)
No osteopenic/osteoporotic obesity	9 (23)	6 (19.3)	4 (17.3)	19 (20.4)
Osteosarcopenic[h] obesity	9 (23)	9 (29)	2 (8.6)	20 (21.5)
No osteosarcopenic obesity	30 (76.9)	22 (70.9)	21 (91.3)	73 (78.4)

Table 19. *Continued.*

	HI (*n* = 39)	M (*n* = 31)	C (*n* = 23)	All (*n* = 93)
Healh status				
Comorbidities, n (%)				
0-1	18 (46.1)	17 (54.8)	13 (56.5)	48 (51.6)
2-3	15 (38.4)	9 (29)	5 (21.7)	29 (31.1)
≥4	6 (15.3)	5 (16.1)	5 (21.7)	16 (17.2)
Prescribed medication, n (%)				
0-1	20 (51.2)	20 (64.5)	12 (52.1)	52 (55.9)
2-3	14 (35.8)	6 (19.3)	8 (34.7)	28 (30.1)
≥4	5 (12.8)	5 (16.1)	3 (13)	13 (13.9)
Smoking, n (%)				
Current	11 (28.2)	9 (29)	10 (43.4)	30 (32.2)
Past (ex-smoker)	8 (20.5)	2 (6.4)	3 (13)	13 (13.9)
Never (non-smoker)	20 (51.2)	20 (64.5)	10 (43.4)	50 (53.7)
Alcohol drinkers, n (%)				
Past	4 (10.2)	2 (6.4)	2 (8.6)	8 (8.6)
Current	2 (5.1)	1 (3.2)	-	3 (3.2)
Non-user	33 (84.6)	28 (90.3)	19 (82.6)	80 (86)
Type of assistive devices, n (%)				
None	38 (97.4)	31 (100)	22 (95.6)	91 (97.8)
Cane	1 (2.5)	-	1 (4.3)	2 (2.1)
Walker	-	-	-	-
Questionnaires				
BADLs[i], mean ± SD [95%CI]	93.59 ± 16.26 [88.32–98.86]	96.88 ± 5.49 [94.89–98.86]	97.17 ± 4.72 [95.13–99.22]	95.59 ± 11.23 [93.28–97.89]
IADLs[j], mean ± SD [95%CI]	7.46 ± 1.58 [6.95–7.98]	7.94 ± 0.24 [7.85–8.03]	7.78 ± 0.60 [7.52–8.04]	7.70 ± 1.08 [7.48–7.92]
Cognitive status[k], mean ± SD [95%CI]	29.79 ± 0.52 [29.63–29.96]	29.75 ± 0.56 [29.55–29.95]	29.74 ± 0.54 [29.51–29.97]	29.77 ± 0.53 [29.66–29.88]

Note. HI; high-intensity group; M: moderate-intensity group; C: control group; SD: standard deviation; CI: coefficient interval; yr: year; BMI: body mass index; aBMD: areal bone mineral density; BADLs: basic activities of daily living; IADLs:instrumental activities of daily living; **a:** BMI-referenced classification provided by the WHO (WHO, 2000); **b:** classification of percentage of fat mass in base of the cut-off points by sex, age, and ethnicity published by Gallagher et al. (2000) (Gallagher et al., 2000); **c:** classification of aBMD according to the WHO definition (Kanis, 1994) (osteoporosis: T-score of lumbar spine and /or proximal femur: ≤ - 2.5; osteopenia: T-score of lumbar spine and/or proximal femur: -1 to -2.49; normal aBMD: T-score of lumbar spine and/or proximal femur: ≥ 0.99); **d:** classification of sarcopenia adapted from Cruz-Jentoft et al. (2019) and Baumgartner et al. (1999) where the ASM, which is the sum of arm and leg muscle mass, adjusted by squared height, have to be lower than < 5.45 or 5.50 kg/m² in women (Baumgartner et al.,1999; Cruz-Jentoft et al., 2019); **e:** classification of sarcopenic obesity in base on NHANES III criteria (ASM < 6.53 and % of body mas > 40.01) (Davison et al., 2002); **f:** classification of sarcopenic obesity in base on NEW MEXICO study criteria (ASM < 5.45 and % of body mas > 38) (Baumgartner, 2000); **g:** classification of osteopenic/osteoporotic obesity in base on Ilich et al., (2015) (T-score of lumbar spine and/or proximal femur: < -1 and & body fat > 32); **h:** classification of osteosarcopenic obesity in base on Ilich et al., (2015) (T-score of lumbar spine and/or proximal femur: < -1, body fat > 32 and ASM < 5.45); **i:** in base on Barthel index (Mahoney& Barthel, 1965); **j:** in base on Lawton and Brody scale (Lawton & Brody, 1969); **k:** in base on MMSE (Folstein et al., 1975).

Briefly, all subjects were older women between the ages of 60 and 88 years (HI: 60–83; M: 60–84; C: 60–88). The majority of participants were married, Caucasian, with secondary studies, living with partners, and working at home doing housework and caring for their families. Based on BMIs assessed by DXA, 61.2% of the women can be classified as overweight or normal weight, while 39.7% of the participants were obese (BMI-referenced cut-off points provided by the WHO, 2000). Taking into account that the mean BMI value of the Spanish population over 65 years of age is 28.3 kg/m^2 for healthy older adults (Mera-Gallego et al., 2017), the sample of this study is representative of the target population in terms of body composition, as the total BMI was only 0.4 points above the Spanish average (28.7 ± 4.25). However, if we take into account the percentage of body mass, the 61.2% exceed the cut-off point of 43% of body fat that determine obesity in older women (Gallagher et al., 2000). Thus, the sample can be classified as overweight to mildly obese at baseline. Moreover, 77.3% showed low BMD at the lumbar spine or proximal femur based on WHO's classification system (Kanis, 1994). Meanwhile, 23% had sarcopenia, only if we consider the cut-off values for appendicular skeletal mass proposed by Baumgartner et al. (1999) and Cruz-Jentoft et al. (2019), not strength or functional measures. There were no sarcopenic women if we include the functional outcomes (e.g. grip strength). A combination of two to all of these pathologic conditions (high body fat, low BMD, and low muscle mass) was present among 20–80% of the women.

With regard to health status, the number of comorbid conditions most frequency reported were: hypertension, osteoporosis, obesity, hypercholesterolemia, osteoarthritis, arthritis, and mild chronic neuromuscular pain. Half of the total sample took zero or one prescribed medication and never smoked, and only a small proportion of the participants had a history of alcohol use. All the women presented high independence and autonomy, as

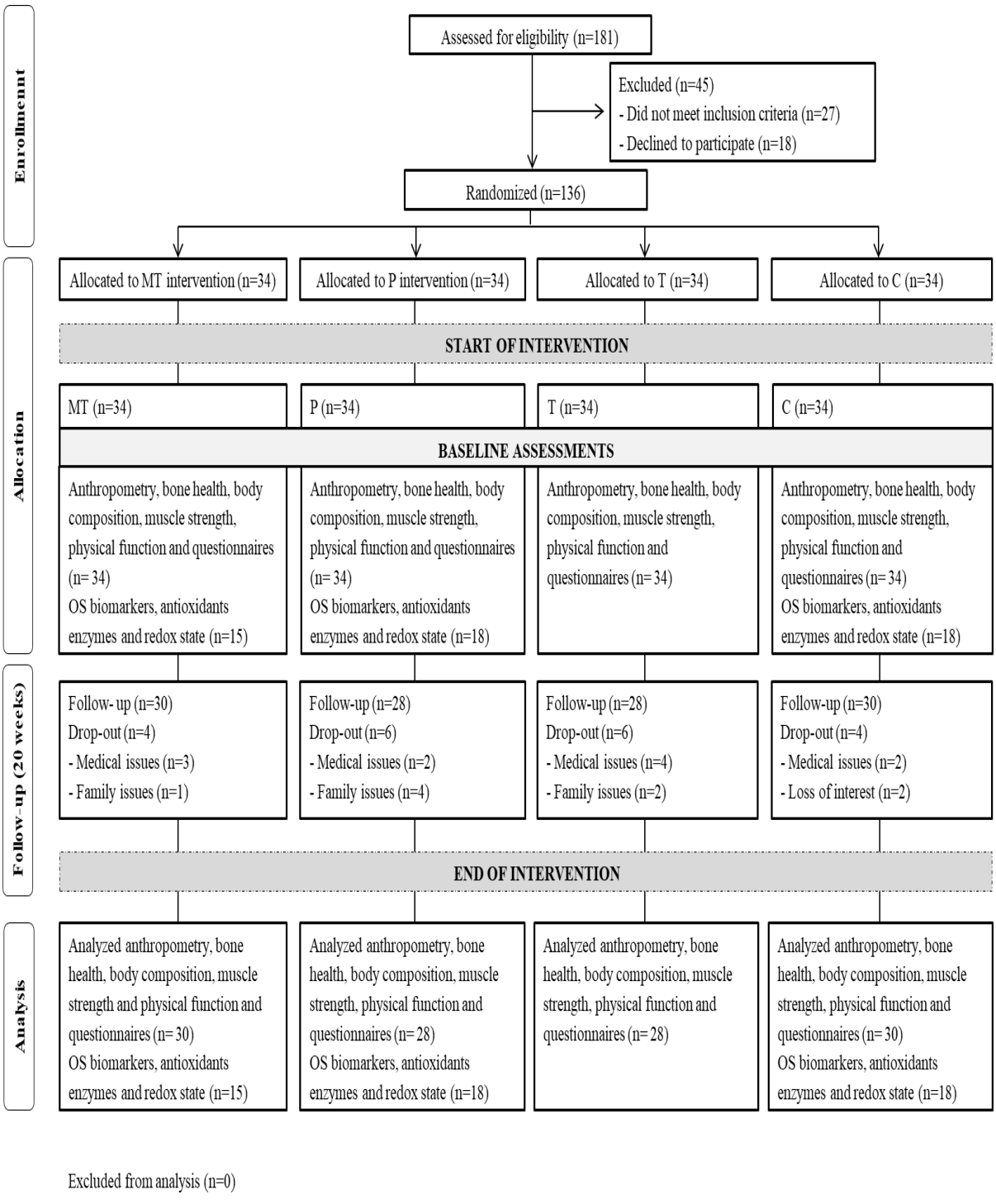
reported by the BADLs, IADLs, and the assistive devices needed for ambulation. In addition, they all had normal cognitive statuses (>24).

V.I.II. Project two

Details of the participant flow throughout the study are displayed in Figure 101. Due to the high cost of oxidative stress biomarkers and the lack of funding, it was not possible to analyze these biomarkers in all the groups and in the entire sample. Since multi-component and power strength trainings are recent exercise modalities, and, according to the current scientific literature, they may have a greater benefit in the elderly population than traditional resistance training regimes, the MT and P groups were eventually selected to analyze oxidative stress against the T group.

From the local community, a total of 181 women responded to the recruitment notices. Among them, 45 were excluded. Eighteen declined to participate upon receiving a detailed description of the commitments of the study, and 27 did not meet the eligibility requirements for the following reasons: severe cardiovascular problems (n = 4), severe neurological disorders (n = 3), chronic renal failure (n = 1), ongoing treatment with specific medications [diuretic (n = 2), hormone replacement therapy (n = 3), and corticosteroids (n = 2)], physical dependence (n = 2), age below 60 years (n = 2), MMSE below 23 (n = 1), engagement in regular strength training (n = 2), plans to leave the area during the intervention for a long period (n = 2), and inability to commit due to scheduling conflicts or time constraints (n = 3). There was a good recruitment rate for participants (136/181 = 75%). The 136 women were randomized into the four groups (MT = 34; P = 34; T = 34; C = 34), and 116 finished the five-month study (MT = 30; P = 28; T = 28; C = 30). Further details about dropout and exclusion are provided in Section V.II.II. An outline of the participant flowchart from recruitment to final analysis is displayed in Figure 101.

Figure 101. *Flowchart of participation.*



Note. MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; OS: oxidative stress.

The baseline participant characteristics (demographic indicators and other descriptive parameters) of the subjects by group and of the entire sample are detailed in Table 20. There were no significant differences ($p > 0.05$) between the groups at baseline in terms of sample characteristics. In addition, there were significant differences between the groups at baseline in total glutathione (MT vs T), 10-year probability of a hip fracture (MT vs T) and OC (MT vs C; P vs C). No other significant baseline differences between the groups were found.

Briefly, all subjects were older women between the ages of 60 and 82 years (MT: 61–81; P: 60–82; T: 61–75; C: 61–78). Most of the subjects were married, Caucasian, with vocational and secondary studies, living with their partner, and working at home doing housework and caring for family. Based on the BMIs assessed by DXA, three-quarters were overweight or obese; the overweight group was the largest, followed by obese and normal weight women (BMI-referenced cut-off points provided by the WHO, 2000). In this project, the sample was below the mean BMI value of the Spanish population of healthy older adults (27.44 kg/m^2 vs 28.3 kg/m^2), and it can be categorized as an overweight sample. However, if we take into account the percentage body fat, more than 50% of the participants exceeded the cut-off point of 43% body fat that determines the obesity condition in older women (Gallagher et al., 2000). Furthermore, 85.2% of the women had waist circumferences greater than 88 cm, which is the cut-off point for obesity in women. Thus, based on the three available body-composition indicators, the sample can be classified as overweight to obese at baseline. Moreover, around 70% of the women showed low BMDs at the lumbar spine or proximal femur, based on the WHO taxonomy (Kanis, 1994). Meanwhile, 30% had sarcopenia, only if we consider the cut-off values of appendicular skeletal mass proposed by Baumgartner et al. (1999) and Cruz-Jentoft et al. (2019), not the strength or functional measures.

Table 20. *Baseline characteristics.*

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)	All (*n* = 136)
Demographics					
Age					
Total, mean ± SD [95%CI]	69.15 ± 4.78 [67.48–70.82]	67.79 ± 5.27 [64.95–69.94]	66.44 ± 3.45 [65.23–67.65]	68.50 ± 5.15 [66.70–70.30]	67.97 ± 4.77 [67.16–68.78]
<69, n (%)	23 (67.6)	25 (73.5)	26 26 (76.4)	22 (67.7)	96 (70.5)
>70, n (%)	11 (32.3)	9 (26.4)	8 (23.5)	12 (35.2)	40 (29.4)
Ethnicity or race, n (%)					
Caucasian	30 (88.2)	28 (82.3)	28 (82.3)	30 (88.2)	116 (85.2)
Non-hispanic	-	1 (2.9)	-	-	1 (0.7)
Latino	3 (8.8)	4 (11.7)	5 (14.7)	4 (11.7)	16 (11.7)
Asian	1 (2.9)	-	-	-	1 (0.7)
Indian	-	1 (2.9)	-	-	1 (0.7)
African/caribbean	-	-	1 (2.9)	-	1 (0.7)
Education level, n (%)					
No education	1 (2.9)	-	2 (5.8)	1 (2.9)	4 (2.9)
<High school (primary)	6 (17.6)	4 (11.7)	4 (11.7)	7 (20.5)	21 (15.4)
High School (secondary)	7 (20.5)	12 (35.2)	14 (41.1)	10 (29.4)	43 (31.6)
Vocational	12 (35.2)	11 (32.3)	8 (23.5)	9 (26.4)	40 (29.4)
University<4 yr (tertiary) (pre-U/diploma)	8 (23.5)	6 (17.6)	4 (11.7)	5 (14.7)	23 (16.9)
University ≥ 4yr (tertiary) (degree and above)	-	1 (2.9)	2 (5.8)	2 (5.8)	5 (3.6)
Living situation, n (%)					
Alone	5 (14.7)	6 (17.6)	7 (20.5)	8 (23.5)	38 (27.9)
With partner	26 (76.4)	25(73.5)	23(67.6)	21 (61.7)	83 (61)
With family (children and others)	3 (8.8)	3 (8.8)	4 (11.7)	5 (14.7)	15 (11)
Marital status, n (%)					
Single (never married)	1 (2.9)	2 (5.8)	2 (5.8)	1 (2.9)	6 (4.4)
Married	24 (70.5)	23 (67.6)	21 (61.7)	22 (67.7)	90 (66.1)
Separated	1 (2.9)	1 (2.9)	-	1 (2.9)	3 (2.2)
Divorced	2 (5.8)	1 (2.9)	2 (5.8)	3 (8.8)	8 (5.8)
Widowed	6 (17.6)	7 (20.5)	7 (20.5)	9 (26.4)	29 (21.32)
Employment status, n (%)					
Employed	2 (5.8)	3 (8.8)	1 (2.9)	2 (5.8)	8 (5.8)
Retired	6 (17.6)	8 (23.5)	6 (17.6)	5 (14.7)	25 (18.3)
Full time student /voluntary work / unemployed	3 (8.8)	5 (14.7)	2 (5.8)	6 (17.6)	16 (11.7)
At home doing housework /caring for family	22 (67.7)	16 (47)	24 (70.5)	20 (58.8)	82 (60.2)
Unemployed due to sickness /disability	1 (2.9)	2 (5.8)	1 (2.9)	1 (2.9)	5 (3.6)

Table 20. Continued.

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)	All (*n* = 136)
Anthropometry					
Height (cm), mean ± SD [95%CI)]	158.73 ± 7.54 [156.1–161.37]	152.44 ± 5.81 [150.4–154.4]	154.51 ± 5.27 [152.6–156.3]	156.75 ± 6.12 [154.6–158.88	155.61 ± 6.61 [154.4–156.7]
Body mass (kg), mean ± SD [95%CI)]	69.64 ± 13.39 [65.96–73.31]	66.32 ± 10.14 [62.65–69.99]	68.50 ± 10.26 [64.83–72.17]	71.19 ± 8.99 [67.52–74.87]	68.91 ± 10.84 [67.07–74.87]
% body fat (%), mean ± SD [95%CI)]	42.76 ± 4.36 [41.22–44.30]	42.53 ± 3.91 [40.99–44.07]	43.91 ± 5.54 [42.37–45.45]	43.31 ± 4.17 [41.77–44.85]	43.13 ± 4.52 [42.36–43.89]
BMI (Kg/m^2), mean ± SD [95%CI)]	27.48 ± 4.46 [25.93–29.04]	28.63 ± 4.70 [26.99–30.28]	28.67 ± 4.13 [27.22–30.11]	28.96 ± 4.08 [27.53–30.38]	27.44 ± 4.34 [27.70–29.17]
BMI classification[a], n (%)					
Obese (BMI: ≥30)	7 (20.5)	13 (38.2)	13 (38.2)	13 (38.2)	46 (33.8)
Overweight (BMI: 25-29.9)	15 (44.1)	14 (41.1)	14 (41.1)	14 (41.1)	57 (41.9)
Normal weight (BMI: 18.5-24.99)	12 (35.2)	7 (20.5)	7 (20.5)	7 (20.5)	33 (24.2)
Underweight (BMI: ≤ 18.49)	-	-	-	-	-
Percentage body mass classification[b], n (%)					
Obese (%: ≥ 43)	15 (44.1)	16 (47)	21 (61.7)	22 (64.7)	74 (54.4)
Overweight (%: 38-42.9)	14 (41.1)	13 (38.2)	7 (20.5)	6 (17.6)	40 (29.4)
Normal weight (%: 25-37.9)	5 (14.7)	5 (14.7)	6 (17.6)	6 (17.6)	22 (16.1)
Underweight (%: ≤ 24.9)	-	-	-	-	-
Waist circumference classification[c], n (%)					
Obese (cm: ≥ 88)	27 (79.4)	28 (82.3)	30 (88.2)	31 (91.1)	116 (85.2)
Overweight (cm: 80-87.9)	5 (14.7)	4 (11.7)	3 (8.8)	2 (5.8)	14 (10.2)
Normal weight (cm: ≤ 79.9)	2 (5.8)	2 (5.8)	1 (2.9)	1 (2.9)	6 (4.4)
aBMD classification[d], n (%)					
Osteoporosis	12 (35.2)	3 (8.8)	6 (17.6)	3 (8.8)	24 (17.6)
Osteopenia	13 (38.2)	21 (61.7)	18 (52.9)	21 (61.7)	73 (53.6)
Normal	9 (26.4)	10 (29.4)	10 (29.4)	10 (29.4)	39 (28.6)
Others body composition disorders, n (%)					
Sarcopenic[e]	15 (44.1)	7 (20.5)	8 (23.5)	11 (32.3)	41 (30.1)
No sarcopenic	19 (55.8)	27 (79.4)	26 (76.4)	23 (67.6)	95 (69.8)
Sarcopenic obesity[f]	23 (67.6)	23(67.6)	19 (55.8)	19 (55.8)	84 (61.7)
No sarcopenic obesity	11 (32.3)	11 (32.3)	15 (44.1)	15 (44.1)	52 (38.2)
Sarcopenic obesity[g]	16 (47)	8 (23.5)	11 (32.3)	11 (32.3)	46 (33.8)
No sarcopenic obesity	18 (52.9)	26 (76.4)	23 (67.6)	23 (67.6)	90 (66.1)

Table 20. *Continued*.

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)	All (*n* = 136)
Anthropometry					
Others body composition disorders, n (%)					
Sarcopenic[e]	15 (44.1)	7 (20.5)	8 (23.5)	11 (32.3)	41 (30.1)
No sarcopenic	19 (55.8)	27 (79.4)	26 (76.4)	23 (67.6)	95 (69.8)
Sarcopenic obesity[f]	23 (67.6)	23(67.6)	19 (55.8)	19 (55.8)	84 (61.7)
No sarcopenic obesity	11 (32.3)	11 (32.3)	15 (44.1)	15 (44.1)	52 (38.2)
Sarcopenic obesity[g]	16 (47)	8 (23.5)	11 (32.3)	11 (32.3)	46 (33.8)
No sarcopenic obesity	18 (52.9)	26 (76.4)	23 (67.6)	23 (67.6)	90 (66.1)
Osteopenic/osteoporotic[h] obesity	26 (76.4)	27 (79.4)	27 (79.4)	28 (82.3)	108 (79.4)
No osteopenic/osteoporotic obesity	8 (23.5)	7 (20.5)	7 (20.5)	6 (17.6)	28 (20.5)
Osteosarcopenic[i] obesity	14 (41.1)	8 (23.5)	8 (23.5)	8 (23.5)	38 (27.9)
No osteosarcopenic obesity	20 (58.8)	26 (76.4)	26 (76.4)	26 (76.4)	98 (72)
Cardiovascular risk[j], n (%)					
Low	-	1 (2.9)	-	1 (2.9)	2 (1.4)
High	14 (41.1)	9 (26.4)	7 (20.5)	6 (17.6)	36 (26.4)
Very high	20 (58.8)	24 (70.5)	27 (79.4)	27 (79.4)	98 (72)
Healh status					
Comorbidities, n (%)					
0-1	19 (55.8)	21 (61.7)	22 (67.7)	17 (50)	79 (58)
2-3	9 (26.4)	8 (23.5)	7 (20.5)	8 (23.5)	32 (23.5)
≥4	7 (20.5)	5 (14.7)	4 (11.7)	9 (26.4)	25 (18.3)
Prescribed medication, n (%)					
0-1	12 (35.2)	14 (41.1)	16 (47)	7 (20.5)	49 (36)
2-3	18 (52.9)	16 (47)	14 (41.1)	20 (58.8)	68 (50)
≥4	4 (11.7)	4 (11.7)	4 (11.7)	7 (20.5)	19 (13.9)
Smoking, n (%)					
Current	10 (29.4)	9 (26.4)	7 (20.5)	14 (41.1)	40 (29.4)
Past (ex-smoker)	6 (17.6)	8 (23.5)	4 (11.7)	5 (14.7)	23 (16.9)
Never (non-smoker)	18 (52.9)	17 (50)	23 (67.6)	15 (44.1)	73 (53.6)
Alcohol drinkers, n (%)					
Past	3 (8.8)	2 (5.8)	3 (8.8)	4 (11.7)	12 (35.2)
Current	2 (5.8)	1 (2.9)	1 (2.9)	2 (5.8)	6 (17.6)
Non-user	29 (85.2)	31 (91.1)	30 (88.2)	28 (82.3)	118 (86.7)
Type of assistive devices, n (%)					
None	33 (97)	34 (100)	33 (97)	32 (94.1)	132 (97)
Cane	1 (2.9)	-	1 (2.9)	2 (5.8)	4 (2.9)
Walker	-	-	-	-	-

Table 20. *Continued.*

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)	All (*n* = 136)
Questionnaires					
BADLs[k], mean ± SD [95%CI]	97.50 ± 4.96 [95.77–99.23]	91.62 ± 12.59 [87.22–96.01]	93.68 ± 17.11 [87.71–99.65]	95.15 ± 7.63 [92.48–97.81]	94.49 ± 11.63 [92.51–96.46]
IADLs[l], mean ± SD [95%CI]	7.94 ± 0.23 [7.86–8.02]	7.38 ± 1.82 [6.75–8.02]	7.62 ± 1.25 [7.18–8.06]	7.85 ± 0.70 [7.61–8.10]	7.70 ± 1.17 [7.50–7.90]
Cognitive status[m], mean ± SD [95%CI]	29.76 ± 0.55 [29.57–29.96]	29.79 ± 0.53 [29.61–29.98]	29.79 ± 0.53 [29.61–29.98]	29.76 ± 0.55 [29.57–29.96]	29.78 ± 0.54 [29.69–29.87]
Anxiety[n], mean ± SD [95%CI]	1.18 ± 3.26 [0.6–2.87]	2.09 ± 3.13 [0.99–3.18]	2.65 ± 3.40 [1.46–3.83]	2.06 ± 3.30 [0.91–3.21]	1.99 ± 3.11 [1.46–2.52]
Depression[o], mean ± SD [95%CI]	1.74 ± 3.26 [0.6–2.87]	2.76 ± 3.90 [1.4–4.13]	2.32 ± 3.57 [1.08–3.57]	1.91 ± 2.65 [0.99–2.84]	2.18 ± 3.36 [1.61–2.75]

Note. MT; multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; SD: standard deviation; CI: coefficient interval; yr: year; BMI: body mass index; aBMD: areal bone mineral density; BADLs: basic activities of daily living; IADLs:instrumental activities of daily living; **a:** BMI-referenced classification provided by the WHO (WHO, 2000); **b:** classification of percentage of fat mass in base of the cut-off points by sex, age, and ethnicity published by Gallagher et al. (2000) (Gallagher et al., 2000); **c:** classification of waist circumference accordingly to the WHO (WHO et al., 2000) [Central obesity is characterized as a waist circumference greater than 88cm in women (Lean et al., 1995; Pi-Sunyer, 2000) or a waist to hip ratio >0.80 in women (Center for Disease Control and Prevention, 2011)]; **d:** classification of aBMD according to the WHO definition (Kanis, 1994) (osteoporosis: T-score of lumbar spine and /or proximal femur: ≤ - 2.5; osteopenia: T-score of lumbar spine and/or proximal femur: -1 to -2.49; normal aBMD: T-score of lumbar spine and/or proximal femur: ≥ 0.99); **e:** classification of sarcopenia adapted from Cruz-Jentoft et al. (2019) and Baumgartner et al. (1999) where the ASM, which is the sum of arm and leg muscle mass, adjusted by squared height, have to be lower than < 5.45 or 5.50 kg/m² in women (Baumgartner et al.,1999; Cruz-Jentoft et al., 2019); **f:** classification of sarcopenic obesity in base on NHANES III criteria (ASM < 6.53 and % of body mas > 40.01) (Davison et al., 2002); **g:** classification of sarcopenic obesity in base on NEW MEXICO study criteria (ASM < 5.45 and % of body mas > 38) (Baumgartner, 2000); **h:** classification of osteopenic/osteoporotic obesity in base on Ilich et al., (2015) (T-score of lumbar spine and/or proximal femur: < -1 and & body fat > 32); **i:** classification of osteosarcopenic obesity in base on Ilich et al., (2015) (T-score of lumbar spine and/or proximal femur: < -1, body fat > 32 and ASM < 5.45); **j:** classification of cardiovascular risk in base of waist/height2 ratio (Ashweell & Gibson ,2016) (low risk: waist/height2 ratio: ≤ 0.49; high risk: waist/height2 ratio: 0.50-0.59; very high risk: waist/height2 ratio: ≥0.60); **k:** in base on Barthel index (Mahoney& Barthel, 1965); **l:** in base on Lawton and Brody scale (Lawton & Brody, 1969); **m:** in base on MMSE (Folstein et al., 1975); **n:** in base on OASIS scale (Norman et al., 2006) ; **o:** in base on ODSIS scale (Bentley et al., 2014).

There were no sarcopenic women if we introduce functional outcomes such as grip strength. A combination of two to all of these pathologic conditions (high body fat, low BMD, and low muscle mass) was present among 28–80% of the women.

In terms of health status, more than half of the sample showed at least zero or one comorbidity (58%), the most common ones being hypertension, hypercholesterolemia, osteoarthritis, arthritis and mild chronic neuromuscular pain, osteoporosis, and obesity. Furthermore, 64% of the women took more than two prescribed medications, most had never

smoked, and only a small proportion of the participants had a history of alcohol consumption. All the women presented high independence and autonomy, as reported by the BADLs, IADLs, and the assistive devices needed for ambulation In addition, they all presented normal cognitive statuses (>24) and no symptoms of anxiety or depression.

V.II. PROGRAM FEASIBILITY AND SAFETY: ATTENDANCE, COMPLIANCE AND ADVERSE EVENTS

V.II.I. Project one

At the mid-point assessments (Week 16), the attendance rate (number of training sessions attended divided by sessions held) for the exercise program was very similar for the two groups: 83.33% for the HI and 83.74% for the M group (30 of 36 sessions, including the familiarization sessions, in both cases), and the study adherence rate was greater than 90% in all three groups [HI = 92.30% (36 of 39 participants), M = 90.32% (28 of 31 participants), and C = 91.30% (21 of 23 participants)]. At the end of the training program (Week 32), the attendance rates were 74.2% and 75.15% for the HI and the M group, respectively. These rates are equivalent to an attendance of 47–48 sessions out of 64 (including familiarization). Furthermore, compliance at the end of the study was around 80% in the three groups [HI = 87.17% (34 of 39 participants), M = 80.64% (25 of 31 participants), and C = 78.26% (18 of 23 participants)], with no significant differences between the groups. The reasons reported by the participants for not attending the sessions include transportation problems, spouse's health, personal health problems, and appointments with doctors or other services. The overall attendance rate after 16 weeks was 91.4% (85 subjects out of 93), while the drop-out rate at this point was 8.6% (8 subjects). At the end of the intervention, the overall adherence rate was 82.8% (77 subjects out of 93) while the drop-out rate was slightly over 15% (exactly 17.2%; 16 subjects). No sessions had to be cancelled due to rain or other specific adverse situation.

During the intervention period, 16 women dropped out of the study. Nine withdrew due to medical reasons (n = 3: endocrine problems; n = 2: vascular health problems; n = 2: renal failure; n = 1: cancer diagnosis; n = 1: infection), 5 due to family issues, and 2 due to loss of interest. It is important to highlight that none of the dropouts left the program as a result of injuries or adverse responses to the intervention (training or testing sessions). The adverse events due to the training program or testing sessions are shown in Table 21. Throughout the study period, any adverse events due to the data-collection procedures were reported. Only mild and moderate adverse events caused by the training sessions were observed (i.e., there were no serious adverse events in any of the categories), and musculoskeletal events were the most common type. It is necessary to clarify that the adverse events reported by the participants were either "possibly related" or "not related" to the intervention, but it is difficult determine if an adverse event was "definitely related." In total, 21 adverse events (HI: 12; M: 9) were reported by 15 participants (16.1%). The most common musculoskeletal adverse events were muscle soreness, joint discomfort, and increased levels of pain (mainly in the knee and lower back). In addition, one subject in the M group reported gastrointestinal problems (stomach pain) that needed healthcare utilization, while two subjects reported a non-injurious fall. In terms of cardiovascular adverse events, two subjects showed mild hematoma.

Most of the musculoskeletal adverse events were reported in the first weeks (third and fourth week). Two participants reported the use of analgesics to decrease musculoskeletal symptoms. None of the participants missed any exercise sessions because of these adverse effects. Modifications to the training program (range of motion of the exercise, number of exercises, number of repetitions or sets, and rest between sets or exercises) were made on an individual basis if the adverse events caused discomfort or inconvenience. However, these

modifications never exceeded two weeks and only needed to be applied on few occasions (eight times in six participants).

Table 21. *Adverse events.*

	HI (*n* = 39)	M (*n* = 31)	C (*n* = 23)	All (*n* = 93)
Musculoskeletal				
Mild	8	5	-	13
Moderate	2	1	-	3
Severe	-	-	-	-
Life-threatening consequences	-	-	-	-
Death	-	-	-	-
Cardiovascular				
Mild	1	1	-	2
Moderate	-	-	-	-
Severe	-	-	-	-
Life-threatening consequences	-	-	-	-
Death	-	-	-	-
Falls				
Mild	1	1	-	2
Moderate	-	-	-	-
Severe	-	-	-	-
Life-threatening consequences	-	-	-	-
Death	-	-	-	-
Health care utilization				
Mild	-	1	-	1
Moderate	-	-	-	-
Severe	-	-	-	-
Life-threatening consequences	-	-	-	-
Death	-	-	-	-

Note. HI: high-intensity group; M: moderate-intensity group; C: control group.

Based on the attendance rate, compliance, dropout rate, reasons for withdrawals, and adverse events reported in all the groups, both training programs can be identified as safe and feasible for older women.

V.II.II. Project two

The attendance rate at the end of the exercise program (Week 20) was very similar for the three groups, which all fared above 80%: 88.09% (37 of 42 sessions) for the MT group, 87.80% (36 of 41 sessions) for P, and 85.36% (35 of 41 sessions) for T, including the familiarization sessions. Without taking into account the four familiarization sessions, the attendance rate was 86.84% (33 of 38 sessions), 86.48% (32 of 37 sessions), and 83.78% (31 of 37 sessions) for MT, P, and T, respectively. The reasons reported by participants for not

attending the sessions were transportation problems, spouse's health, family matters, personal health problems, and appointments with doctors or other services. In addition, the study compliance was greater than 80% in all the groups [MT = 88.23% (30 of 34 participants), P = 82.35% (28 of 34 participants), T = 82.35 (28 of 34 participants), and C: 88.23% (30 of 34 participants)]. The overall adherence rate at the end of the intervention was 85.3% (116 subjects out of 136), while the dropout rate was below 15% (exactly 14.7%; 20 subjects). No sessions had to be cancelled due to rain or other specific adverse situation.

During the intervention period, 20 women dropped out of the study. Eleven withdrew due to medical reasons (n = 4: vascular health problems; n = 3: prior musculoskeletal problems; n = 2: endocrine health problems; n = 2: cancer diagnoses), 7 due to family issues, and 2 due to loss of interest. It is important to highlight that none of the dropouts left the program as a result of injuries or adverse responses to the intervention (training or testing sessions). The adverse events due to the training program or testing sessions are shown in Table 22. Throughout the study period, any adverse events caused by the data-collection procedures were reported. Only mild and moderate adverse events due to the training sessions were observed, with musculoskeletal events being the most common. Again, it is necessary to clarify that the adverse events reported by participants were either "possibly related" or "not related" to the intervention, but it is difficult determine if they were "definitely related." In total, 30 adverse events (MT: 9; P: 9; T: 12) were reported by 23 participants (16.9%). The most common musculoskeletal adverse events were the same as the ones reported in the first project. In addition, four subjects reported a non-injurious fall, and three had to access healthcare due to gastrointestinal problems and the seasonal flu.

Most of the musculoskeletal adverse events were reported in the first month. None of the participants reported the use of analgesics to decrease the symptoms or missed exercise sessions because of these adverse effects. Again, modifications to the exercise protocol were

made on an individual basis as needed if the event caused discomfort or inconvenience. These modifications were only needed for 10 participants (13 times) within a period of less than two weeks at the beginning of the program.

Table 22. *Adverse events.*

	MT (*n* = 39)	P (*n* = 31)	T (*n* = 23)	C (*n* = 23)	All (*n* = 93)
Musculoskeletal					
Mild	7	6	7	-	20
Moderate	-	1	2	-	3
Severe	-	-	-	-	-
Life-threatening consequences	-	-	-	-	-
Death	-	-	-	-	-
Cardiovascular					
Mild	-	-	-	-	-
Moderate	-	-	-	-	-
Severe	-	-	-	-	-
Life-threatening consequences	-	-	-	-	-
Death	-	-	-	-	-
Falls					
Mild	1	1	2	-	4
Moderate	-	-	-	-	-
Severe	-	-	-	-	-
Life-threatening consequences	-	-	-	-	-
Death	-	-	-	-	-
Health care utilization					
Mild	1	1	1	-	3
Moderate	-	-	-	-	-
Severe	-	-	-	-	-
Life-threatening consequences	-	-	-	-	-
Death	-	-	-	-	-

Note. MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training group; C: control group.

Based on the attendance rate, compliance, overall dropout rate, reasons for withdrawals, and adverse events reported in all the groups, the training programs of each training modality carried out in this study were well tolerated by older women and can be identified as safe and feasible for the study population.

V.III. POTENTIAL CONFOUNDING VARIABLES

V.III.I. Project one

Potential confounding variables such as age, basic physical function reflected in the BADLs and IADLs questionnaires, and cognitive status assessed by the MMSE showed no significant differences between the groups at baseline.

V.III.II. Project two

Potential confounds such as age, basic physical function reflected in the BADLs and IADLs questionnaires, and cognitive status assessed by the MMSE, along with the anxiety and depression states recorded by the OASIS and ODSIS scales, respectively, showed no significant differences between the groups at baseline. In addition, two main potential confounding parameters, nutritional status and physical-activity level, were recorded in this second project.

A. Nutritional status

Changes in nutritional status from the ITT analysis at the different time points of the study are presented in Tables 23 to 26. At baseline, there were no differences between the groups in terms of daily macronutrients and total energy intake, except for protein intake between the P and C groups (~10g/day more in the P group; $p = 0.047$; Tables 23 and 24). For the rest of the parameters, only magnesium intake (MT vs C, $p = 0.008$; T vs C, $p = 0.002$) and vitamin H (MT vs C, $p = 0.004$) – also called B8 or biotin – showed differences between groups at the beginning of the training program (Tables 25 and 26). Repeated-measures ANOVA revealed significant differences by time in total energy intake (MT; $p = 0.018$), magnesium (T; $p = 0.019$), and selenium intake (C; $p = 0.000$), with no significant differences in the rest of the parameters. After adjusting for age and baseline values, the same differences were found along with protein intake in the P group ($p = 0.040$). Repeated-measures ANOVA also revealed a significant time × group interaction in magnesium (T vs

C, p = 0.001), selenium (MT vs C, p = 0.032; T vs C, p = 0.001), fluoride (MT vs C, p = 0.040; P vs C, p = 0.044; T vs C: p = 0.002), vitamin H (MT vs C, p = 0.002; T vs C, p = 0.042), and vitamin E (T vs C, p = 0.005) intake, without differences in the rest of the variables. After correction with the ANCOVA, no time × group interactions were found in any of the variables analyzed.

Results from the PPA (n = 116) on nutritional status are presented in Supplementary Material A (Tables A.1–A.4). At baseline, there were differences between the T and C groups in lipid (p = 0.041) and vitamin E (p = 0.032) intake. No significant differences were found in the rest of the parameters. Regarding the main effects of time and time × group interactions, the results were similar to those of the ITT analysis, although there were significant differences by time in CHO intake within the P group (ANOVA, p = 0.043; ANCOVA, p = 0.028), while the differences in protein intake for this group disappeared in this analysis. There were no significant time × group interactions except for the lipid intake between the MT and C groups as measured by the ANOVA (p = 0.041) and between T and C (p = 0.047) after the covariate adjustment in the ANCOVA analysis.

Table 23. *Daily macronutrients and total energy intake from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
CHO intake (g/d)	MT	141.92	142.11 ± 33.83 (130.68–153.54)	141.43 ± 31.71 (129.8–153.07)	-0.48	0.793 (0.02)	0.786 (0.02)	MT vs P: 1.000 (0.3)	MT vs P: 0.741 (0.18)
	P		146.46 ± 34.57 (135.03–157.89)	151.01 ± 32.18 (139.37–162.65)	3.11	0.079 (0.14)	0.056 (0.15)	MT vs T: 1.000 (0.2)	MT vs T: 1.000 (0.09)
	T		146.15 ± 33.46 (134.72–157.58)	148.23 ± 37.15 (136.59–159.87)	1.42	0.421 (0.06)	0.341 (0.07)	MT vs C: 1.000 (0.26)	MT vs C: 1.000 (0.01)
	C		132.95 ± 32.84 (121.52–144.38)	132.50 ± 35.85 (120.86–144.13)	-0.34	0.861 (0.01)	0.644 (0.03)	P vs T: 1.000 (0.08)	P vs T: 1.000 (0.07)
								P vs C: 0.167 (0.54)	P vs C: 0.576 (0.18)
								T vs C: 0.365 (0.43)	T vs C: 1.000 (0.1)
Protein intake (g/d)	MT	72.60	75.95 ± 16.45 (70.67–81.22)	75.88 ± 17.10 (70.84–81.29)	-0.09	0.872 (0)	0.778 (0.01)	MT vs P: 1.000 (0)	MT vs P: 1.000 (0.04)
	P		76.71 ± 18.25 (71.44–81.89)	75.92 ± 18.01 (70.52–81.33)	-1.03	0.051 (0.04)	**0.040** (0.05)	MT vs T: 1.000 (0.28)	MT vs T: 1.000 (0.01)
	T		71.22 ± 15.19 (65.94–76.49)	71.27 ± 16.42 (65.87–76.68)	0.07	0.895 (0)	0.848 (0)	MT vs C: 0.122 (0.63)	MT vs C: 1.000 (0.03)
	C		66.52 ± 11.48 (61.25–71.80)	66.81 ± 11.32 (61.40–72.21)	0.43	0.477 (0.03)	0.375 (0.03)	P vs T: 1.000 (0.27)	P vs T: 0.670 (0.05)
								P vs C: 0.119 (0.27)	P vs C: 0.245 (0.05)
								T vs C: 1.000 (0.61)	T vs C: 1.000 (0.08)
Lipids intake (g/d)	MT	58.01	60.15 ± 14.34 (55.06–65.24)	60.34 ± 14.22 (55.25–65.43)	0.31	0.646 (0.01)	0.694 (0.01)	MT vs P: 1.000 (0.2)	MT vs P: 1.000 (0.05)
	P		58.12 ± 12.95 (53.02–63.21)	57.65 ± 12.48 (52.55–62.74)	-0.81	0.244 (0.04)	0.254 (0.04)	MT vs T: 1.000 (0.03)	MT vs T: 1.000 (0.01)
	T		60.61 ± 18.20 (55.52–65.70)	60.82 ± 18.39 (55.73–65.91)	0.34	0.610 (0.01)	0.444 (0.02)	MT vs C: 0.210 (0.54)	MT vs C: 0.880 (0.06)
	C		53.17 ± 14.00 (48.08–58.26)	52.58 ± 14.28 (47.49–57.67)	-1.11	0.146 (0.04)	0.098 (0.05)	P vs T: 1.000 (0.2)	P vs T: 1.000 (0.05)
								P vs C: 0.998 (0.38)	P vs C: 1.000 (0.02)
								T vs C: 0.152 (0.5)	T vs C: 0.550 (0.06)

Table 23. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total energy intake (Kcal/d)	MT	1429.02	1457.11 ± 260.32 (1361.87–1552.35)	1427.85 ± 234.48 (1333.55–1522.15)	-2.01	**0.018** (0.12)	**0.017** (0.12)	MT vs P: 1.000 (0.18)	MT vs P: 0.524 (0.12)
	P		1475.29 ± 272.69 (1380.05–1570.53)	1473.11 ± 273.47 (1378.81–1567.42)	-0.15	0.859 (0.01)	0.996 (0)	MT vs T: 1.000 (0.13)	MT vs T: 0.514 (0.1)
	T		1468.64 ± 331.46 (1373.40–1563.88)	1465.64 ± 346.35 (1371.34–1559.94)	-0.20	0.806 (0.01)	0.956 (0)	MT vs C: 0.410 (0.52)	MT vs C: 1.000 (0.05)
	C		1315.05 ± 251.53 (1219.81–1410.29)	1303.97 ± 243.63 (1209.66–1398.27)	-0.84	0.365 (0.049)	0.179 (0.007)	P vs T: 1.000 (0.02)	P vs T: 1.000 (0)
								P vs C: 0.080 (0.65)	P vs C: 1.000 (0.06)
								T vs C: 0.107 (0.54)	T vs C: 1.000 (0.06)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: n = 34. MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CHO: carbohydrates; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

Table 24. *Daily macronutrients and total energy intake relative to body mass from ITT analysis.*

Variables	Group	Baseline	Post-test	Variables	Group	Baseline	Post-test
CHO intake (g/Kg/d)	MT	2.04 (51.08%)	2.04 (50.93%)	Lipids intake (g/Kg/d)	MT	0.87 (21.62%)	0.87 (21.73%)
	P	2.20 (52.06%)	2.29 (53.06%)		P	0.87 (20.66%)	0.87 (20.25%)
	T	2.13 (52.57%)	2.16 (52.87%)		T	0.88 (21.8%)	0.88 (21.69%)
	C	1.86 (52.62%)	1.85 (52.6%)		C	0.74 (21.04%)	0.73 (20.87%)
Protein intake (g/Kg/d)	MT	1.09 (27.29%)	1.09 (27.32%)	Total energy intake (Kcal/Kg/d)	MT	20.92	20.62
	P	1.15 (27.27%)	1.15 (26.67%)		P	22.24	22.34
	T	1.03 (25.62%)	1.04 (25.42%)		T	21.44	21.38
	C	0.93 (26.32%)	0.93 (26.52%)		C	18.47	18.25

Table 25. *Daily minerals intake from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Calcium intake (mg/d)	MT	657.96	701.11 ± 157.84 (638.87–736.35)	693.64 ± 160.65 (629.26–758.02)	-1.07	0.158 (0.05)	0.131 (0.05)	MT vs P: 1.000 (0.14) MT vs T: 1.000 (0.22)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.04)
	P		671.50 ± 159.11 (609.26–733.44)	670.41 ± 172.83 (606.03–734.79)	-0.16	0.836 (0.01)	0.788 (0.01)	MT vs C: 0.339 (0.44)	MT vs C: 0.969 (0.05)
	T		655.44 ± 179.77 (593.20–717.68)	655.05 ± 185.40 (590.67–719.44)	-0.06	0.942 (0)	0.896 (0)	P vs T: 1.000 (0.09)	P vs T: 1.000 (0)
	C		603.78 ± 228.23 (541.54–666.02)	605.07 ± 232.41 (540.69–669.45)	0.21	0.806 (0.01)	0.631 (0.01)	P vs C: 0.949 (0.32) T vs C: 1.000 (0.24)	P vs C: 1.000 (0.02) T vs C: 1.000 (0.02)
Ferrous intake (mg/d)	MT	11.31	10.99 ± 2.52 (9.76–12.21)	11.19 ± 2.82 (9.96–12.42)	1.82	0.479 (0.07)	0.306 (0.1)	MT vs P: 1.000 (0.25) MT vs T: 1.000 (0.22)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.05)
	P		12.04 ± 3.50 (10.82–13.27)	12.01 ± 3.58 (10.78–13.24)	-0.29	0.901 (0.01)	0.952 (0)	MT vs C: 1.000 (0.19)	MT vs C: 1.000 (0.03)
	T		11.93 ± 5.09 (10.71–13.16)	12.08 ± 5.02 (10.85–13.31)	1.26	0.595 (0.03)	0.800 (0.01)	P vs T: 1.000 (0.02)	P vs T: 1.000 (0.01)
	C		10.27 ± 2.70 (9.04–11.49)	10.67 ± 2.53 (9.44–11.90)	3.95	0.152 (0.15)	0.188 (0.14)	P vs C: 0.786 (0.02) T vs C: 0.663 (0.43)	P vs C: 1.000 (0.11) T vs C: 1.000 (0.07)
Iodine intake (mg/d)	MT	93.31	95.25 ± 32.13 (84.33–106.17)	94.49 ± 31.47 (83.60–105.37)	-0.80	0.266 (0.02)	0.285 (0.02)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.2)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.01)
	P		91.38 ± 34.00 (80.46–102.30)	91.77 ± 33.41 (80.88–102.65)	0.42	0.577 (0.01)	0.600 (0.01)	MT vs C: 1.000 (0.09)	MT vs C: 0.511 (0.02)
	T		89.16 ± 23.97 (78.24–100.08)	88.81 ± 24.31 (77.92–99.70)	-0.40	0.607 (0.01)	0.568 (0.02)	P vs T: 1.000 (0.1)	P vs T: 1.000 (0.03)
	C		97.46 ± 37.16 (86.54–108.38)	97.46 ± 37.70 (86.57–108.35)	0.00	1.000 (0)	0.948 (0)	P vs C: 1.000 (0.16) T vs C: 1.000 (0.27)	P vs C: 1.000 (0.03) T vs C: 1.000 (0.01)
Magnesium intake (mg/d)	MT	253.57	268.47 ± 50.49 (245.57–291.36)	270.64 ± 59.35 (246.57–294.71)	0.81	0.669 (0.04)	0.530 (0.06)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.24)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.13)
	P		255.44 ± 50.16 (232.54–278.33)	259.97 ± 54.52 (235.9–284.04)	1.77	0.375 (0.09)	0.373 (0.09)	MT vs C: 1.000 (0.66)	MT vs C: 1.000 (0.03)
	T		275.50 ± 86.63 (252.60–298.39)	287.58 ± 79.12 (263.51–311.65)	4.39	**0.019** (0.15)	**0.018** (0.15)	P vs T: 1.000 (0.41) P vs C: 0.171 (0.41)	P vs T: 1.000 (0.12) P vs C: 1.000 (0.01)
	C		214.89 ± 75.16 (191.99–237.79)	221.86 ± 85.91 (197.79–245.93)	3.24	0.173 (0.09)	0.307 (0.07)	T vs C: **0.001** (0.53)	T vs C: 1.000 (0.09)

Table 25. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Zinc intake (mg/d)	MT	8.04	8.04 ± 1.45 (7.21–8.86)	8.15 ± 1.16 (7.47–8.84)	1.46	0.615 (0.09)	0.600 (0.08)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.32)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.18)
	P		8.28 ± 2.63 (7.46–9.11)	8.25 ± 2.28 (7.57–8.94)	-0.35	0.900 (0.01)	0.807 (0.02)	MT vs C: 1.000 (0.18)	MT vs C: 0.975 (0.19)
	T		7.76 ± 2.05 (6.93–8.58)	7.67 ± 1.77 (6.98–8.36)	-1.14	0.706 (0.05)	0.418 (0.08)	P vs T: 1.000 (0.29)	P vs T: 1.000 (0.1)
	C		8.09 ± 3.23 (7.26–8.92)	7.80 ± 2.59 (7.11–8.48)	-3.63	0.210 (0.1)	0.148 (0.1)	P vs C: 1.000 (0.19) T vs C: 1.000 (0.06)	P vs C: 1.000 (0.1) T vs C: 1.000 (0.1)
Selenium intake (mg/d)	MT	94.36	92.39 ± 21.11 (81.62–103.16)	91.12 ± 19.97 (80.52–101.73)	-1.37	0.292 (0.06)	0.345 (0.05)	MT vs P: 1.000 (0.12)	MT vs P: 1.000 (0.02)
	P		96.02 ± 32.57 (85.24–106.79)	94.25 ± 32.48 (83.65–104.85)	-1.84	0.142 (0.05)	0.142 (0.05)	MT vs T: 1.000 (0.19) MT vs C: **0.032** (0.17)	MT vs T: 1.000 (0.03) MT vs C: 0.333 (0.1)
	T		87.89 ± 28.72 (77.12–98.66)	86.42 ± 28.97 (75.82–97.02)	-1.67	0.221 (0.05)	0.098 (0.07)	P vs T: 0.665 (0.25)	P vs T: 1.000 (0.01)
	C		101.14 ± 41.25 (90.37–111.91)	96.43 ± 40.15 (85.83–107.03)	-4.65	**0.000** (0.12)	**0.000** (0.11)	P vs C: 0.171 (0.25) T vs C: **0.001** (0.06)	P vs C: 0.708 (0.07) T vs C: 0.992 (0.07)
Sodium intake (mg/d)	MT	1355.36	1436.58 ± 466.30 (1297.75–1575.42)	1440.61 ± 469.19 (1296.38–1584.85)	0.28	0.831 (0.01)	0.822 (0.01)	MT vs P: 1.000 (0.09) MT vs T: 0.971 (0.32)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.06)
	P		1381.88 ± 432.18 (1243.04–1520.71)	1397.55 ± 439.24 (1253.32–1541.79)	1.13	0.408 (0.04)	0.418 (0.04)	MT vs C: 0.789 (0.38)	MT vs C: 1.000 (0.01)
	T		1319.29 ± 377.48 (1180.45–1458.12)	1295.55 ± 431.42 (1151.32–1439.79)	-1.80	0.211 (0.06)	0.207 (0.06)	P vs T: 1.000 (0.23)	P vs T: 0.857 (0.09)
	C		1283.70 ± 351.03 (1144.87–1422.54)	1284.14 ± 351.97 (1139.91–1428.38)	0.03	0.981 (0)	0.956 (0)	P vs C: 1.000 (0.28) T vs C: 1.000 (0.03)	P vs C: 1.000 (0.09) T vs C: 1.000 (0.04)
Potassium intake (mg/d)	MT	2753.30	2860.47 ± 502.23 (2642.70–3078.24)	2855.44 ± 514.38 (2633.85–3077.03)	-0.18	0.664 (0.01)	0.503 (0.02)	MT vs P: 1.000 (0.13) MT vs T: 1.000 (0.03)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.01)
	P		2790.82 ± 563.12 (2573.05–3008.59)	2785.00 ± 588.01 (2563.40–3006.59)	-0.21	0.615 (0.01)	0.602 (0.01)	MT vs C: 0.127 (0.61)	MT vs C: 1.000 (0.02)
	T		2875.17 ± 787.72 (2657.40–3092.94)	2874.70 ± 798.11 (2653.11–3096.29)	-0.02	0.968 (0)	0.990 (0)	P vs T: 1.000 (0.13)	P vs T: 1.000 (0.01)
	C		2486.73 ± 677.07 (2268.96–2704.50)	2485.67 ± 677.73 (2264.08–2707.26)	-0.04	0.927 (0)	0.912 (0)	P vs C: 0.366 (0.13) T vs C: 0.092 (0.47)	P vs C: 1.000 (0.01) T vs C: 1.000 (0)

Table 25. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Phosphorus intake (mg/d)	MT	1176.13	1232.82 ± 210.20 (1136.74–1328.9)	250.14 ± 70.09 (1131.6–1325.45)	-79.71	0.661 (0.02)	0.649 (0.02)	MT vs P: 1.000 (0.01)	MT vs P: 1.000 (0.05)
	P		1236.47 ± 253.82 (1140.39–1332.54)	249.52 ± 91.30 (1145.34–1339.18)	-79.82	0.554 (0.03)	0.500 (0.03)	MT vs T: 1.000 (0.27)	MT vs T: 1.000 (0.04)
	T		1163.97 ± 295.11 (1067.89–1260.04)	270.05 ± 74.92 (1072.25–1266.09)	-76.80	0.595 (0.02)	0.530 (0.02)	MT vs C: 0.210 (0.67)	MT vs C: 1.000 (0.04)
	C		1071.26 ± 353.74 (975.18–1167.34)	194.40 ± 94.43 (984.01–1177.86)	-81.85	0.323 (0.02)	0.426 (0.02)	P vs T: 1.000 (0.25)	P vs T: 1.000 (0)
								P vs C: 0.129 (0.59)	P vs C: 1.000 (0)
								T vs C: 1.000 (0.89)	T vs C: 1.000 (0)
Fluoride intake (mg/d)	MT	237.86	244.70 ± 68.38 (216.96–272.43)	250.14 ± 70.09 (221.86–278.41)	2.22	0.177 (0.08)	0.124 (0.09)	MT vs P: 1.000 (0.01)	MT vs P: 1.000 (0.05)
	P		247.32 ± 86.12 (219.58–275.06)	249.52 ± 91.30 (221.25–277.80)	0.89	0.583 (0.02)	0.572 (0.03)	MT vs T: 1.000 (0.27)	MT vs T: 1.000 (0.01)
	T		262.76 ± 74.69 (235.02–290.50)	270.05 ± 74.92 (241.78–298.33)	2.78	0.071 (0.1)	0.098 (0.09)	MT vs C: **0.040** (0.67)	MT vs C: 0.745 (0.11)
	C		196.67 ± 95.23 (168.93–224.41)	194.40 ± 94.43 (166.13–222.68)	-1.15	0.573 (0.02)	0.515 (0.03)	P vs T: 1.000 (0.25)	P vs T: 1.000 (0.05)
								P vs C: **0.044** (0.25)	P vs C: 1.000 (0.05)
								T vs C: **0.002** (0.59)	T vs C: 0.676 (0.11)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: n = 34. MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

Table 26. *Daily vitamins intake from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin B1 intake (mg/d)	MT	1.13	1.17 ± 0.28 (1.04–1.30)	1.19 ± 0.29 (1.06–1.31)	1.25	0.589 (0.05)	0.403 (0.08)	MT vs P: 0.888 (0.36) MT vs T: 1.000 (0.05) MT vs C: 0.822 (0.41) P vs T: 1.000 (0.28) P vs C: 1.000 (0.01) T vs C: 1.000 (0.31)	MT vs P: 0.721 (0.17) MT vs T: 1.000 (0.13) MT vs C: 1.000 (0.14) P vs T: 1.000 (0.03) P vs C: 1.000 (0.03) T vs C: 1.000 (0.04)
	P		1.09 ± 0.43 (0.96–1.22)	1.06 ± 0.39 (0.94–1.18)	-2.69	0.281 (0.07)	0.170 (0.09)		
	T		1.20 ± 0.41 (1.07–1.33)	1.17 ± 0.39 (1.05–1.29)	-2.44	0.281 (0.07)	0.390 (0.06)		
	C		1.07 ± 0.34 (0.94–1.20)	1.06 ± 0.33 (0.94–1.18)	-1.37	0.589 (0.04)	0.389 (0.06)		
Vitamin B2 intake (mg/d)	MT	1.43	1.42 ± 0.26 (1.29–1.56)	1.42 ± 0.26 (1.27–1.57)	-0.21	0.883 (0.01)	0.951 (0.01)	MT vs P: 1.000 (0.28) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.22) P vs T: 1.000 (0.23) P vs C: 0.411 (0.23) T vs C: 1.000 (0.41)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.02) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.06) P vs C: 0.867 (0.09) T vs C: 1.000 (0.03)
	P		1.51 ± 0.53 (1.37–1.65)	1.55 ± 0.57 (1.40–1.70)	2.52	0.058 (0.07)	0.078 (0.06)		
	T		1.42 ± 0.43 (1.28–1.56)	1.43 ± 0.48 (1.28–1.57)	0.41	0.769 (0.01)	0.840 (0.01)		
	C		1.36 ± 0.34 (1.23–1.50)	1.35 ± 0.33 (1.21–1.50)	-0.64	0.660 (0.03)	0.756 (0.02)		
Vitamin B3 (niacin) intake (mg/d)	MT	31.13	32.16 ± 6.94 (29.63–34.69)	32.31 ± 7.04 (29.69–34.94)	0.46	0.716 (0.02)	0.647 (0.03)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0.33) MT vs C: 0.651 (0.43) P vs T: 0.665 (0.36) P vs C: 0.339 (0.44) T vs C: 1.000 (0.08)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.1) MT vs C: 1.000 (0.03) P vs T: 1.000 (0.09) P vs C: 1.000 (0.09) T vs C: 1.000 (0.02)
	P		32.71 ± 9.08 (30.18–35.24)	32.89 ± 9.11 (30.26–35.51)	0.54	0.663 (0.02)	0.649 (0.02)		
	T		30.38 ± 7.02 (27.85–32.91)	29.88 ± 7.51 (27.25–32.5)	-1.65	0.218 (0.07)	0.186 (0.08)		
	C		29.28 ± 6.49 (26.75–31.81)	29.28 ± 7.07 (26.65–31.9)	0.00	1.000 (0)	0.994 (0)		
Vitamin B6 intake (mg/d)	MT	1.90	1.98 ± 0.39 (1.81–2.15)	1.99 ± 0.51 (1.80–2.18)	0.59	0.781 (0.03)	0.805 (0.02)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.24) MT vs C: 0.712 (0.37) P vs T: 1.000 (0.22) P vs C: 0.700 (0.22) T vs C: 1.000 (0.35)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.06) MT vs C: 1.000 (0.01) P vs T: 1.000 (0.04) P vs C: 1.000 (0) T vs C: 1.000 (0.04)
	P		1.98 ± 0.59 (1.81–2.15)	1.99 ± 0.61 (1.80–2.18)	0.30	0.889 (0.01)	0.941 (0)		
	T		1.88 ± 0.46 (1.71–2.05)	1.87 ± 0.5 (1.67–2.06)	-0.93	0.676 (0.04)	0.668 (0.04)		
	C		1.77 ± 0.52 (1.60–1.94)	1.77 ± 0.65 (1.58–1.97)	0.00	1.000 (0)	0.912 (0.01)		

Table 26. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin B9 (folic acid) intake (µg/d)	MT	248.15	248.05 ± 61.93 (222.7–273.41)	249.85 ± 69.52 (222.36–277.34)	0.72	0.693 (0.03)	0.725 (0.02)	MT vs P: 1.000 (0.2) MT vs T: 0.971 (0.32) MT vs C: 1.000 (0.37) P vs T: 0.174 (0.45) P vs C: 1.000 (0.1) T vs C: 0.066 (0.62)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.05) MT vs C: 1.000 (0.01) P vs T: 1.000 (0.04) P vs C: 1.000 (0.04) T vs C: 1.000 (0.11)
	P		240.26 ± 80.35 (214.91–265.61)	234.08 ± 89.07 (206.59–261.58)	-2.57	0.175 (0.07)	0.194 (0.07)		
	T		279.41 ± 96.57 (254.06–304.76)	277.50 ± 102.57 (250–304.99)	-0.68	0.674 (0.02)	0.600 (0.02)		
	C		224.90 ± 52.13 (199.54–250.25)	226.75 ± 54.59 (199.26–254.24)	0.82	0.683 (0.03)	0.609 (0.04)		
Vitamin B12 intake (µg/d)	MT	4.23	4.40 ± 1.29 (3.64–5.16)	4.43 ± 1.32 (3.68–5.18)	0.73	0.360 (0.02)	0.277 (0.03)	MT vs P: 1.000 (0.11) MT vs T: 1.000 (0.28) MT vs C: 1.000 (0.37) P vs T: 0.889 (0.28) P vs C: 0.818 (0.28) T vs C: 1.000 (0.31)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.01) P vs T: 1.000 (0) P vs C: 1.000 (0.01) T vs C: 1.000 (0.01)
	P		4.73 ± 3.50 (3.97–5.49)	4.73 ± 3.42 (3.98–5.48)	0.00	1.000 (0)	0.842 (0)		
	T		3.92 ± 2.04 (3.16–4.68)	3.95 ± 2.01 (3.2–4.7)	0.75	0.405 (0.01)	0.571 (0.01)		
	C		3.89 ± 1.36 (3.13–4.65)	3.92 ± 1.40 (3.18–4.67)	0.91	0.318 (0.03)	0.369 (0.02)		
Vitamin C intake (mg/d)	MT	127.21	129.97 ± 61.92 (111.25–148.68)	131.88 ± 65.87 (90–173.75)	1.47	0.920 (0.03)	0.976 (0.01)	MT vs P: 1.000 (0.24) MT vs T: 1.000 (0.08) MT vs C: 1.000 (0.2) P vs T: 1.000 (0.36) P vs C: 0.686 (0.29) T vs C: 1.000 (0.17)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.15) MT vs C: 1.000 (0.21) P vs T: 1.000 (0.17) P vs C: 1.000 (0.17) T vs C: 1.000 (0.22)
	P		117.85 ± 57.92 (99.13–136.57)	116.91 ± 56.64 (75.04–158.78)	-0.80	0.961 (0.02)	0.948 (0.02)		
	T		132.45 ± 52.90 (113.74–151.17)	136.92 ± 54.24 (95.05–178.8)	3.38	0.815 (0.08)	0.667 (0.16)		
	C		128.56 ± 46.77 (109.84–147.27)	164.50 ± 224.61 (122.62–206.37)	27.96	0.062 (0.22)	0.072 (0.21)		
Vitamin A intake (µg/d)	MT	188.38	855.50 ± 351.06 (741.6–969.39)	856.11 ± 344.65 (742.3–969.92)	0.07	0.876 (0)	0.802 (0)	MT vs P: 0.681 (0.37) MT vs T: 0.454 (0.49) MT vs C: 0.096 (0.54) P vs T: 1.000 (0.05) P vs C: 1.000 (0.19) T vs C: 1.000 (0.17)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.01) P vs T: 0.747 (0.03) P vs C: 1.000 (0.03) T vs C: 1.000 (0.01)
	P		732.25 ± 355.12 (618.36–846.15)	726.46 ± 355.49 (612.65–840.27)	-0.79	0.146 (0.02)	0.147 (0.02)		
	T		707.29 ± 226.24 (593.4–821.18)	710.41 ± 233.67 (596.6–824.22)	0.44	0.433 (0.01)	0.467 (0.01)		
	C		661.00 ± 387.68 (547.11–774.9)	657.45 ± 387.86 (543.63–771.26)	-0.54	0.371 (0.01)	0.351 (0.01)		

Table 26. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin B5 (Pantothenic acid) intake (mg/d)	MT	4.73	4.90 ± 0.87 (4.45–5.35)	4.99 ± 0.99 (4.52–5.45)	1.68	0.529 (0.09)	0.362 (0.13)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.13)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.04)
	P		4.89 ± 2.04 (4.44–5.34)	5.01 ± 2.03 (4.45–5.47)	2.40	0.369 (0.06)	0.284 (0.07)	MT vs C: 0.523 (0.6)	MT vs C: 1.000 (0.11)
	T		4.75 ± 1.19 (4.3–5.2)	4.84 ± 1.21 (4.38–5.3)	1.86	0.500 (0.07)	0.557 (0.06)	P vs T: 1.000 (0.1)	P vs T: 0.608 (0.04)
	C		4.36 ± 0.79 (3.91–4.81)	4.42 ± 0.91 (3.95–4.88)	1.35	0.653 (0.07)	0.906 (0.02)	P vs C: 0.459 (0.1) T vs C: 1.000 (0.37)	P vs C: 0.011 (0.08) T vs C: 0.837 (0.06)
Vitamin H intake (B8 or biotin) (µg/d)	MT	25.19	28.25 ± 8.42 (25.71–30.78)	28.07 ± 7.98 (25.64–30.50)	-0.62	0.648 (0.02)	0.697 (0.02)	MT vs P: 0.094 (0.6) MT vs T: 1.000 (0.2)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.01)
	P		24.17 ± 6.74 (21.64–26.71)	23.82 ± 6.15 (21.39–26.25)	-1.46	0.361 (0.05)	0.225 (0.07)	MT vs C: **0.002** (0.88)	MT vs C: 1.000 (0.09)
	T		26.42 ± 8.08 (23.89–28.96)	26.48 ± 7.90 (24.06–28.91)	0.22	0.879 (0.01)	0.803 (0.01)	P vs T: 0.765 (0.38)	P vs T: 1.000 (0.08)
	C		21.93 ± 6.49 (19.39–24.47)	21.72 ± 6.38 (19.29–24.15)	-0.94	0.594 (0.03)	0.219 (0.07)	P vs C: 1.000 (0.33) T vs C: **0.042** (0.66)	P vs C: 1.000 (0.08) T vs C: 1.000 (0)
Vitamin D intake (µg/d)	MT	2.16	2.63 ± 1.90 (1.94–3.31)	2.67 ± 1.91 (1.96–3.37)	1.57	0.611 (0.02)	0.675 (0.02)	MT vs P: 1.000 (0.21) MT vs T: 0.501 (0.50)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.07)
	P		2.21 ± 2.12 (1.53–2.89)	2.23 ± 2.11 (1.53–2.94)	1.06	0.771 (0.01)	0.766 (0.01)	MT vs C: 1.000 (0.18)	MT vs C: 1.000 (0.02)
	T		1.65 ± 1.42 (0.96–2.33)	1.79 ± 1.58 (1.09–2.49)	8.73	0.077 (0.1)	0.069 (0.1)	P vs T: 1.000 (0.24)	P vs T: 1.000 (0.07)
	C		2.17 ± 2.45 (1.49–2.85)	2.26 ± 2.54 (1.56–2.96)	4.06	0.277 (0.04)	0.295 (0.03)	P vs C: 1.000 (0.24) T vs C: 1.000 (0.01)	P vs C: 1.000 (0.03) T vs C: 1.000 (0.03)

Table 26. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin E intake (mg/d)	MT	6.51	6.64 ± 2.25 (5.85–7.43)	6.52 ± 1.92 (5.78–7.26)	-1.81	0.429 (0.06)	0.469 (0.05)	MT vs P: 1.000 (0.06)	MT vs P: 1.000 (0.07)
	P		6.61 ± 2.21 (5.81–7.40)	6.64 ± 2.11 (5.9–7.38)	0.44	0.847 (0.01)	0.767 (0.02)	MT vs T: 0.963 (0.31)	MT vs T: 1.000 (0.1)
	T		7.23 ± 2.98 (6.44–8.03)	7.27 ± 2.80 (6.53–8.01)	0.49	0.817 (0.01)	0.358 (0.05)	MT vs C: 0.271 (0.58)	MT vs C: 1.000 (0.08)
	C		5.57 ± 1.70 (4.78–6.36)	5.45 ± 1.73 (4.71–6.19)	-2.11	0.440 (0.07)	0.094 (0.14)	P vs T: 1.000 (0.25)	P vs T: 1.000 (0.04)
								P vs C: 0.161 (0.61)	P vs C: 0.969 (0.04)
								T vs C: **0.005** (0.78)	T vs C: 0.439 (0.15)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: n = 34. MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

B. Physical activity level

Levels of physical activity, sedentary behavior, and compliance recommendations for physical activity are presented in Table 27. No significant differences were found between groups at the beginning of the study. The T group was the most active in terms of total min/week of physical activity, followed by the P, MT, and C groups, respectively. On the contrary, the P group showed the largest amount of time spent in sedentary activities, followed by the C, MT, and T groups. Overall, a high percentage of subjects complied with at least one of the WHO recommendations on physical activity for health, although only around 30% met all the recommendations.

Table 27. *Total, domain-specific, intensity-specific physical activity levels, sedentary behaviour and compliance recommendations.*

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)
Physical activity domains				
Physical activity at work				
Vigorous (min/week), mean ± SD [95%CI]	51.18 ± 90 [19.77–82.58]	88.24 ± 200.08 [18.42–158.05]	73.94 ± 164.27 [16.62–131.26]	47.65 ± 89.58 [16.39–78.90]
Moderate (min/week), mean ± SD [95%CI]	75 ± 167.98 [16.39–133.61]	79.41 ± 159.41 [23.79–135.03]	139 ± 221.74 [61.63–216.37]	135.59 ± 283.19 [36.78–234.40]
Total (min/week), mean ± SD [95%CI]	126.18 ± 179.02 [63.71–188.64]	167.65 ± 294.93 [64.74–270.56]	212.94 ± 319 [101.63–324.25]	183.24 ± 292.2 [81.28–285.19]
Vigorous (MET-minutes/week), mean ± SD [95%CI]	409.41 ± 720.07 [158.17–660.66]	705.88 ± 1600.6 [147.38–1264.3]	591.53 ± 1314.2 [132.98–1050.8]	381.18 ± 716.64 [131.13–631.22]
Moderate (MET-minutes/week), mean ± SD [95%CI]	300 ± 671.94 [65.55–534.45]	317.67 ± 637.64 [95.16–540.13]	556 ± 886.92 [246.51–865.49]	542.35 ± 1132.7 [147.1–937.6]
Total (MET-minutes/week), mean ± SD [95%CI]	709.41 ± 912.84 [390.9–1027.92]	1023.53 ± 1912.61 [356.19–1690.87]	1147.53 ± 1825.74 [510.5–1784.56]	923.53 ± 1306.11 [467.81–1379.25]
Physical activity to move, travel to and from places (to transport)				
Travel physical activity (min/week), mean ± SD [95%CI]	403.53 ± 303.37 [297.68–509.38]	336.18 ± 335.35 [219.17–453.19]	354.21 ± 353.58 [230.83–477.58]	339.85 ± 346.83 [218.84–460.87]
Travel physical activity (MET-minutes/week), mean ± SD [95%CI]	1614.12 ±1213.49 [1190.71–2037.53]	1344.71 ± 1341.4 [876.67–1812.74]	1416.82 ± 1414.33 [923.34–1910.31]	1359.41 ± 1387.35 [875.34–1843.48]
Recreational physical activity				
Vigorous (min/week), mean ± SD [95%CI]	67.06 ± 132.74 [20.74–113.38]	89.71 ± 145.79 [38.83–140.58]	82.94 ± 216.59 [7.37–158.51]	39.71 ± 86.35 [9.57–69.84]
Moderate (min/week), mean ± SD [95%CI]	197.09 ± 209.53 [123.98–270.2]	202.94 ± 174.23 [142.15–263.74]	208.71 ± 182.63 [144.98–272.43]	168.82 ± 180.18 [105.96–231.69]
Total (min/week), mean ± SD [95%CI]	264.15 ± 244.57 [178.81–349.48]	292.65 ± 214.68 [217.74–367.56]	291.65 ± 280.7 [193.71–389.59]	208.53 ± 200.86 [138.44–278.61]
Vigorous (MET-minutes/week), mean ± SD [95%CI]	536.47 ± 1061.96 [165.93–907.01]	717.65 ± 1166.39 [310.67–1124.62]	663.53 ± 1732.74 [58.95–1268.11]	317.65 ± 690.85 [76.6–558.7]
Moderate (MET-minutes/week), mean ± SD [95%CI]	788.35 ± 838.12 [495.92–1080.79]	811.76 ± 696.95 [568.59–1054.94]	834.82 ± 730.53 [579.93–1089.72]	675.29 ± 720.72 [423.82–926.77]
Total (MET-minutes/week), mean ± SD [95%CI]	1324.82 ± 1332.51 [859.89–1789.76]	1529.41 ± 1292.05 [1078.59–1980.23]	1498.35 ± 1867.86 [846.62–2150.08]	992.94 ± 1005.12 [642.24–1343.65]
Sedentary behaviour				
Sitting or sedentary time (min/week), mean ± SD [95%CI]	1741.88 ± 1127.61 [1348.44–2135.32]	1868.38 ± 1293.43 [1417.08–2319.68]	1686.18 ± 437.1 [1533.66–1838.69]	1745.88 ± 642.01 [110.1–1521.87]
Sitting or sedentary time (MET-minutes/week), mean ± SD [95%CI]	2612.82 ± 1691.41 [2022.66–3202.99]	2802.57 ± 1940.15 [2125.62–3479.53]	2529.26 ± 655.65 [2300.5–2758.03]	2618.82 ± 963.01 [2282.81–2954.84]

Table 27. *Continued.*

	MT (*n* = 34)	P (*n* = 34)	T (*n* = 34)	C (*n* = 34)
Total physical activity				
Vigorous (min/week), mean ± SD [95%CI]	118.24 ± 180.59 [55.22–181.25]	177.94 ± 229.85 [97.74–258.14]	156.88 ± 277.75 [59.97–253.79]	87.35 ± 119.17 [45.77–128.93]
Moderate (min/week), mean ± SD [95%CI]	675.62 ± 405.11 [534.27–816.97]	618.53 ± 450.96 [461.18–775.88]	701.91 ± 505.92 [525.39–878.44]	644.26 ± 531.52 [458.81–829.72]
Total (min/week), mean ± SD [95%CI]	793.85 ± 389.25 [658.04–929.67]	796.47 ± 499.41 [622.22–970.72]	858.79 ± 597.02 [650.48–1067.1]	731.62 ± 515.34 [551.81–911.43]
Vigorous (MET-minutes/week), mean ± SD [95%CI]	945.88 ± 1444.76 [441.78–1449.99]	1423.53 ± 1838.87 [781.92–2065.14]	1255.06 ± 2221.99 [479.77–2030.35]	698.82 ± 953.37 [366.18–1031.47]
Moderate (MET-minutes/week), mean ± SD [95%CI]	2702.47 ± 1620.44 [2137.07–3267.87]	2474.12 ± 1803.87 [1844.72–3103.52]	2807.65 ± 2023.68 [2101.55–3513.74]	2577.06 ± 2126.06 [1835.23–3318.88]
Total (MET-minutes/week), mean ± SD [95%CI]	3648.35 ± 1807.31 [3017.75–4278.96]	3897.65 ± 2533.35 [3013.72–4781.58]	4062.71 ± 3127.17 [2971.58–5153.83]	3275.88 ± 2105.38 [2541.28–4010.49]
Daily physical activity				
Average daily physical activity (min), mean ± SD [95%CI]	113.4 ± 55.6 [94–132.8]	113.78 ± 71.34 [88.88–138.67]	122.68 ± 85.28 [92.92–152.44]	104.51 ± 73.62 [78.82–130.2]
Average daily physical activity at work (min), mean ± SD [95%CI]	18.02 ± 25.57 [9.1–26.94]	23.94 ± 42.13 [9.24–38.65]	30.42 ± 45.57 [14.51–46.32]	26.17 ± 41.74 [11.61–40.74]
Average daily physical activity to transport (min), mean ± SD [95%CI]	57.64 ± 43.33 [42.52–72.76]	48.02 ± 47.9 [31.3–64.7]	50.6 ± 50.51 [32.97–68.22]	48.55 ± 49.54 [31.26–65.83]
Average daily recreational physical activity (min), mean ± SD [95%CI]	37.73 ± 34.93 [25.54–49.92]	41.8 ± 30.66 [31.1–52.5]	41.66 ± 40.1 [27.67–55.65]	29.78 ± 28.69 [19.77–39.8]
Average daily sedentary activities time (min), mean ± SD [95%CI]	248.84 ± 161.08 [192.63–305.05]	266.91 ± 184.77 [202.44–331.38]	240.88 ± 62.44 [219.09–262.66]	249.41 ± 91.71 [217.41–281.41]
Compliance recommendations				
Health physical activity METs, n (%)	34 (100)	32 (94.1)	34 (100)	33 (97.1)
Health vigorous physical activity, n (%)	13 (38.2)	15 (44.1)	14 (41.2)	13 (38.2)
Health moderate physical activity, n (%)	32 (94.1)	29 (85.3)	31 (91.2)	29 (85.3)
Compliance of all recommendations, n (%)	11 (32.4)	12 (35.3)	11 (32.4)	9 (26.5)

Note. MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; SD: standard deviation; CI: confident interval; METs: Metabolic equivalent of tasks.

V.IV. RESULTS ON OXIDATIVE STRESS, ANTIOXIDANT ENZYMES, AND THIOL REDOX STATE

V.IV.I. Project one

A. Oxidative stress of DNA, lipids, and protein carbonyls

Changes in DNA oxidation, lipid peroxidation, and oxidative stress of protein carbonyls from the ITT analysis are displayed in Table 28. Repeated-measures ANOVA showed a main effect of time on urinary 8-oxo-dG [$F(1, 57) = 16.86$, $p < 0.000$, $\eta^2p = 0.372$, $1-\beta = 1$], 8-iso-P [$F(1, 67) = 5.41$, $p < 0.007$, $\eta^2p = 0.139$, $1-\beta = 0.829$], and MDA [$F(1, 67) = 1.94$, $p < 0.048$, $\eta^2p = 0.055$, $1-\beta = 0.393$]. Pairwise comparisons revealed significant decreases in all three parameters in the M group, with moderate ESs for all of them, and a significant increase in the HI group in 8-oxo-dG (large ES) and 8-iso-P (moderate ES). No significant differences by time were found in protein carbonyls. In addition, significant time × group interaction was found in MDA between the M and C groups (large ES). The ANCOVA showed a main effect of time on the same parameters: 8-oxo-dG [$F(1, 55) = 11.67$, $p < 0.001$, $\eta^2p = 0.175$, $1-\beta = 0.919$], 8-iso-P [$F(1, 65) = 32.41$, $p < 0.000$, $\eta^2p = 0.333$, $1-\beta = 1$], and MDA [$F(1, 65) = 59.66$, $p < 0.000$, $\eta^2p = 0.479$, $1-\beta = 1$]. After the adjustment, the HI group maintained significant changes in 8-oxo-dG and 8-iso-P with decreased ESs, whereas for the M group, only MDA improved significantly after 16 weeks of training (small ES), but neither 8-oxo-dG nor 8-iso-P did. No changes in protein carbonyls were found. The ANCOVA revealed significant group interactions in 8-oxo-dG [$F(2, 55) = 6.14$, $p < 0.004$, $\eta^2p = 0.183$, $1-\beta = 0.873$] and MDA [$F(2, 65) = 3.09$, $p < 0.050$, $\eta^2p = 0.087$, $1-\beta = 0.477$]. Differences were found between the HI and the M group (large ES) and between HI and C (moderate ES) in 8-oxo-dG, and between M and C in MDA (moderate ES). The results of the PPA found the same significant differences as the ITT analysis, with higher ESs. The PPA results are presented in Supplementary Material B (Table B.1).

Table 28. *Intervention effects on oxidative stress of DNA, lipid and protein biomarkers from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Urinary 8-oxo-dG (nmol/mmol creatinine)	M	2.83	3.80 ± 1.15 (3.31–4.28)	2.98 ± 1.18 (2.43–3.54)	-21.34	**0.004** (0.69)	0.166 (0.34)	M vs HI: 0.988 (0.29)	M vs HI: **0.006** (1.06)
	HI		2.09 ± 0.97 (1.64–2.54)	3.35 ± 1.32 (2.85–3.86)	60.49	**0.000** (1.09)	**0.000** (0.81)	M vs C: 1.000 (0.2)	M vs C: 1.000 (0.3)
	C		2.75 ± 1.18 (2.20– 3.29)	2.75 ± 1.18 (2.20–3.29)	0.00	1.000 (0)	0.888 (0.03)	HI vs C: 0.404 (0.48)	HI vs C: **0.030** (0.77)
8-iso-P (nmol/mmol creatinine)	M	36.90	43.65 ± 15.62 (36.89–50.42)	36.77 ± 11.92 (30.59–42.94)	-15.78	**0.043** (0.5)	0.298 (0.22)	M vs HI: 1.000 (0.27)	M vs HI: 0.127 (0.63)
	HI		32.43 ± 15.38 (26.29–38.56)	40.34 ± 14.48 (34.74 –45.94)	24.40	**0.011** (0.53)	**0.043** (0.36)	M vs C: 1.000 (0.1)	M vs C: 1.000 (0.14)
	C		35.31 ± 18.18 (27.86–42.75)	35.31 ± 18.18 (27.86–42.75)	0.00	1.000 (0)	0.766 (0.05)	HI vs C: 0.773 (0.31)	HI vs C: 0.364 (0.39)
MDA (nmol/mg protein)	M	0.20	0.20 ± 0.10 (0.17–0.24)	0.16 ± 0.05 (0.14–0.19)	-19.12	**0.024** (0.49)	**0.012** (0.42)	M vs HI: 0.800 (0.34)	M vs HI: 0.677 (0.36)
	HI		0.18 ± 0.06 (0.15–0.21)	0.18 ± 0.06 (0.16–0.21)	1.74	0.837 (0.05)	0.341 (0.18)	M vs C: **0.031** (0.84)	M vs C: **0.046** (0.74)
	C		0.22 ± 0.07 (0.18–0.25)	0.22 ± 0.07 (0.18–0.25)	0.00	1.000 (0)	0.329 (0.17)	HI vs C: 0.286 (0.46)	HI vs C: 0.543 (0.35)
Protein carbonyls (nmol/mg protein)	M	19.43	20.21 ± 3.67 (18.98–21.43)	20.23 ± 1.90 (19.27–21.18)	0.11	0.973 (0.01)	0.368 (0.14)	M vs HI: 0.653 (0.35)	M vs HI: 1.000 (0.03)
	HI		18.77 ± 2.68 (17.66 –19.88)	19.42 ± 2.61 (18.56–20.29)	3.47	0.267 (0.25)	0.406 (0.13)	M vs C: 0.881 (0.37)	M vs C: 1.000 (0.2)
	C		19.47 ± 2.22 (18.13–20.82)	19.47 ± 2.22 (18.13–20.82)	0.00	1.000 (0)	0.986 (0)	HI vs C: 1.000 (0.02)	HI vs C: 1.000 (0.14)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size in 8-oxo-dG: M = 20; HI = 24; C = 16. Sample size in the rest of the parameters: M = 23; HI= 28; C = 19. M: moderate-intensity group; HI: high-intensity group; C: control group; DNA: deoxyribonucleic acid; 8-oxo-dG: 8-oxo-2-deoxyguanosine; 8-iso-P: 8-isoprostane; MDA: malonaldehyde; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17 (70.12 for the analysis of 8-oxo-dG).

B. Antioxidant enzymes

The antioxidant-enzymes results from the ITT analysis are presented in Table 29. Repeated-measures ANOVA showed a significant increase ($p < 0.005$) of the antioxidant enzyme CAT in the M group and a significant decrease of the GPx enzyme in the HI group after 16 weeks of training. The magnitude of the pre-post differences (at 16 weeks) for the CAT improvements was considered small, while the change in GPx was moderate. Moreover, significant time × group interaction was found in GPx between the M and C groups (large ES). No significant differences within and between groups were found in the rest of the parameters. Repeated-measures ANCOVA showed the same significant main effect by time on CAT [$F(1, 65) = 7.67$, $p < 0.007$, $\eta^2p = 0.106$, $1-\beta = 0.779$] and GPx [$F(1, 65) = 61.54$, $p < 0.000$, $\eta^2p = 0.486$, $1-\beta = 1$], with similar ESs. It also showed the same differences between groups, with no changes in the magnitude of the adaptations. The results of the PPA found the same significant differences as the ITT analysis, with larger ESs. These results are presented in Supplementary Material B (Table B.2).

Table 29. *Intervention effects on antioxidants enzymes from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
CAT (U/mg protein)	M	207.61	203.60 ± 25.80 (192.44–214.76)	214.60 ± 27.20 (202.44–226.76)	5.40	**0.028** (0.41)	**0.048** (0.37)	M vs HI: 1.000 (0.1)	M vs HI: 1.000 (0.21)
	HI		208.15 ± 26.47 (198.04–218.27)	211.54 ± 31.20 (200.52–222.56)	1.63	0.448 (0.12)	0.403 (0.13)	M vs C: 1.000 (0.11)	M vs C: 0.697 (0.31)
	C		211.65 ± 28.48 (199.37–223.93)	211.65 ± 28.48 (199.37–223.93)	0.00	1.000 (0)	0.823 (0.4)	HI vs C: 1.000 (0)	HI vs C: 1.000 (0.08)
GPx (U/mg protein)	M	57.37	54.91 ± 9.59 (50.22–59.60)	54.61 ± 5.67 (51.09–58.12)	-0.54	0.888 (0.04)	0.185 (0.27)	M vs HI: 0.897 (0.4)	M vs HI: 0.593 (0.45)
	HI		57.25 ± 11.59 (52.99–61.50)	52.12 ± 6.71 (48.93–55.31)	-8.95	**0.009** (0.54)	**0.001** (0.52)	M vs C: 0.082 (0.63)	M vs C: 0.266 (0.43)
	C		60.52 ± 12.59 (55.36–65.68)	60.52 ± 12.59 (55.36–65.68)	0.00	1.000 (0)	0.261 (0.15)	M vs C: **0.004** (0.88)	M vs C: **0.009** (0.72)
SOD (U/mg protein)	M	4.94	5.01 ± 0.40 (4.78–5.24)	5.08 ± 0.46 (4.85–5.32)	1.43	0.560 (0.17)	0.340 (0.24)	M vs HI: 0.779 (0.36)	M vs HI: 1.000 (0.17)
	HI		4.82 ± 0.54 (4.61–5.03)	4.90 ± 0.54 (4.69–5.12)	1.59	0.492 (0.14)	0.860 (0.03)	M vs C: 1.000 (0.09)	M vs C: 1.000 (0.1)
	C		5.03 ± 0.70 (4.77–5.28)	5.03 ± 0.70 (4.77–5.28)	0.00	1.000 (0)	0.700 (0.06)	HI vs C: 1.000 (0.21)	HI vs C: 1.000 (0.05)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 23), HI (*n* = 28), C (*n* = 19). M: moderate-intensity group; HI: high-intensity group; C: control group; CAT: catalase; GPx: glutathione peroxidase; SOD: superoxide dismutase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17.

C. Thiol redox state

Changes in thiol redox state from the ITT analysis are presented in Table 30. Repeated-measures ANOVA showed a significant decrease ($p < 0.005$) of the GSH in the HI group, with a moderate ES. No other significant main pairwise comparison changes by time or group × time interactions were found in the rest of the parameters. All the ESs in the pre-post adaptations are considered small, except for the changes in the GSSG/GSH ratio in the HI group (moderate ES). Despite the lack of significant changes between groups at the end of the intervention, the ESs between the M and the C group, as well as between HI and C, were small to moderate. After controlling for baseline values and age, the repeated-measures ANCOVA found no differences in the thiol-redox-state outcomes. Again, a main effect by time was revealed only in the GSH parameter [$F(1, 65) = 20.15$, $p < 0.000$, $\eta^2p = 0.237$, $1-\beta = 0.993$]. The results of the PPA found the same significant differences as the ITT analysis, with greater ESs. These results are presented in Supplementary Material B (Table B.3).

Table 30. *Intervention effects on thiol redox state from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
GSH (nmol/mg protein)	M	22.19	21.21 ± 3.17 (19.84–22.58)	21.08 ± 4.12 (19.61–22.54)	-0.64	0.861 (0.04)	0.305 (0.2)	M vs HI: 1.000 (0.1)	M vs HI: 0.084 (0.27)
	HI		22.81 ± 3.69 (21.57–24.05)	20.69 ± 3.45 (19.36–22.02)	-9.31	**0.003** (0.59)	**0.007** (0.49)	M vs C: 0.625 (0.39)	M vs C: 1.000 (0.24)
	C		22.46 ± 2.72 (20.96–23.97)	22.46 ± 2.72 (20.96–23.97)	0.00	1.000 (0)	0.853 (0.05)	HI vs C: 0.284 (0.56)	HI vs C: 0.176 (0.59)
GSSG (nmol/mg protein)	M	0.24	0.24 ± 0.07 (0.20–0.28)	0.23 ± 0.0 (0.18–0.27)	-6.37	0.532 (0.19)	0.594 (0.15)	M vs HI: 1.000 (0.19)	M vs HI: 1.000 (0.22)
	HI		0.23 ± 0.09 (0.20–0.27)	0.25 ± 0.12 (0.20–0.29)	6.66	0.488 (0.14)	0.528 (0.12)	M vs C: 1.000 (0.09)	M vs C: 1.000 (0.12)
	C		0.23 ± 0.10 (0.19–0.28)	0.23 ± 0.10 (0.19–0.28)	0.00	1.000 (0)	0.988 (0)	HI vs C: 1.000 (0.1)	HI vs C: 1.000 (0.11)
GSSG/GSH ratio	M	1.11	1.20 ± 0.41 (0.99–1.41)	1.15 ± 0.55 (0.99–1.41)	-4.19	0.722 (0.1)	0.977 (0.01)	M vs HI: 1.000 (0.18)	M vs HI: 1.000 (0.25)
	HI		1.07 ± 0.51 (0.87–1.43)	1.27 ± 0.78 (0.88–1.26)	19.20	0.112 (0.31)	0.157 (0.26)	M vs C: 1.000 (0.13)	M vs C: 1.000 (0.04)
	C		1.08 ± 0.58 (1.02–1.53)	1.08 ± 0.58 (0.84–1.31)	0.00	1.000 (0)	0.899 (0.03)	HI vs C: 0.955 (0.28)	HI vs C: 0.940 (0.27)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). M: moderate-intensity group; HI: high-intensity group; C: control group; GSH: reduced glutathione; GSSG: oxidized glutathione; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17.

IV.IV.II. Project two

A. Oxidative stress of DNA, lipids, and antioxidant enzymes

Changes in DNA oxidation, lipid peroxidation, and antioxidant enzymes from the ITT analysis are displayed in Table 31. Repeated-measures ANOVA showed a main effect of time in urinary 8-oxo-dG [$F(1, 48) = 8.59$, $p < 0.005$, $\eta^2p = 0.152$, $1-\beta = 0.819$], 8-iso-P [$F(1, 48) = 4.52$, $p < 0.039$, $\eta^2p = 0.086$, $1-\beta = 0.549$], and SOD [$F(1, 48) = 4.51$, $p < 0.016$, $\eta^2p = 0.158$, $1-\beta = 0.744$]. Pairwise comparisons revealed significant decreases in the oxidative-stress parameters (8-oxo-dG and 8-iso-P) in both training groups, achieving moderate and large ESs on the DNA damage among the MT and P groups, respectively. In addition, the magnitude of change in lipid peroxidation for the MT group was also considered moderate, whereas the magnitude for the P group was small. In terms of antioxidant enzymes, the MT group saw a significant increase in the values of the SOD enzyme (small ES) after 20 weeks of training. No significant differences by time were found in GPx. In addition, significant time × group interaction was found in 8-oxo-dG between the P and the C group, and in the SOD antioxidant enzyme between both exercise groups and the C group, with large ESs for all of them. The ANCOVA showed a main effect of time on the same parameters: 8-oxo-dG [$F(1, 46) = 156$, $p < 0.000$, $\eta^2p = 0.772$, $1-\beta = 1$], 8-iso-P [$F(1, 46) = 9.37$, $p < 0.004$, $\eta^2p = 0.169$, $1-\beta = 0.850$], and SOD [$F(1, 46) = 6.085$, $p < 0.05$, $\eta^2p = 0.209$, $1-\beta = 0.865$]. The MT and P groups maintained significant differences in the parameter mentioned above. However, pairwise comparison also showed a new significant effect by time on SOD in the P group (moderate ES). No changes were found in GPx. Regarding the group × time interactions, the ANCOVA revealed the same significant interactions in 8-oxo-dG [$F(2, 46) = 4.81$, $p < 0.013$, $\eta^2p = 0.173$, $1-\beta = 772$] and in SOD [$F(2, 46) = 6.085$, $p < 0.05$, $\eta^2p = 0.209$, $1-\beta = 0.865$], again with large ESs. In this case, PPA was not carried out, because there was no experimental mortality associated with these parameters.

Table 31. *Intervention effects on oxidative stress and antioxidant enzymes from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Urinary 8-oxo-dG (nmol/mmol creatinine)	MT	2.96	3.03 ± 2.89 (1.73–4.33)	1.56 ± 1.34 (0.83–2.28)	-48.56	**0.048** (0.65)	**0.000** (0.61)	MT vs P: 1.000 (0.41) MT vs C: 0.058 (0.71) P vs C: **0.003** (1.14)	MT vs P: 1.00 (0.35) MT vs C: 0.105 (0.64) P vs C: **0.013** (1)
	P		3.30 ± 3.06 (2.11–4.49)	1.13 ± 0.69 (0.47–1.79)	-65.79	**0.002** (0.98)	**0.000** (0.79)		
	C		2.56 ± 1.24 (1.37–3.75)	2.73 ± 1.86 (2.07–3.39)	6.67	0.798 (0.11)	0.314 (0.21)		
8-iso-P (nmol/mmol creatinine)	MT	52.01	59.74 ± 31.22 (40.21–79.27)	41.52 ± 31.75 (22.36–60.68)	-30.49	**0.024** (0.58)	**0.031** (0.51)	MT vs P: 1.000 (0.04) MT vs C: 1.000 (0.12) P vs C: 0.773 (0.07)	MT vs P: 1.000 (0.03) MT vs C: 0.154 (0.59) P vs C: 0.177 (0.48)
	P		59.03 ± 48.16 (41.20–76.87)	43.10 ± 41.39 (25.61–60.60)	-26.98	**0.030** (0.35)	**0.031** (0.33)		
	C		38.55 ± 29.56 (20.72–56.38)	45.65 ± 36.08 (28.16–63.14)	18.42	0.323 (0.22)	0.551 (0.12)		
SOD (U/mL)	MT	1.73	1.82 ± 1.10 (1.46–2.18)	2.28 ± 1.11 (1.84–2.72)	25.36	**0.011** (0.42)	**0.007** (0.44)	MT vs P: 1.000 (0.05) MT vs C: **0.003** (1.35) P vs C: **0.003** (1.4)	MT vs P: 1.000 (0.13) MT vs C: **0.006** (1.03) P vs C: **0.027** (0.94)
	P		1.95 ± 0.35 (1.62–2.28)	2.23 ± 0.96 (1.83–2.63)	14.12	0.088 (0.38)	**0.034** (0.49)		
	C		1.44 ± 0.47 (1.12–1.77)	1.23 ± 0.27 (0.83–1.64)	-14.52	0.191 (0.54)	0.068 (0.8)		
GPx (nmol/min/ml)	MT	107.25	109.18 ± 35.56 (84.98–133.38)	117.05 ± 42.62 (94.30–139.81)	7.21	0.602 (0.2)	0.409 (0.24)	MT vs P: 1.000 (0.1) MT vs C: 0.568 (0.46) P vs C: 0.291 (0.56)	MT vs P: 1.000 (0.1) MT vs C: 0.649 (0.44) P vs C: 0.361 (0.54)
	P		108.99 ± 42.12 (86.90–131.08)	121.38 ± 43.48 (100.61–142.15)	11.37	0.370 (0.29)	0.194 (0.32)		
	C		103.90 ± 57.60 (81.81–125.99)	96.65 ± 45.12 (75.88–117.42)	-6.97	0.599 (0.14)	0.346 (0.19)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 15), P (*n* = 18), C (*n* = 18). MT: multi-component training group; P: power strength training group; C: control group; 8-oxo-dG: 8-oxo-2-deoxyguanosine; 8-iso-P: 8-isoprostane; SOD: superoxide dismutase; GPx: glutathione peroxidase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 68.49.

B. Thiol redox state

Details of the thiol-redox-state results from the ITT analysis can be observed in Table 32. Repeated-measures ANOVA showed a main effect of time on all the parameters: total glutathione [$F(1, 48) = 1.12$, $p < 0.029$, $\eta^2p = 0.023$, $1-\beta = 0.180$], GSH [$F(1, 48) = 5.27$, $p < 0.026$, $\eta^2p = 0.099$, $1-\beta = 0.614$], GSSG [$F(1, 48) = 4.02$, $p < 0.024$, $\eta^2p = 0.144$, $1-\beta = 0.691$], and GSSG/GSH ratio [$F(1, 48) = 5.25$, $p < 0.009$, $\eta^2p = 0.180$, $1-\beta = 0.810$]. Pairwise comparisons revealed that the P group was the only one that showed significant increases (total glutathione, GSH and GSSG/GSH ratio) and a significant decrease (GSSG) at the end of the 20 weeks of the training period. The ESs of these changes ranged from small (total glutathione) to moderate (GSG and GSSG) and large (GSSG/GSH ratio). No significant effects by time were found in the MT and C groups. Furthermore, the analyses showed significant time × group interactions after 20 weeks of intervention in all outcomes (total glutathione: MT vs P and P vs C; GSH: MT vs P and P vs C; GSSG: MT vs C and P vs C; GSSG/GSH ratio: MT vs C and P vs C). The magnitude of all of these between-group differences were considered large (≥ 0.80). After correcting for baseline values and age, the ANCOVA analysis revealed a significant decrease in GSSG and GSSG/GSH ratio in the MT group after the end of the intervention. The rest of the effects achieved by time were the same as those from the ANOVA analysis: total glutathione [$F(1, 46) = 14$, $p < 0.001$, $\eta^2p = 0.233$, $1-\beta = 0.956$], GSH [$F(1, 46) = 8.39$, $p < 0.006$, $\eta^2p = 0.154$, $1-\beta = 0.810$], GSSG [$F(1, 46) = 48.71$, $p < 0.000$, $\eta^2p = 0.514$, $1-\beta = 1$], and GSSG/GSH ratio [$F(1, 46) = 44.97$, $p < 0.000$, $\eta^2p = 0.494$, $1-\beta = 1$]. The ESs were similar, and no additional significant effects between groups were found. In fact, the significant differences between the MT and the P group in total glutathione disappeared after the correction. The magnitudes of the changes were also similar (large ESs for all the parameters).

Table 32. *Intervention effects on thiol redox state from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total glutathione (μmol/L)	MT	5.42	5.25 ± 0.27 (5.01–5.49)	5.30 ± 0.31 (5.07–5.52)	0.96	0.608 (0.17)	0.833 (0.06)	MT vs P: **0.002** (1.21) MT vs C: 1.000 (0.09) P vs C: **0.001** (1.22)	MT vs P: 0.070 (0.66) MT vs C: 1.000 (0.23) P vs C: **0.009** (0.8)
	P		5.66 ± 0.56 (5.44–5.88)	5.84 ± 0.53 (5.64–6.04)	3.21	**0.046** (0.33)	**0.002** (0.5)		
	C		5.33 ± 0.46 (5.11–5.55)	5.27 ± 0.39 (5.06–5.47)	-1.20	0.475 (0.15)	0.223 (0.23)		
GSH (μmol/L)	MT	4.84	4.71 ± 0.37 (4.49–4.93)	4.84 ± 0.35 (4.61–5.07)	2.81	0.186 (0.36)	0.378 (0.23)	MT vs P: **0.003** (1.26) MT vs C: 0.630 (0.48) P vs C: **0.000** (1.57)	MT vs P: **0.039** (0.77) MT vs C: 0.229 (0.55) P vs C: **0.000** (1.18)
	P		5.04 ± 0.47 (4.83–5.24)	5.40 ± 0.50 (5.19–5.61)	7.14	**0.000** (0.74)	**0.000 (**0.87)		
	C		4.76 ± 0.42 (4.56–4.97)	4.64 ± 0.45 (4.43–4.85)	-2.57	0.179 (0.28)	0.097 (0.33)		
GSSG (μmol/L)	MT	0.57	0.53 ± 0.17 (0.43–0.64)	0.45 ± 0.11 (0.36–0.54)	-15.23	0.213 (0.55)	**0.018** (0.77)	MT vs P: 1.000 (0.0 8) MT vs C: **0.030** (1.12) P vs C: **0.011** (0.92)	MT vs P: 1.000 (0.13) MT vs C: **0.048** (1.06) P vs C: **0.015** (0.91)
	P		0.62 ± 0.22 (0.52–0.72)	0.44 ± 0.22 (0.35–0.52)	-28.70	**0.004** (0.79)	**0.003** (0.61)		
	C		0.56 ± 0.21 (0.46–0.66)	0.62 ± 0.17 (0.54–0.70)	10.40	0.327 (0.3)	0.304 (0.22)		
GSSG/GSH ratio	MT	0.12	0.11 ± 0.04 (0.09–0.14)	0.09 ± 0.02 (0.07–0.11)	-18.25	0.136 (0.59)	**0.024** (0.66)	MT vs P: 1.000 (0.35) MT vs C: **0.012** (1.12) P vs C: **0.000** (1.25)	MT vs P: 1.000 (0.35) MT vs C: **0.019** (1.07) P vs C: **0.001** (1.22)
	P		0.12 ± 0.04 (0.10–0.14)	0.08 ± 0.04 (0.06–0.10)	-32.90	**0.003** (0.93)	**0.000** (0.85)		
	C		0.11 ± 0.04 (0.09–0.14)	0.13 ± 0.04 (0.11–0.15)	14.50	0.182 (0.38)	0.095 (0.35)		
GSH/GSSG ratio	MT	9.91	10.11 ± 4.82 (7.59–12.63)	11.66 ± 4.57 (9.16–14.17)	15.38	0.328 (0.33)	0.177 (0.36)	MT vs P: 0.224 (0.6) MT vs C: 0.186 (0.74) P vs C: **0.001** (1.28)	MT vs P: 0.201 (0.62) MT vs C: 0.202 (0.73) P vs C: **0.001** (1.29)
	P		9.55 ± 4.60 (7.25–11.85)	14.74 ± 5.57 (12.45–17.02)	54.26	**0.001** (1.01)	**0.000** (0.95)		
	C		10.11 ± 5.11 (7.81–12.41)	8.44 ± 4.16 (6.15–10.73)	-16.48	0.252 (0.36)	0.204 (0.32)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 15), P (*n* = 18), C (*n* = 18). MT: multi-component training group; P: power strength training group; C: control group; GSH: reduced glutathione; GSSG: oxidized glutathione; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 68.49.

V.V. DISCUSSION ON OXIDATIVE STRESS, ANTIOXIDANT ENZYMES, AND THIOL REDOX STATE

To the best of our knowledge, the studies presented in this PhD dissertation are the first to investigate the effects of two key training parameters (intensity and modality training) using elastic resistance during a medium to long training period (16, 20 and 32 weeks) on the oxidative stress of DNA, lipids and proteins, antioxidant enzymes and redox thiol state in older women. Regarding the intensity, the first study's main and novel finding is that high-intensity progressive resistance training increases oxidative stress, as shown by the increase in urine 8-oxo-dG and 8-iso-P concentrations and the decrease in the antioxidant tripeptide GSH and GPx enzymes. However, the progressive resistance training at moderate intensity demonstrated a decrease in DNA damage and lipid peroxidation through the two biomarkers tested, 8-iso-P and MDA, with a significant increase in the levels of the antioxidant enzyme CAT and no significant changes in GSH. Furthermore, regarding the training modality, the second study's main and novel finding is that both training modalities – multi-component and power strength training – are effective for decreasing the oxidative stress of DNA and lipids by decreasing their concentration levels and improving the activity of the antioxidant enzymes, especially SOD, and the thiol redox state by increasing GSH and reducing GSSG, the latter particularly in the P group.

We had hypothesized in H1 and H10 (Chapter III, Section III.I.III.) that a 16-week program of progressive resistance training with elastic bands at high intensity in older women increases oxidative stress by increasing the concentrations of 8-oxo-dG, 8-iso-P, MDA, and protein carbonyls biomarkers, while a moderate intensity routine produces a reduction of the values in the same parameters, finding significant differences between the training intensities. These hypotheses were partially refuted, because we only found significant differences between the effects of the two intensities on 8-oxo-dG when values were adjusted by age and

baseline scores. In the rest of the parameters, no differences between the training intensities were found, though 8-iso-P and MDA did decrease significantly in the M group and increase in the H group (significantly in 8-iso-P and not significantly in MDA). Additionally, neither the HI nor M groups produced significant changes in protein carbonyls. Next, we had hypothesized in H2 and H10 (Chapter III, Section III.I.III.) that both training intensities produce similar increases in the concentration of thiol redox state and antioxidant enzymes parameters after 16 weeks of progressive resistance training with elastic bands, finding significant differences between the training intensities. However, our findings partially refuted these hypotheses, because only the M group demonstrated improved antioxidant activity by an increase of CAT, while the HI group had decreased activity of GPx and GSH. Additionally, no other significant changes or differences between training intensities were found in the antioxidant enzymes and thiol redox state.

Regarding the influence of the training modality, we had hypothesized in H1 and H10 (Chapter III, Section III.II.III) that both, the multi-component and power strength training modalities, produce similar improvements in the oxidative stress state by decreasing the concentrations of 8-oxo-dG and 8-iso-P and increasing the activity of the thiol redox state and antioxidant enzymes after an intervention period of 20 weeks using elastic resistance. Our findings largely confirmed this hypothesis, as we found no differences between the training modalities in the improvements of DNA and lipid peroxidation and the antioxidant enzymes, but differences between multi-component and power strength were found between the parameters of thiol redox state, particularly in total glutathione and GSH.

V.V.I. Specific discussion of the first project

To date, few studies have investigated the chronic effect of resistance training on oxidative stress biomarkers (Alikhani et al., 2019; Bobeuf et al., 2011; Dantas et al., 2016; Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer, Wagner, 2015; Franzke et al., 2018; Gargallo et al., 2018; Liao et al., 2016; Padilha et al., 2015; Parise et al., 2005, 2005b; Rall et al., 2000; Ribeiro et al., 2017; Shahar et al., 200; Vezzoli et al., 2019;Vincent et al., 2002;Vincent et al., 2006), and more specifically on DNA damage (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer, Wagner, 2015; Franzke et al., 2018; Gargallo et al., 2018; Mota et al., 2019; Parise et al., 2005; Rall et al., 2000; Soares et al., 2015;Vezzoli et al., 2019). The results obtained in the first study are consistent with those by Parise et al. (2005), which showed that in older individuals (mean age 71 years), 14 weeks of circuit resistance training three times a week at 50–80% of their 1RM significantly reduced their urinary levels of 8-oxo-dG while producing no change in GSH (Parise et al., 2005). However, it is necessary to note that the authors did not report the percentages of the changes, and the sample was composed of men and women, not differentiating between genders in the results provided.

Additionally, our results in the M group agree with those obtained by Soares et al. (2015), which showed that 16 weeks of resistance training three times a week at 75% of 1RM + aerobic training significantly decreased DNA damage, as evaluated in men with different DNA damage biomarkers (DNA strand breaks and FPG-sensitive sites) (Soares et al., 2015). Similar results were also reported by Mota et al. (2019) with a significant decrease in DNA damage after a 16-week period of resistance + aerobic training performed three times a week by women over 40 years old, although the intensity of the strength component was not reported, and the biomarkers assessed were the same as Soares et al. (2015). In both studies, concurrent training (resistance plus aerobic) was performed, not resistance training alone, as

in our first study. Nevertheless, a study more similar to ours was conducted by Vezzoli et al. (2019) who found that a 12-week resistance training program performed 3 days a week at 60% of 1RM in sarcopenic elderly community dwelling individuals (men and women) decreased the values of 8-oxo-dG by 36%.

However, our results contrast with those from Rall et al. (2000), who found that 12 weeks of resistance training in older adults with rheumatoid arthritis, two times a week at 50–80% of 1RM, did not result in any significant change in urinary 8-oxo-dG, although this finding may have been due to their small sample size. Again, the authors did not report the results separated by gender, making it difficult to compare the findings. Focusing on the studies that analyzed the effects of elastic resistance training, detrimental (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer, Wagner, 2015; Franzke et al., 2018) or no-change (Franzke et al., 2018) effects were found for DNA damage in the institutionalized elderly after 6 months of resistance training twice a week (Franzke, Halper, Hofmann et al., 2015; Franzke, Neubauer, Wagner, 2015). However, there are a number of important differences between Franzke's studies and our first study. The most relevant is that the authors did not specify the intensity at which their participants worked in any of the three studies, so the discrepancy between our findings and theirs may be related to exercise intensity. Moreover, DNA damage was assessed with different biomarkers; the studies were conducted in very old, institutionalized individuals; the resistance training protocols were performed in conjunction with protein and vitamin supplementation in both men and women; and the results were reported by gender only in the study by Franzke et al. (2018).

Our results also contrast the findings reported in a recent review on this topic. Cuyul-Vasquez et al. (2020) noted that a progressive 8–24 weeks of resistance training at 40–80% of 1RM in healthy older people generated favorable chronic adaptations but without significant changes in redox homeostasis in terms of molecular oxidation and antioxidant capacity

markers. However, this review showed some important bias: the inclusion of a healthy and pathologic sample, the exclusion of studies performed with variable resistance, and the low quality of the studies included (Cuyul-Vasquez et al., 2020). It is important to note that no previous study has compared the effects of different training intensities on DNA damage in older adults, with our first study being the first one. Additionally, some of the discrepancies in findings may be related to the time that elapsed between the performed exercises and the measurement of 8-oxo-dG. Several acute metabolic changes resulting from exercise can persist for at least 72 hr after exercise (Cakir- Atabek et al., 2010), which is why we collected the blood samples from the participants 72 hr after their last training session. Additionally, the use of different biomarkers of DNA damage across studies further confounds comparisons.

In terms of lipid peroxidation, our results in the first study revealed the same trend as the DNA damage. Moderate intensities seem to be beneficial, while high intensities are harmful. These findings align with previous studies that found positive effects for resistance training on 8-iso-P (Vezzoli et al, 2019) or MDA (Alikhani et al., 2019; Carru et al., 2018; Dantas et al., 2016; Mota et al., 2019; Raungthai et al., 2019) when it was performed at moderate intensities. However, much of the research until now has been conducted in subjects with pathological conditions (Dantas et al., 2016; Raungthai et al., 2019; Vezzoli et al, 2019) or combined resistance training with aerobic training or supplementation regimens (Carru et al., 2018; Mota et al., 2019; Raungthai et al., 2019; Vezzoli et al, 2019).

Alikhani et al. (2019) have the only previous study to analyze the effect of a resistance training program without an aerobic component or supplementation in healthy older women (55–65 years old). The authors found that 12 weeks of resistance training, 3 days a week at 75% of 1RM (six exercises, 4 sets of 10 repetitions) significantly decreased the values of MDA by 17.45%. Interestingly, our study found similar improvements with less

training frequency (two vs three sessions per week) but with similar total work in terms of sets and repetitions. However, the paper by Alikhani et al. (2019) fails to not analyze the effect size of their changes, as happen with most studies in the field. It is also necessary to highlight the study by Carru et al. (2018), which demonstrates statistically significant reductions in plasma MDA only in female participants (not male) after 18 weeks of resistance training, 2 days a week at 70% of 1 RM, suggesting that strength training might have beneficial effects on lipid peroxidation, particularly in older women (Carru et al., 2018). Additionally, other studies have also observed positive effects on lipid peroxidation but in other biomarkers (Amaral et al., 2020; Bachi et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Vicent et al., 2002, 2006), though MDA and 8-iso-P, in particular, are the gold standard for analyzing lipid peroxidation.

By contrast, some investigators reported no effects on lipid peroxidation after the resistance training period in older adults (Bobeuf et al., 2011; Franzke et al., 2018; Giolo et al., 2018; Liao et al., 2016; Ribero et al., 2017; Shahar et al., 2013). For example, a study by Bobeuf et al. (2011) did not detect any differences in plasma MDA and 8-iso-P levels after a 6-month resistance training and supplement of vitamin C and E, 3 days a week, in older men and women (Bobeuf et al., 2011). Nevertheless, the intensity of the training program was not reported. Alternatively, Vincent and colleagues (Vincent et al., 2002) were the first to examine the effects of different intensities of resistance training on lipid peroxidation. Authors found that long-term (24 weeks) resistance training with an intensity of 50% (1 set x 13 repetitions) and 80% of 1 RM (1 set x 8 repetitions) 3 days a week using 12 exercise machines in older men and women (Vincent et al., 2002) produced a significant reduction in MDA in both groups of 14% in low intensity and 18% in high intensity. Discrepancies between Vincent's study and ours, where high intensity significantly increased the levels of 8-iso-P but did not produce changes in MDA, may be attributed to the higher volume used in

our study (3–4 sets vs 1 set). Regarding the studies that used elastic devices in their resistance training programs, our results differs from the previous investigations, where no changes were found on lipid peroxidation after 12 weeks (Shakar et al., 2013) and 6 months (Franzke et al., 2018; Liao et al., 2016) of resistance training. None used a proper method to control the training intensity with elastic bands. Additionally, the specific training intensity was not reported in any study.

Aside from DNA and lipid oxidation, a few investigators have measured protein oxidation following resistance training in older adults, with protein carbonyls being the biomarkers most commonly analyzed. Our results are similar to those reported by previous investigations; no changes in the oxidation of proteins were found after the resistance training period performed with machines/free weights (Padihla et al 2015; Parise et al., 2005b) or elastic bands (Shahar et al 2013). Conversely, Vezzoli et al. (2019) was the only study to report a decrease in protein carbonyl levels following 12 weeks of resistance training 3 days a week at 60% of 1 RM (Vezzoli et al., 2019). However, our study is the first that allows us to know that protein carbonyls react differently to the effects of exercise than DNA and the lipid biomarkers of oxidative stress, as their levels were not affected by the training. It seems that is not an intensity-dependent biomarker.

Regarding the thiol redox state, the results of the first study provide preliminary data that redox activity is dose dependent in older adults, depending on the intensities applied. The significant decrease in GSH activity (9.31%), alongside the increase in GSSG (6.66%), produced by high-intensity resistance training in the HI cohort could be interpreted as evidence of insufficient antioxidant defenses to cope with the enhanced free radical production resulting from the intervention. In contrast, the reduction in GSSG (6.37%) and absence of changes in GSH resulting from moderate-intensity resistance training demonstrate that moderate levels are the optimal training intensity for older women, because these levels

produce the necessary stimulus to generate effective adaptive changes in the enzymatic antioxidant system while reducing levels of DNA damage and lipid peroxidation.

Our results regarding GSH contrast with previous studies, which have suggested that GSH increases after a resistance training exercise program at moderate (50% 1RM, 1 set x 13 repetitions, 8 exercises) and high (80% 1RM, 1 set x 8 repetitions, 8 exercises) intensities in elderly subjects between 60 and 83 years old after 24 weeks of resistance training (Vincent et al., 2002), with the higher increases achieved in the moderate-intensity group. It could be possible that the training intensities (between 50% and 80% of 1RM) and volumes (only 1 set per exercise) reported by Vicent et al. (2002) were not high stimulus, with both intensities between the thresholds where antioxidant defenses can remove the excess RONS produced. Similar results were also shown in young, untrained men after 6 weeks of progressive resistance training; the improvement of GSH (24.74% in the moderate-intensity group and 27.55% in the high-intensity group) were independent of the training intensity applied (moderate intensity: 3 sets of 12 repetitions at an intensity corresponding to 70% of 1RM; high intensity: 3 sets of 6 repetitions at an intensity corresponding to 85% of 1RM) (Cakir-Atabek et al., 2010). After 8 weeks of progressive resistance training in young men, Azizbeigi, et al. (2015) found similar behavior in other antioxidant enzymes due to SOD and GPx activity increased in both the moderate- (65–70% 1RM) and high-intensity (85–90% 1RM) groups (Azizbeigi, et al., 2015).

Generally, studies have shown that resistance training results in an increase of all or some of the antioxidant enzymes (Alikhani et al., 2019; Amaral et al., 2020; Bachi et al., 2019; Dantas et al., 2016; Franzke, Halper, Hofmann et al., 2015; Mora et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Padilha et al., 2015; Parise et al., 2015b; Raungthai et al., 2019; Ribeiro et al., 2017; Soares et al., 2015; Vezzoli et al., 2019), or produces no changes (Bobeuf et al., 2011; Carru et al., 2018; Franzke, Halper,

Hofmann et al., 2015; Franzke et al, 2018; Gargallo et al., 2018; Giodo et al., 2018; Liao et al., 2016; Mora et al., 2019; Parise et al., 2005; Ribero et al., 2017; Shahar et al., 2013; Valls et al., 2014). Interestingly, a compensatory balance appears to exist among the various components contributing to the overall antioxidant defense system in blood (Kłapcin´ska et al., 2000). This balance seems to result from how antioxidant enzymes work in networks, where a decrease in a particular antioxidant can be compensated for by an increase in another, as can be observed in the first and second studies. As with oxidative stress biomarkers, their response seems to be conditioned by the training dose.

Previous publications have reported mixed results regarding antioxidant defense depending on the antioxidant enzymes analyzed. Findings in the literature on enzymatic antioxidants are contradictory, supporting this hypothesis. In the case of SOD, which is the major defense against O2- and the first line of defense against oxidative stress, our results in the first study showed no significant changes in this parameter for moderate- or high-intensity resistance training. These results align with previous studies (Frantzke et al., 2018; Giolo et al., 2018; Parise et al., 2005). However, contrary to our results, some investigation failed to note the effect of resistance training on this antioxidant enzyme (Amaral et al., 2020; Franzke, Halper, Hofmann et al., 2015; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Cavalcante et al., 2019; Parise et al 2005b). Only the study by Shahar et al. (2013) demonstrates that SOD levels decrease after a resistance training program. These conflicting results are also common for the remaining antioxidants enzymes. For example, the GPx and CAT enzymes, which both have the similar primary function of decomposing H_2O_2 to H_2O, have different responses to resistance training. After 12 weeks of resistance training in older men and women with hypertension, only Raungthai et al. (2019) found an increase in this antioxidant enzyme (Raungthai et al., 2019). In the rest of the studies, no changes were found (Liao et al., 2016, Franzke, Halper, Hofmann et al., 2015; Franzke et al., 2018). It seems that

this enzyme is less sensitive to the effects of resistance training than other endogenous enzymatic enzymes. However, the behavior of CAT is more similar to SOD, with previous work that found an increase (Franzke, Halper, Hofmann et al., 2015; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Parise et al., 2005b), no changes (Franzke et al., 2018, Mora et al., 2019; Parise et al., 2005), or a decrease (Amaral et al., 2020).

Our results in GPx and SOD reflect the trends in the evidence mentioned above, because they had different behavior within and between groups. Both enzymes are intensity-dependent in different ways. Moderate intensity increased the CAT concentration while GPx remained stable. Alternatively, high intensity produced no changes in CAT but a significant decrease in GPx. A possible explanation for these responses might be that, as aging progresses, humans gradually become less adaptable to increases in ROS when undergoing high-intensity training, thus increasing their susceptibility to oxidative stress (Ji, 2001; Radak, et al., 2013). Thus, the production of RONS may exceed hormesis and overwhelm the antioxidant system. This observation was clearly manifested in our study, as resistance training at a moderate intensity generated a beneficial adaptive response to oxidative stress, while high intensity produced an imbalance in favor of ROS production and a decrease in antioxidant enzymes. In fact, if the exercise intensity during training resistance is too low and thus insufficient, the majority of free radicals produced during the training sessions are eliminated by the antioxidant defenses; consequently, there is no change in the antioxidant system (Lovlin et al., 1987). However, if it is too high, the body's antioxidant system may not be able to effectively remove the excess RONS produced (Kerksick & Willoughby, 2005).

It is important to highlight that biological antioxidant adaptations are dependent on the magnitude of RONS produced acutely by each exercise session (Radak et al., 2001) with training intensity a key factor to achieve adaptations in the antioxidant system. In fact, in the review by Bouzi and colleagues, the authors recommend that resistance training protocols for

older adults contain sufficient volume for each muscle group (3–5 sets, 10 repetitions) with intensities between 50% and 80% of 1RM to improve the antioxidant defenses (Bouzi et al., 2015). However, this recommendation regarding intensity in 2015 was made only on the basis of seven articles, only one of which compares different intensities. Is not clear whether variation in the intensities of exercise can generate changes in such markers, but Dixon et al. (2006) and Cakır-Atabek et al. (2015) hypothesize that there is an exercise intensity threshold beyond which oxidative stress increases (Cakır-Atabek et al., 2015; Dixon et al., 2006).

The mechanism by which antioxidants act to decrease oxidative damage is still not well defined. Reducing oxidized substrates (Nordberg & Arner, 2001), stimulating the transcription of other antioxidant systems (Burke-Gaffney et al., 2005), and intercepting the attack of RONS (Halliwell & Gutteridge, 1995) are some, but their effects depend on the type of ROS produced, the location where it is generated, the manner in which it is generated, and what objective of damage is measured (Halliwell & Gutteridge, 1995).

The results we obtained in the first study correspond to those of previous studies, wherein very intense or very long exercise regimes induced increased chromosomal damage (Schiffl et al., 1997) and lipid peroxidation, but lower intensities, even the practice of Tai Chi, produced significantly lower oxidative stress (Goon et al., 2008). Radak et al. (2013) highlights that a moderate level of oxidative stress is essential for adaptive responses to exercise, but very prolonged or exhausting exercise or exercise to which the person is unaccustomed can impair the balance between ROS production and the antioxidant defense system (Radak et al., 2013). However, the results vary notably across studies due to the exercise protocol [intensity (low, moderate, high), mode (aerobic/anaerobic training, resistance, power, multi-component, eccentric, isometric, dynamic, jump training, HIIT), volume, frequency, duration], redox products (different oxidative stress and antioxidant biomarkers analyzed), sample matrix (different fluids and tissues), biochemical analysis

methods (HPLC, ELISA, etc.), nutritional status and training level of the subjects, and sampling time points (minutes, hours, days), which vary markedly too. These differences make it difficult to draw a conclusion about the effect of resistance training on oxidative stress damage markers.

V.V.II. Specific discussion of the second project

Regarding the second study, where the effects of multi-component and power strength training programs on oxidative stress were compared, the results showed that the participants of both training modalities notably improved their oxidative stress state by significantly reducing (moderate to large ES) the concentrations of 8-oxo-dG and 8-iso-P and significantly improving the antioxidant defenses, with no significant differences between the groups except in the thiol state. In the case of the multi-component program, this decrease of damage promoted by regular physical exercise was also measured in studies that performed only aerobic exercises (Inoue et al., 2008; Siu et al., 2011) or aerobic amd resistance exercises (concurrent training) (Bachi et al., 2019; Mota et al., 2019; Raungthai et al., 2019; Soares et al., 2015). In fact, the results from a recent systematic review indicate that exercise programs increase antioxidant capacity markers and decrease molecular oxidation markers, regardless of intensity, volume, exercise type or population, when aerobic programs were performed in older adults (de Sousa et al., 2017). Furthermore, data from the literature suggest that improving oxidative/antioxidant balance can be achieved with intensities between the two ventilator thresholds (50-80% of VO2 max) (Bouzid et al. 2015; Goto , Naito et al., 2007; Leaf et al., 1997; Lovlin et al., 1987), which corresponds with the intensity performed in the aerobic component of the MT group. However, despite the current evidence, most of the studies performed to date have a low statistical power and low quality, making difficult to extract conclusions.

If we focus on the studies that performed only a multi-component training, not concurrent or aerobic training, only the study of Trapé et al. (2017) analyzed the effect of this modality on oxidative stress biomarkers. The authors found that after 12 weeks of multi-component training with elastic bands and free weight in circuit, 2 days a week, MDA levels decreased significantly in older women, producing an adaptive response to oxidative stress related to exercise (Trapé et al., 2017). As we can see, this training modality seems to be effective at improving at least the lipid peroxidation by reducing the concentration levels of 8-iso-P or MDA in older adults. Indeed, our study was the first that reported evidence of the influence of this kind of training program on DNA damage. Both in the case of 8-oxo-dG and 8-iso-P, the percentage of changes and the ES were higher than in the first project in both training groups, probably due to the longer length of the training program or just because the type of exercise regimen performed. Furthermore, the significant increase of SOD activity and decrease of GSSG concentration levels also shows an increase of enzyme protection.

Our results about the antioxidant activity in the multi-component group were similar to those found by Carvarhlo et al. (2010), who showed that a moderate-intensity multi-component exercise program, performed 3 days/week, results in significant and beneficial effects on plasma antioxidant capacity through an increase in the total antioxidant status, GSH and GPx biomarkers in older women (Carvarho et al., 2010). In our study, the improvements in these two biomarkers in the MT group were not significant, probably because the training frequency was lower than in the study of Carvarho and colleagues (two vs three; Carvarho et al., 2010). Moreover, Gonçalves et al. (2019) found similar results after 12 weeks of multi-component training, 2 sessions/week, 90 min/session, with an exercise intensity between 13 and 15 on the Borg scale; there was an improvement in redox status in older women (Gonçalves et al., 2019). However, Trapé et al. (2017) found that the multi-component induced response to antioxidant defense varies between antioxidant enzymes.

They observed a significant improvement in the total antioxidant capacity parameter, but at the same time, no changes were found in GSH activity after 12 weeks of multi-component training in older women performed with the same training frequency as our study. As happened in the first study, behavior following the exercise training differs between antioxidants enzymes.

But if we must highlight a training modality from the modalities analyzed in our two studies, due to its effects on oxidative stress, it is power strength training. The P group decreased the DNA damage at a higher rate than the MT training (MT: -48.56% vs P: -60.79%), achieving large ES by time and a similar decrease in the lipid peroxidation as the MT group (MT: -30.49% vs P: -26.98%). Additionally, this exercise regimen produced similar responses in SOD and GPx but a better response in the thiol antioxidant system than the multi-component training, with significant differences between groups in total glutathione and GSH in favor of power training. Supporting our results, previous studies also found a significant decrease in the lipid peroxidation biomarkers after a power strength training program in older adults. For example, Dimauro and colleagues (Dimauro et al., 2016) demonstrated that 12 weeks of explosive-type resistance training 2 days a week at moderate intensity (40–70% of 1RM) could be proposed as an effective exercise intervention for improving lipid peroxidation through a significant decrease in myeloperoxidase. Indeed, Valls et al. (2014), with the same training protocol, also found a significant improvement in lipid peroxidation by a decrease in the 4-HNE biomarker (Valls et al., 2014).

Different to our results, previous investigations found no changes in MDA and protein carbonyls after 12 weeks (2 days a week) of high-speed resistance training and an acute session in healthy elderly subjects (Ceci et al., 2014). However, the studies from Venorjarvi et al. (2013) and Alcazar et al. (2019) – which were conducted with clinical samples (impaired glucose regulation and COPD, respectively) – found conflicting results. Venorjarvi

and colleagues observed that a 12-week power training program, in combination with aerobic training, 3 days a week between 50–85% of 1 RM results in no change in MDA in middle-aged men with impaired glucose regulation (Venorjarvi et al., 2013). Otherwise, Alcazar and colleagues showed a significant decrease in protein carbonylation after an applied 12 weeks of power training plus HIIT 3 days a week at 50–85% of 1RM in elderly participants with COPD (Alcazar et al., 2019). The reasons for these contrasting results remain unclear but may relate to differences in the characteristics of the studied population (the health status of participants or initial level of oxidative stress) and methodological issues [level of social interaction or supervision association with each intervention (e.g., group vs individual training), differences in the training doses (e.g., frequency, intensity, duration), and/or differences in oxidative and antioxidants biomarkers used].

It should be noted that our study is the first to analyze the effects of this training modality on DNA damage. Compared to other training modalities or traditional resistance training, it appears that power training produces at least the same beneficial effects as moderate resistance training or aerobic training in older adults, or even greater effects than these modalities, based on the results achieved in our study. The mechanisms by which power training confers a positive effect on oxidative stress have yet to be fully elucidated; however, the present study may provide some insights. As we mentioned in previous sections, not all the fibers are equally affected by aging. In fact, type II fibers have a faster age-induced decline, partially attributable to greater apoptosis and oxidative injury, as this type of fiber has lower mitochondrial content and is more susceptible to atrophy than type I fibers with a high mitochondrial content (Lexell et al., 1988; Phillips & Leeuwenburgh, 2005). It is well-known the organs that produce more oxidative stress are the most oxygen dependent, with brain and muscle being the largest factors of oxidative stress products. Thus, the higher involvement of this kind of muscle fiber through power strength training could reduce the

oxidative stress rate in the muscle content, making the oxidative stress response to exercise mode dependent. Additionally, the healthy amount of ROS generated during the contractions probably increases the expression of genes involved in mitochondrial biogenesis as well as antioxidant defense (Bouzi et al., 2015; Cartee et al., 2016; Yoo et al., 2018). Conversely, as we saw in the first study, exercise may aggravate oxidative damage if the exercise dose is not adequate in terms of intensity, duration, or exercise type.

As with the oxidative stress biomarkers, the body of evidence that supports the use of power strength training for improving antioxidant defenses is weak; only a few studies have analyzed this link (Ceci et al., 2014; Dimuro et al., 2016; Valls et al., 2014; Venorjarvi et al., 2013). In contrast to earlier findings, our results demonstrated a good specific response from the thiol antioxidant group, with moderate to large ES. Most of the previous studies found no changes in the antioxidant's parameters after the power training in older adults (Ceci et al., 2014; Valls et al., 2014; Venorjarvi et al., 2013). For example, Valls et al. (2014) and Ceci et al. (2014) demonstrated that in the absence of clinical disease, 12 weeks of high-speed resistance training could be well tolerated by old adults (70–75 years), but this program did not induce any change in GSH, GSSG, GSH/GSSG ratio or total antioxidant capacity (Valls et al., 2014; Cerci et al., 2014).

Similarly, Venorjarvi et al. (2013) also observed no changes in the antioxidant enzyme levels analyzed after 12 weeks of power training in combination with aerobic training in men with impaired glucose regulation (Venorjarvi et al., 2013). Only Dimauro et al. (2016) found negative effects on antioxidant defenses after an applied 12 weeks of high-speed resistance training in healthy older adults, with a significant decrease in MnSOD (Dimauro et al., 2016). The positive effects in our study may stem from a longer duration of training program, since they performed 8 weeks longer than the previous studies (12 vs 20 weeks). Additionally, we cannot forget that the use of variable resistance could also influence

the final outcomes, as the way in which it offers resistance during the ROM is different, producing different adaptations.

One of the most important knowledge gaps in the literature is the lack of reference values regarding oxidative stress biomarkers. Reference values are essential for the correct interpretation of the evaluations and establishment of appropriate treatment goals. They can be used as a motivation for the subjects during the interventions and are also useful for evaluating the effectiveness of interventions. However, there are no reference values for the oxidative and antioxidants biomarkers of the elderly population without a main pathologic condition. Rrecently, Hernando-Espinilla and colleagues (Hernando-Espinilla et al., 2020) established the reference values of a cohort of 41 healthy older adults (60 to 90 years of age, men and women) for the same biomarkers that were analyzed in our studies. The reference values for the oxidative stress biomarkers were as follows: 8-oxo-dG: 3.27 ± 0.34 (nmol/mmol creatinina); 8-iso-P: 60.55 ± 3.91(Pg/mmol crea); MDA: 0.23 ± 0.01 (nmol/ mg Prot); and protein carbonyls: 0.21 ± 0.08 (nmol/ mg Prot). Indeed, the reference values for the antioxidant enzymes were as follows: SOD: 4.70 ± 0.82 (U/mg Prot); GPx: 51.53 ± 8.81 (U/g Prot); CAT: 205.19 ± 28.70 (U/g Prot); GSH: 20.74 ± 3.52 (nmol /mg Prot); GSSG: 0.25 ± 0.06 (nmol/ mg Prot); and GSSG/GSH: 1.25 ± 0.33.

Using these values as a reference, the oxidative stress levels of the samples analyzed in the first and second studies were lower, while the levels of antioxidant enzymes were higher. However, the differences are minimal, which ensures that the samples present values similar to the representative healthy older population. It is reasonable to speculate that the older age of the participants in the reference cohort – along with the fact that there are both men and women in the same sample – is what produces the difference in values between the different samples. One possible explanation for the lack of significant changes in GPx enzyme in both studies may be because this enzyme is more efficient with high ROS

concentration (Antunes et al., 2002; Jenkins & Goldfarb, 1993), and higher levels are characteristic of people with disease processes.

It is necessary to highlight the difficulties encountered when comparing our results with previous studies. The use of different biomarkers, data reported in most cases from men and women combined, strength programs usually coupled with aerobic training or supplementation, or the fact that the biomarkers are expressed in different units are some of the most important limitations to be aware of.

The findings on 8-oxo-dG and 8-iso-P – and the antioxidant defense – reinforce the idea that exercise must be performed at moderate intensities or a sufficient intensity through resistance strength, multi-component, or power strength training to result in the accumulation of RONS and subsequent oxidative stress in a single bout to produce and increase of the antioxidant enzymes, resulting in a chronic adaptation reflected in a decrease in oxidative stress and an increase in part of antioxidant enzymes. The positive results of resistance training at moderate intensity and the multi-component and power strength modalities – presented as a decrease in the oxidative stress biomarkers and the increase in the antioxidant enzymes – have a direct impact in the prevention of diseases related to the most oxygen-dependent tissues, brain, and skeletal muscles. Thus, the incidence and prevalence of neurodegenerative diseases, such as Alzheimer's or Parkinson's (Fugere et al., 2006; Gianni et al., 2004; Radak et al., 2002; Terman & Brunk, 2004); the loss of muscle mass, termed as sarcopenia (Fulle et al., 2004; Gianni et al., 2004); and the reduction of muscle strength and function, termed as dynapenia (Baumann et al., 2016; Clanton et al., 1999), frailty and even pre-frailty (Liu et al., 2016; Saum et al., 2015; Soysal et al., 2017) could be reduced by implementing such training protocols to the extent that these pathologies are directly related to higher levels of oxidative stress than the healthy elderly population.

It is necessary to remark that the effects found in both studies are especially relevant, because the effects of oxidative stress are especially marked in older women, who are exposed to particular risk from the loss of the antioxidant effects of estrogen during menopause (Moreau & Hildreth, 2014). Indeed, one of the most relevant consequences is that older women are particularly susceptible to the damaging effects of sarcopenia and dynapenia associated with chronic oxidative stress (Cesari et al., 2012; Howard et al., 2007), as this population possess also lower levels of muscular strength and muscle mass than men (Brady et a., 2014; Goodpaster et al., 2006; Hughes et al., 2001).

Though the relationship between exercise and oxidative stress is complex and multifactorial, as we have seen from the results obtained, the phenomenon of the "exercise paradox" proposed by Radak et al. (2005) has been met (Radak et al., 2005). The modalities of resistance training at moderate intensity, multi-component training, and power strength training produced eustress in the aging population, while the high-intensity resistance training generated negative stress. Thus, in our case, physical exercise also acted as a double-edged sword. The behavior of each ROS and antioxidant enzyme was specific to the exercise type and exercise intensity.

In view of the findings from both studies, it may be assumed that resistance training at moderate intensity, multi-component training, and the power strength training modalities – all performed with elastic variable resistance – could modify the redox state in older women by improving antioxidant and thiol defenses and reducing DNA damage and lipid peroxidation, with no changes in protein oxidation. It would appear that these improvements are related to the intensity and type of training. However, more research is required to provide further evidence of exercise-induced oxidative stress during different types of exercise interventions, and additional studies are needed in this area before answers to these questions can be

accurately provided due to the lack of research that directly compares the effects of different exercise training modalities or intensities on the redox status in elderly population.

V.VI. RESULTS ON BONE HEALTH

V.VI.I. Project one

A. areal bone mineral density and T-score at lumbar spine

Changes in aBMD on the lumbar spine found in the ITT analysis are displayed in Table 33. Pairwise comparison after repeated-measures ANOVA revealed a significant effect by time in the M group by increasing L1-vertebra and total lumbar spine aBMD and decreasing the T-scores of the same areas. The ESs of these changes were trivial. At the same time, the HI group also found significant differences by time, with increases in the aBMD of L2, the total lumbar spine, and the L2–L4 segment and decreases in the T-scores of the same variables plus the L1 vertebra. As with the M group, the ESs of the changes achieved by the HI group were trivial. No significant differences by time were found in the aBMD and T-scores of the L3 and L4 segments for any group. In addition, the C group did not find significant changes by time in the parameters analyzed. Moreover, no significant time × group interaction was found with the ANOVA analysis. After controlling for baseline values and age, repeated-measures ANCOVA showed the same significant effects by time and similar ESs as the ANOVA analysis, except that the significant difference in the M group for L1 aBMD disappeared. However, significant main effects of time × group interaction were found in both parameters of the total lumbar spine: aBMD [$F(2, 88) = 4.8$, $p < 0.010$, $\eta^2p = 0.098$, $1-\beta = 0.784$] and T-score [$F(2, 88) = 3.97$, $p < 0.022$, $\eta^2p = 0.083$, $1-\beta = 0.699$]. Differences were found between the HI and C groups in both parameters (trivial ESs). The results of the PPA were similar to those of the ITT analysis, but with some differences. In the ANOVA and ANCOVA analyses, there were no significant effects by time in L1 aBMD and total-lumbar-spine T-score for the HI and the M group, respectively. Furthermore, significant between-group effects on L1 T-score and total-lumbar-spine aBMD were found between the M and C groups. The PPA results are presented in Supplementary Material C (Table C.1).

Table 33. *Intervention effects on BMD at lumbar spine from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L1vertebra aBMD (g/cm^2)	M	0.79	0.76 ± 0.12 (0.72–0.81)	0.77 ± 0.13 (0.73–0.82)	1.32	**0.050** (0.08)	0.059 (0.08)	M vs HI: 0.783 (0.28) M vs C: 1.000 (0.15) HI vs C: 1.000 (0.11)	M vs HI: 1.000 (0.02) M vs C: 0.103 (0.13) HI vs C: 0.130 (0.12)
	HI		0.80 ± 0.10 (0.76–0.84)	0.80 ± 0.11 (0.77–0.85)	1.04	0.069 (0.08)	0.074 (0.07)		
	C		0.80 ± 0.13 (0.75–0.85)	0.79 ± 0.13 (0.74–0.84)	-0.90	0.222 (0.05)	0.237 (0.05)		
L1 vertebra T-score (SD)	M	-1.83	-2.04 ± 1.16 (-2.43 to -1.65)	-1.95 ± 1.18 (-2.34 to -1.55)	-4.57	**0.013** (0.08)	**0.020** (0.08)	M vs HI: 0.858 (0.27) M vs C: 1.000 (0.16) HI vs C: 1.000 (0.09)	M vs HI: 1.000 (0.01) M vs C: 0.063 (0.11) HI vs C: 0.077 (0.12)
	HI		-1.74 ± 0.94 (-2.09 to -1.39)	-1.66 ± 0.95 (-2.01 to -1.31)	-4.41	**0.022** (0.08)	**0.021** (0.08)		
	C		-1.71 ± 1.25 (-2.17 to -1.25)	-1.76 ± 1.21 (-2.21 to -1.30)	2.77	0.271 (0.04)	0.297 (0.04)		
L2 vertebra aBMD (g/cm^2)	M	0.83	0.80 ± 0.13 (0.76–0.85)	0.81 ± 0.13 (0.76–0.85)	0.83	0.201 (0.05)	0.225 (0.05)	M vs HI: 0.156 (0.46) M vs C: 1.000 (0.2) HI vs C: 0.871 (0.29)	M vs HI: 1.000 (0.02) M vs C: 0.417 (0.09) HI vs C: 0.155 (0.11)
	HI		0.86 ± 0.13 (0.82–0.90)	0.87 ± 0.12 (0.83–0.91)	1.06	**0.049** (0.07)	**0.045** (0.07)		
	C		0.84 ± 0.11 (0.78–0.89)	0.83 ± 0.11 (0.78–0.88)	-0.67	0.348 (0.05)	0.363 (0.04)		
L2 vertebra T-score (SD)	M	-1.7	-1.89 ± 1.33 (-2.32 to -1.46)	-1.93 ± 1.16 (-2.33 to -1.53)	2.04	0.633 (0.03)	0.491 (0.04)	M vs HI: 0.271 (0.4) M vs C: 1.000 (0.19) HI vs C: 1.000 (0.23)	M vs HI: 0.590 (0.12) M vs C: 1.000 (0.02) HI vs C: 0.976 (0.1)
	HI		-1.54 ± 1.15 (-1.92 to -1.16)	-1.47 ± 1.12 (-1.83 to -1.11)	-4.64	0.321 (0.06)	0.233 (0.07)		
	C		-1.69 ± 1.05 (-2.19 to -1.19)	-1.72 ± 1.03 (-2.19 to -1.26)	1.79	0.746 (0.03)	0.749 (0.03)		

Table 33. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L3 vertebra aBMD (g/cm^2)	M	0.88	0.86 ± 0.14 (0.81–0.91)	0.86 ± 0.14 (0.81–0.92)	0.58	0.424 (0.04)	0.418 (0.03)	M vs HI: 0.491 (0.33) M vs C: 1.000 (0.01) HI vs C: 0.651 (0.33)	M vs HI: 1.000 (0.03) M vs C: 0.787 (0.07) HI vs C: 0.334 (0.1)
	HI		0.90 ± 0.15 (0.86–0.95)	0.91 ± 0.14 (0.87–0.96)	0.97	0.119 (0.06)	0.109 (0.06)		
	C		0.87 ± 0.14 (0.81–0.93)	0.87 ± 0.13 (0.81–0.93)	-0.60	0.472 (0.04)	0.435 (0.04)		
L3vertebra T-score (SD)	M	-1.78	-2.00 ± 1.29 (-2.47 to -1.52)	-1.94 ± 1.32 (-2.41 to -1.48)	-2.58	0.299 (0.04)	0.336 (0.04)	M vs HI: 0.408 (0.36) M vs C: 1.000 (0.01) HI vs C: 0.554 (0.35)	M vs HI: 1.000 (0.03) M vs C: 0.687 (0.07) HI vs C: 0.254 (0.1)
	HI		-1.55 ± 1.34 (-1.97 to -1.13)	-1.47 ± 1.32 (-1.89 to -1.06)	-4.95	0.084 (0.06)	0.064 (0.06)		
	C		-1.89 ± 1.35 (-2.44 to -1.34)	-1.93 ± 1.23 (-2.47 to -1.39)	2.06	0.497 (0.03)	0.449 (0.03)		
L4 vertebra aBMD (g/cm^2)	M	0.88	0.86 ± 0.15 (0.81–0.92)	0.87 ± 0.14 (0.82–0.92)	0.86	0.306 (0.05)	0.256 (0.05)	M vs HI: 0.673 (0.3) M vs C: 1.000 (0.02) HI vs C: 0.716 (0.31)	M vs HI: 1.000 (0.01) M vs C: 0.782 (0.08) HI vs C: 0.569 (0.08)
	HI		0.90 ± 0.15 (0.86–0.95)	0.92 ± 0.15 (0.87–0.96)	1.11	0.122 (0.07)	0.134 (0.06)		
	C		0.87 ± 0.14 (0.81–0.94)	0.87 ± 0.15 (0.81–0.93)	-0.44	0.647 (0.03)	0.617 (0.03)		
L4 vertebra T-score (SD)	M	-1.60	-1.76 ± 1.40 (-2.26 to -1.27)	-1.70 ± 1.33 (-2.19 to -1.21)	-3.65	0.244 (0.05)	0.198 (0.05)	M vs HI: 0.870 (0.26) M vs C: 1.000 (0.01) HI vs C: 1.000 (0.25)	M vs HI: 1.000 (0.01) M vs C: 0.661 (0.07) HI vs C: 0.414 (0.09)
	HI		-1.44 ± 1.40 (-1.88 to -1.00)	-1.35 ± 1.36 (-1.78 to -0.92)	-6.22	0.070 (0.06)	0.076 (0.06)		
	C		-1.66 ± 1.36 (-2.24 to -1.08)	-1.69 ± 1.40 (-2.26 to -1.13)	1.83	0.635 (0.02)	0.614 (0.02)		

Table 33. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total lumbar spine aBMD (g/cm^2)	M	0.85	0.83 ± 0.12 (0.78–0.87)	0.83 ± 0.13 (0.79–0.88)	0.89	**0.036** (0.06)	**0.038** (0.05)	M vs HI: 0.395 (0.36) M vs C: 1.000 (0.06) HI vs C: 0.736 (0.31)	M vs HI: 1.000 (0.02) M vs C: 0.054 (0.09) HI vs C: **0.011** (0.12)
	HI		0.87 ± 0.12 (0.83–0.91)	0.88 ± 0.12 (0.84–0.92)	1.12	**0.002** (0.08)	**0.002** (0.08)		
	C		0.85 ± 0.12 (0.79–0.90)	0.84 ± 0.11 (0.79–0.89)	-0.64	0.182 (0.04)	0.179 (0.04)		
Total lumbar spine T-score (SD)	M	-1.78	-1.97 ± 1.17 (-2.39 to -1.55)	-1.90 ± 1.18 (-2.31 to -1.49)	-3.43	**0.022** (0.06)	**0.030** (0.05)	M vs HI: 0.551 (0.32) M vs C: 1.000 (0.07) HI vs C: 1.000 (0.25)	M vs HI: 1.000 (0.02) M vs C: 0.105 (0.08) HI vs C: **0.022** (0.1)
	HI		-1.62 ± 1.16 (-1.99 to -1.25)	-1.53 ± 1.13 (-1.90 to -1.17)	-5.06	**0.002** (0.07)	**0.001** (0.07)		
	C		-1.79 ± 1.14 (-2.27 to -1.30)	-1.82 ± 1.10 (-2.29 to -1.34)	1.70	0.369 (0.03)	0.362 (0.03)		
L2-L4 lumbar spine segment aBMD (g/cm^2)	M	0.87	0.84 ± 0.13 (0.80–0.89)	0.85 ± 0.13 (0.80–0.90)	0.78	0.114 (0.05)	0.114 (0.05)	M vs HI: 0.231 (0.42) M vs C: 1.000 (0.05) HI vs C: 0.446 (0.38)	M vs HI: 1.000 (0.02) M vs C: 0.210 (0.08) HI vs C: 0.063 (0.1)
	HI		0.90 ± 0.14 (0.86–0.94)	0.91 ± 0.14 (0.87–0.95)	1.03	**0.014** (0.06)	**0.014** (0.06)		
	C		0.86 ± 0.12 (0.81–0.92)	0.86 ± 0.12 (0.80–0.91)	-0.55	0.323(0.04)	0.304 (0.04)		
L2-L4 lumbar spine segment T-score (SD)	M	-1.76	-2.10 ± 1.21 (-2.57 to -1.63)	-2.05 ± 1.24 (-2.51 to -1.59)	-2.36	0.177 (0.04)	0.173 (0.04)	M vs HI: 0.057 (0.55) M vs C: 1.000 (0.07) HI vs C: 0.163 (0.5)	M vs HI: 1.000 (0.02) M vs C: 0.297 (0.08) HI vs C: 0.083 (0.09)
	HI		-1.38 ± 1.45 (-1.80 to -0.96)	-1.30 ± 1.44 (-1.72 to -0.89)	-5.56	**0.020** (0.05)	**0.020** (0.05)		
	C		-1.93 ± 1.16 (-2.47 to -1.39)	-1.97 ± 1.10 (-2.51 to -1.43)	2.02	0.358 (0.03)	0.321 (0.04)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (n = 31), HI (n = 39), C (n = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; BMD: bone mineral density; aBMD: areal bone mineral density; CIs: confidence intervals;
ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

B. areal bone mineral density and T-score at proximal femur and fracture risk

The aBMD at the proximal femur and the fracture-risk outcomes from the ITT analysis are presented in Table 34. Repeated-measures ANOVA showed a main effect of time on femoral neck aBMD [$F(1, 90) = 8.67$, $p < 0.004$, $\eta^2p = 0.088$, $1-\beta = 0.830$], femoral neck T-score [$F(1, 90) = 8.73$, $p < 0.004$, $\eta^2p = 0.088$, $1-\beta = 0.832$], trochanter aBMD [$F(1, 90) = 4.68$, $p < 0.033$, $\eta^2p = 0.049$, $1-\beta = 0.572$], trochanter T-score [$F(1, 90) = 3.88$, $p < 0.042$, $\eta^2p = 0.041$, $1-\beta = 0.496$], Ward's triangle aBMD [$F(1, 90) = 8.003$, $p < 0.006$, $\eta^2p = 0.082$, $1-\beta = 0.799$], Ward's triangle T-score [$F(1, 90) = 8.25$, $p < 0.005$, $\eta^2p = 0.084$, $1-\beta = 0.811$], total hip aBMD [$F(1, 90) = 17.56$, $p < 0.000$, $\eta^2p = 0.163$, $1-\beta = 0.986$], and total hip T-score [$F(1, 90) = 8.09$, $p < 0.005$, $\eta^2p = 0.083$, $1-\beta = 0.804$]. Pairwise comparisons revealed significant increases in aBMD from the M group in the femoral neck, Ward's triangle, and total hip, while the HI group achieved significant improvements in the same parameters and in the trochanter area. These increases in aBMD were accompanied by significant decreases in T-scores. The magnitude of change in all the variables analyzed was considered trivial. No significant time × group interaction was found with the ANOVA analysis in aBMD and T-score. Repeated-measures ANCOVA showed the same effects by time with similar ESs. However, after the corrections, a significant time × group interaction was found in the trochanter aBMD [$F(2, 88) = 3.34$, $p < 0.040$, $\eta^2p = 0.071$, $1-\beta = 0.619$], trochanter T-score [$F(2, 88) = 3.98$, $p < 0.022$, $\eta^2p = 0.083$, $1-\beta = 0.700$], and Ward's triangle T-score [$F(2, 88) = 3.13$, $p < 0.048$, $\eta^2p = 0.067$, $1-\beta = 0.589$]. Between-group differences were found between the HI and the C group in the case of trochanter aBMD and T-score (trivial ESs), and between the M and C groups for the Ward's triangle T-score (small ES).

With regard to fracture risk, both training groups achieved significant within changes in the 10-year probability of a major osteoporotic fracture and the 10-year probability of hip fracture, decreasing the probability of fracture risk after the 8-month training period.

Moreover, the magnitudes of change ranged from trivial to small. In addition, while no significant changes were found in the rest of the variables between the training groups, significant time × group interaction was found through the repeated-measures ANOVA analysis between M and HI for both variables and between the M and C groups for the 10-year probability of a major osteoporotic fracture. In this case, the ESs were moderate to large. Furthermore, the repeated-measures ANCOVA revealed a new significant difference between the HI and C groups in the 10-year probability of hip fracture variable.

The results of the PPA were similar in direction, but the statistical significance changed for some variables. After the ANOVA analysis, some differences by time were found, adding a significant difference for the M group in terms of trochanter aBMD. No changes from the ITT results were found between groups, and the ANCOVA showed the same differences by time as in the ITT analysis. The most notable differences were in the between-group differences when performing the ANCOVA. In the PPA, significant differences were found between the M and the C group for the femoral and trochanter aBMD. However, the differences between the H and C groups in terms of trochanter aBMD and T-score as well as total hip aBMD disappeared. The PPA results are presented in Supplementary Material C (Table C.2).

Table 34. *Intervention effects on BMD at proximal femur from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Femoral neck aBMD (g/cm^2)	M	0.66	0.66 ± 0.09 (0.63–0.70)	0.67 ± 0.09 (0.64–0.71)	1.57	**0.005** (0.11)	**0.002** (0.13)	M vs HI: 1.000 (0.06) M vs C: 1.000 (0.03) HI vs C: 1.000 (0.03)	M vs HI: 1.000 (0.04) M vs C: 0.085 (0.13) HI vs C: 0.262 (0.1)
	HI		0.66 ± 0.09 (0.63–0.69)	0.67 ± 0.08 (0.64–0.70)	1.39	**0.005** (0.1)	**0.010** (0.09)		
	C		0.67 ± 0.09 (0.63–0.71)	0.67 ± 0.10 (0.63–0.71)	-0.13	0.836 (0.01)	0.873 (0.01)		
Femoral neck T-score (SD)	M	-1.63	-1.64 ± 0.81 (-1.94 to -1.34)	-1.56 ± 0.81 (-1.86 to -1.26)	-5.09	**0.011** (0.1)	**0.008** (0.11)	M vs HI: 1.000 (0) M vs C: 1.000 (0) HI vs C: 1.000 (0.01)	M vs HI: 1.000 (0) M vs C: 0.169 (0.11) HI vs C: 0.133 (0.11)
	HI		-1.66 ± 0.82 (-1.92 to -1.39)	-1.56 ± 0.82 (-1.83 to -1.29)	-5.71	**0.001** (0.12)	**0.003** (0.11)		
	C		-1.55 ± 0.89 (-1.90 to -1.20)	-1.56 ± 0.91 (-1.91 to -1.21)	0.56	0.818 (0.01)	0.850 (0.01)		
Trochanter aBMD (g/cm^2)	M	0.65	0.66 ± 0.09 (0.63–0.70)	0.67 ± 0.09 (0.63–0.70)	0.73	0.098 (0.05)	0.063 (0.05)	M vs HI: 1.000 (0.19) M vs C: 1.000 (0.21) HI vs C: 1.000 (0.04)	M vs HI: 1.000 (0.19) M vs C: 0.222 (0.21) HI vs C: **0.036** (0.04)
	HI		0.64 ± 0.08 (0.61–0.67)	0.65 ± 0.09 (0.62–0.68)	1.38	**0.001** (0.1)	**0.002** (0.09)		
	C		0.65 ± 0.10 (0.61–0.69)	0.64 ± 0.10 (0.61–0.68)	-0.40	0.442 (0.02)	0.452 (0.03)		
Trochanter T-score (SD)	M	-0.51	-0.42 ± 0.88 (-0.75 to -0.09)	-0.38 ± 0.86 (-0.71 to -0.04)	-9.85	0.225 (0.05)	0.184 (0.05)	M vs HI: 1.000 (0.11) M vs C: 1.000 (0.14) HI vs C: 1.000 (0.04)	M vs HI: 0.566 (0.11) M vs C: 0.393 (0.14) HI vs C: **0.018** (0.04)
	HI		-0.59 ± 0.87 (-0.89 to -0.30)	-0.48 ± 0.92 (-0.78 to -0.18)	-18.88	**0.000** (0.13)	**0.001** (0.12)		
	C		-0.48 ± 1.06 (-0.87 to -0.10)	-0.52 ± 1.05 (-0.91 to -0.13)	7.14	0.385 (0.03)	0.396 (0.03)		

Table 34. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Intertro-chanteric area aBMD (g/cm^2)	M	0.99	0.98 ± 0.15 (0.93–1.03)	0.98 ± 0.15 (0.94–1.03)	0.49	0.354 (0.03)	0.392 (0.03)	M vs HI: 1.000 (0.02) M vs C: 1.000 (0.2) HI vs C: 1.000 (0.21)	M vs HI: 1.000 (0.02) M vs C: 0.989 (0.2) HI vs C: 0.625 (0.21)
	HI		0.98 ± 0.12 (0.94–1.03)	0.99 ± 0.12 (0.95–1.03)	0.68	0.146 (0.06)	0.176 (0.06)		
	C		1.02 ± 0.15 (0.96–1.08)	1.01 ± 0.13 (0.96–1.07)	-0.51	0.386 (0.03)	0.581 (0.03)		
Intertro-chanteric area T-score (SD)	M	-0.68	-0.78 ± 0.91 (-1.10 to -0.46)	-0.71 ± 0.89 (-1.02 to -0.41)	-8.23	0.080 (0.07)	0.095 (0.07)	M vs HI: 1.000 (0.08) M vs C: 1.000 (0.18) HI vs C: 1.000 (0.1)	M vs HI: 1.000 (0.08) M vs C: 0.463 (0.18) HI vs C: 0.776 (0.1)
	HI		-0.68 ± 0.84 (-0.97 to -0.40)	-0.64 ± 0.84 (-0.92 to -0.37)	-6.32	0.183 (0.05)	0.200 (0.05)		
	C		-0.53 ± 0.92 (-0.90 to -0.16)	-0.56 ± 0.87 (-0.92 to -0.20)	4.88	0.539 (0.03)	0.660 (0.03)		
Ward's triangle aBMD (g/cm^2)	M	0.50	0.51 ± 0.10 (0.47–0.55)	0.52 ± 0.09 (0.49–0.56)	2.59	**0.007** (0.14)	**0.001** (0.14)	M vs HI: 0.748 (0.28) M vs C: 1.000 (0.23) HI vs C: 1.000 (0.06)	M vs HI: 1.000 (0.28) M vs C: 0.075 (0.23) HI vs C: 0.299 (0.06)
	HI		0.48 ± 0.11 (0.45–0.52)	0.50 ± 0.10 (0.46–0.53)	2.47	**0.006** (0.11)	**0.014** (0.11)		
	C		0.50 ± 0.10 (0.46–0.55)	0.50 ± 0.10 (0.46–0.55)	-0.26	0.816 (0.01)	0.865 (0.01)		
Ward's triangle T-score (SD)	M	-1.98	-1.86 ± 0.85 (-2.19 to -1.53)	-1.74 ± 0.82 (-2.06 to -1.43)	-6.23	**0.005** (0.14)	**0.001** (0.14)	M vs HI: 0.761 (0.27) M vs C: 1.000 (0.24) HI vs C: 1.000 (0.05)	M vs HI: 1.000 (0.27) M vs C: **0.049** (0.24) HI vs C: 0.192 (0.05)
	HI		-2.10 ± 0.97 (-2.39 to -1.80)	-1.99 ± 0.95 (-2.27 to -1.71)	-5.12	**0.004** (0.11)	**0.009** (0.11)		
	C		-1.93 ± 0.90 (-2.31 to -1.54)	-1.94 ± 0.87 (-2.31 to -1.57)	0.90	0.713 (0.02)	0.763 (0.02)		

Table 34. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total hip aBMD (g/cm^2)	M	0.84	0.84 ± 0.12 (0.80–0.88)	0.85 ± 0.12 (0.81–0.89)	1.13	**0.000** (0.08)	**0.000** (0.08)	M vs HI: 1.000 (0.1) M vs C: 1.000 (0.04) HI vs C: 1.000 (0.06)	M vs HI: 1.000 (0) M vs C: **0.029** (0.08) HI vs C: **0.027** (0.09)
	HI		0.83 ± 0.10 (0.79–0.86)	0.84 ± 0.09 (0.80–0.87)	1.21	**0.000** (0.1)	**0.000** (0.1)		
	C		0.85 ± 0.12 (0.80–0.89)	0.84 ± 0.12 (0.80–0.89)	-0.07	0.849 (0)	0.891 (0)		
Total hip T-score (SD)	M	-0.82	-0.85 ± 0.91 (-1.18 to -0.53)	-0.79 ± 0.91 (-1.11 to -0.47)	-7.52	**0.015** (0.07)	**0.014** (0.07)	M vs HI: 1.000 (0.04) M vs C: 1.000 (0.04) HI vs C: 1.000 (0)	M vs HI: 1.000 (0.01) M vs C: 0.178 (0.08) HI vs C: 0.066 (0.1)
	HI		-0.83 ± 0.86 (-1.13 to -0.54)	-0.75 ± 0.84 (-1.04 to -0.47)	-9.48	**0.001** (0.09)	**0.001** (0.09)		
	C		-0.74 ± 1.01 (-1.12 to -0.36)	-0.75 ± 1.00 (-1.13 to -0.38)	1.75	0.666 (0.01)	0.716 (0.01)		
10-year probability of a major osteoporotic fracture (%)	M	0.10	0.12 ± 0.05 (0.11–0.14)	0.11 ± 0.04 (0.10–0.13)	-8.15	**0.000** (0.23)	**0.012** (0.13)	M vs HI: **0.004** (0.98) M vs C: **0.048** (0.72) HI vs C: 1.000 (0.11)	M vs HI: 0.782 (0.18) M vs C: 1.000 (0.1) HI vs C: 0.069 (0.3)
	HI		0.09 ± 0.03 (0.08–0.11)	0.08 ± 0.02 (0.07–0.09)	-11.11	**0.000** (0.34)	**0.000** (0.38)		
	C		0.08 ± 0.04 (0.07–0.10)	0.08 ± 0.04 (0.07–0.10)	0.54	0.886 (0.01)	0.426 (0.05)		
10-year probability of a hip fracture (%)	M	0.02	0.02 ± 0.01 (0.01–0.03)	0.02 ± 0.01 (0.01–0.02)	-6.28	**0.011** (0.1)	**0.024** (0.07)	M vs HI: **0.015** (1.03) M vs C: 1.000 (0.35) HI vs C: 0.775 (0.68)	M vs HI: 1.000 (0.1) M vs C: 0.593 (0.07) HI vs C: **0.032** (0.23)
	HI		0.01 ± 0.00 (0.01–0.01)	0.01 ± 0.00 (0.01–0.01)	-14.93	**0.000** (0.42)	**0.000** (0.39)		
	C		0.01 ± 0.01 (0.01–0.02)	0.01 ± 0.01 (0.01–0.01)	1.47	0.710 (0.02)	0.811 (0)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; BMD: bone mineral density; aBMD: areal bone mineral density; CIs: confidence intervals;
ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

C. Bone turnover markers and bone health related variables

Changes in BTMs and bone health related variables at pre-intervention and midpoint (Week 16) from the ITT analysis are displayed in Tables 35 and 36. Repeated-measures ANOVA showed a main effect of time on P1NP [$F(1, 90) = 8.40$, $p < 0.005$, $\eta^2p = 0.085$, $1-\beta = 0.818$], β-CTx [$F(1, 90) = 8.93$, $p < 0.004$, $\eta^2p = 0.090$, $1-\beta = 0.841$], bALP [$F(1, 90) = 1.91$, $p < 0.47$, $\eta^2p = 0.021$, $1-\beta = 0.277$], bALP/β-CTx ratio [$F(1, 90) = 6.25$, $p < 0.014$, $\eta^2p = 0.065$, $1-\beta = 0.696$], Na [$F(1, 90) = 4.66$, $p < 0.033$, $\eta^2p = 0.049$, $1-\beta = 0.570$], K [$F(1, 90) = 4.74$, $p < 0.032$, $\eta^2p = 0.050$, $1-\beta = 0.577$], and Cl [$F(1, 90) = 22.25$, $p < 0.000$, $\eta^2p = 0.198$, $1-\beta = 0.997$]. Pairwise comparison showed that both training groups significantly improved their measures of P1NP, β-CTx, bALP/β-CTx ratio, and K, while the HI group also exhibited significant increases in the concentrations of bALP, Na, and Cl. For all the parameters, the magnitude of change was considered trivial or small. In addition, a significant time × group interaction was found between the training groups for bALP and bALP/β-CTx ratio, and between the HI and C groups in β-CTx, bALP/β-CTx ratio, and Cl. The ANCOVA revealed a significant effect by time on Cl for the M group and a lack of differences in the same variable within the HI group, with the same effects in the rest of the parameters. Differences between the training groups disappeared after the corrections, along with the difference between the HI and C groups in Cl. The ANCOVA revealed significant between-group effects between the HI and the C group in bALP as well as differences between these two groups in β-CTx and bALP/β-CTx ratio. The results of the PPA found the same differences by time after performing both ANOVA and ANCOVA. In the PPA analysis, no significant time × group interaction were found between the M and HI groups in bALP and bALP/β-CTx ratio after applying the ANOVA. Differences between the M and the C group in β-CTx and between HI and C in terms of bALP/β-CTx ratio also disappeared with the ANCOVA. The PPA results are presented in Supplementary Material C (Tables C.3 and C.4).

Table 35. *Intervention effects on bone biomarkers at pre and midpoint (16 weeks) from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
P1NP (µg/L)	M	36.59	35.28 ± 13.55 (30.53–40.04)	39.25 ± 14.73 (34.55–43.94)	11.24	**0.002** (0.28)	**0.003** (0.27)	M vs HI: 1.000 (0.13)	M vs HI: 0.842 (0.13)
	HI		34.75 ± 11.60 (30.51–39.00)	37.61 ± 10.57 (33.43–41.80)	8.23	**0.011** (0.26)	**0.017** (0.24)	M vs C: 1.000 (0.06)	M vs C: 0.091 (0.26)
	C		40.62 ± 15.62 (35.10–46.14)	40.18 ± 14.77 (34.73–45.63)	-1.08	0.761 (0.03)	0.980 (0)	HI vs C: 1.000 (0.21)	HI vs C: 0.578 (0.18)
β-CTx (pg/mL)	M	313.67	312.22 ± 124.87 (266.68–357.76)	291.45 ± 131.53 (247.64–335.25)	-6.65	**0.010** (0.16)	**0.008** (0.2)	M vs HI: 1.000 (0.17)	M vs HI: 1.000 (0.26)
	HI		294.20 ± 132.62 (253.60–334.80)	270.46 ± 114.04 (231.40–309.51)	-8.07	**0.001** (0.19)	**0.000** (0.05)	M vs C: 0.242 (0.46)	M vs C: 0.080 (2.24)
	C		348.65 ± 122.40 (295.78–401.51)	351.17 ± 124.88 (300.31–402.03)	0.72	0.785 (0.02)	0.513 (2.54)	HI vs C: **0.043** (0.68)	HI vs C: **0.021** (2.71)
bALP (U/L)	M	35.07	32.75 ± 8.36 (29.77–35.74)	33.51 ± 8.17 (30.46–36.56)	2.31	0.264 (0.09)	0.386 (0.47)	M vs HI: **0.027** (0.62)	M vs HI: 0.510 (0.4)
	HI		37.26 ± 8.61 (34.60–39.92)	39.01 ± 9.47 (36.29–41.73)	4.68	**0.005** (0.19)	**0.003** (0.04)	M vs C: 1.000 (0.01)	M vs C: 0.462 (0.99)
	C		34.47 ± 7.89 (31.01–37.94)	33.63 ± 7.28 (30.08–37.17)	-2.46	0.282 (0.11)	0.257 (0)	HI vs C: 0.056 (0.62)	HI vs C: **0.019** (0.5)
bALP/ β-CTx ratio	M	136.79	115.25 ± 36.47 (85.58–144.93)	131.05 ± 46.24 (99.91–162.20)	13.71	**0.015** (0.38)	**0.021** (0.37)	M vs HI: **0.041** (0.55)	M vs HI: 1.000 (0.02)
	HI		167.77 ± 117.58 (141.31–194.23)	183.84 ± 121.95 (156.08–211.61)	9.58	**0.006** (0.13)	**0.005** (0.14)	M vs C: 1.000 (0.44)	M vs C: 0.066 (0.41)
	C		113.31 ± 51.00 (78.85–147.76)	109.70 ± 50.55 (73.55–145.86)	-3.18	0.628 (0.07)	0.552 (0.09)	HI vs C: **0.005** (0.73)	HI vs C: **0.019** (0.21)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; P1NP: N-terminal propeptide of type1 procollagen; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); bALP: bone-specific alkaline phosphatase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

Table 36. *Intervention effects on bone health related variables at pre and midpoint (16 weeks) from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
25OHD (ng/ml)	M	24.74	23.90 ± 8.53 (19.62–28.18)	24.58 ± 11.28 (20.42–28.73)	2.83	0.584 (0.07)	0.611 (0.12)	M vs HI: 0.646 (0.27)	M vs HI: 1.000 (0.13)
	HI		27.30 ± 14.88 (23.49–31.12)	28.07 ± 13.81 (24.37–31.78)	2.82	0.485 (0.05)	0.273 (0.04)	M vs C: 1.000 (0.31)	M vs C: 1.000 (2.65)
	C		21.52 ± 10.29 (16.55–26.48)	21.56 ± 7.19 (16.74–26.39)	0.20	0.976 (0)	0.692 (0)	HI vs C: 0.109 (0.55)	HI vs C: 0.990 (2.05)
Na (mEq/L)	M	140.89	141.03 ± 1.76 (140.35–141.71)	141.22 ± 1.40 (140.60–141.85)	0.14	0.482 (0.12)	0.302 (0.16)	M vs HI: 1.000 (0.04)	M vs HI: 1.000 (0.17)
	HI		140.38 ± 2.03 (139.77–140.99)	141.15 ± 2.05 (140.59–141.71)	0.55	**0.002** (0.38)	**0.012** (0.28)	M vs C: 1.000 (0.29)	M vs C: 1.000 (0.07)
	C		141.56 ± 1.85 (140.77–142.35)	141.65 ± 1.58 (140.92–142.37)	0.06	0.785 (0.05)	0.214 (0.21)	HI vs C: 0.845 (0.26)	HI vs C: 1.000 (0.11)
K (mEq/L)	M	4.57	4.65 ± 0.37 (4.52–4.77)	4.49 ± 0.37 (4.37–4.61)	-3.40	**0.005** (0.42)	**0.018** (0.31)	M vs HI: 1.000 (0.07)	M vs HI: 1.000 (0.01)
	HI		4.58 ± 0.31 (4.46–4.69)	4.46 ± 0.32 (4.36–4.57)	-2.46	**0.022** (0.35)	**0.009** (0.35)	M vs C: 1.000 (0.02)	M vs C: 0.329 (0.36)
	C		4.43 ± 0.38 (4.29–4.58)	4.50 ± 0.28 (4.36–4.63)	1.37	0.338 (0.18)	0.934 (0.01)	HI vs C: 1.000 (0.1)	HI vs C: 0.295 (0.38)
Cl (mEq/L)	M	105.06	105.64 ± 1.95 (104.76–106.52)	106.19 ± 2.05 (105.36–107.02)	0.52	0.130 (0.27)	**0.015** (0.4)	M vs HI: 0.119 (0.5)	M vs HI: 1.000 (0.18)
	HI		104.33 ± 2.72 (103.55–105.11)	105.02 ± 2.51 (104.28–105.76)	0.66	**0.033** (0.26)	0.182 (0.15)	M vs C: 1.000 (0.25)	M vs C: 0.686 (0.27)
	C		105.52 ± 2.57 (104.50–106.54)	106.73 ± 2.32 (105.77–107.70)	1.15	**0.004** (0.5)	**0.000** (0.57)	HI vs C: **0.019** (0.7)	HI vs C: 0.115 (0.41)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; 25OHD: 25-hydroxy-vitamin D; Na: sodium; K: potassium; Cl: chloride; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

Changes in BTM and bone health related variables pre- and post-training period (32 weeks) from the ITT analysis are presented in Tables 37 and 38. Repeated-measures ANOVA showed a main effect of time on P1NP [$F(1, 90) = 30.22$, $p < 0.000$, $\eta^2p = 0.251$, $1-\beta = 1$], β-CTx [$F(1, 90) = 6.23$, $p < 0.014$, $\eta^2p = 0.065$, $1-\beta = 0.695$], bALP [$F(1, 90) = 24.40$, $p < 0.000$, $\eta^2p = 0.213$, $1-\beta = 0.998$], bALP/β-CTx ratio [$F(1, 90) = 15.08$, $p < 0.000$, $\eta^2p = 0.144$, $1-\beta = 0.970$], 25OHD [$F(1, 90) = 7.21$, $p < 0.009$, $\eta^2p = 0.074$, $1-\beta = 0.757$], and Cl [$F(1, 90) = 22.25$, $p < 0.000$, $\eta^2p = 0.198$, $1-\beta = 0.997$]. Pairwise comparison showed that both training groups significantly improved in terms of the parameters mentioned above, with increased levels of bone-formation biomarkers and decreased concentrations of bone-resorption biomarkers. In this case, the magnitude of the ESs were higher than that after 16 weeks, with small and moderate ESs being the most common. In addition, a significant time × group interaction was found in bALP [$F(2, 90) = 4.34$, $p < 0.016$, $\eta^2p = 0.088$, $1-\beta = 0.740$] between exercise groups and between the HI and the C group. Moreover, the ANOVA also showed a significant time × group interaction in the bALP/β-CTx ratio [$F(2, 90) = 5.32$, $p < 0.007$, $\eta^2p = 0.106$, $1-\beta = 0.827$] between the HI and C groups. Repeated-measures ANCOVA revealed the same differences by time. Nevertheless, significant differences between groups were found in P1NP [$F(2, 88) = 6.72$, $p < 0.002$, $\eta^2p = 0.133$, $1-\beta = 0.908$] and β-CTx [$F(2, 88) = 8.96$, $p < 0.000$, $\eta^2p = 0.169$, $1-\beta = 0.969$]. In both cases, the differences were between the M and HI groups vs the C group. Indeed, the significant difference between M and HI in bALP disappeared, and the ESs were similar. The results of the PPA showed no differences between pre- and post-intervention BTMs. In addition, the significant differences between HI and C in β-CTx and between M and HI in the bALP/β-CTx ratio disappeared in the ANOVA analysis. The same time × group interaction as found in the ITT analysis were present in the ANCOVA. The PPA results are presented in Supplementary Material C (Tables C.5–C.6)

Table 37. *Intervention effects on bone biomarkers at pre and post training period (32 weeks) from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
P1NP (µg/L)	M	36.59	35.28 ± 13.55 (30.53–40.04)	42.25 ± 12.65 (38.00–46.51)	19.76	**0.000** (0.53)	**0.000** (0.5)	M vs HI: 1.000 (0.07)	M vs HI: 1.000 (0.08)
	HI		34.75 ± 11.60 (30.51–39.00)	43.06 ± 9.68 (39.27–46.85)	23.89	**0.000** (0.78)	**0.000** (0.74)	M vs C: 1.000 (0.16)	M vs C: **0.011** (0.45)
	C		40.62 ± 15.62 (35.10–46.14)	40.10 ± 14.18 (35.16–45.03)	-1.29	0.765 (0.04)	0.717 (0.04)	HI vs C: 1.000 (0.26)	HI vs C: **0.002** (0.6)
β-CTx (pg/mL)	M	313.67	312.22 ± 124.87 (266.68–357.76)	289.61 ± 125.01 (245.99–333.23)	-7.24	**0.008** (0.18)	**0.006** (0.18)	M vs HI: 1.000 (0.2)	M vs HI:1.000 (0.07)
	HI		294.20 ± 132.62 (253.60–334.80)	265.38 ± 115.36 (226.49–304.27)	-9.80	**0.000** (0.23)	**0.000** (0.25)	M vs C: 0.094 (0.58)	M vs C: **0.004** (0.32)
	C		348.65 ± 122.40 (295.78–401.51)	363.17 ± 129.73 (312.53–413.81)	4.17	0.137 (0.12)	0.056 (0.14)	HI vs C: **0.009** (0.81)	HI vs C: **0.000** (0.41)
bALP (U/L)	M	35.07	32.75 ± 8.36 (29.77–35.74)	35.40 ± 7.89 (32.49–38.31)	8.07	**0.001** (0.33)	**0.002** (0.3)	M vs HI: **0.017** (0.66)	M vs HI: 0.458 (0.18)
	HI		37.26 ± 8.61 (34.60–39.92)	40.97 ± 8.75 (38.38–43.57)	9.95	**0.000** (0.43)	**0.000** (0.45)	M vs C: 1.000 (0.07)	M vs C: 0.191 (0.27)
	C		34.47 ± 7.89 (31.01–37.94)	34.86 ± 7.42 (31.48–38.25)	1.13	0.663 (0.05)	0.706 (0.04)	HI vs C: **0.016** (0.74)	HI vs C: **0.004** (0.43)
bALP/ β-CTx ratio	M	136.79	115.25 ± 36.47 (85.58–144.93)	139.30 ± 51.61 (105.40–173.19)	20.86	**0.002** (0.54)	**0.005** (0.19)	M vs HI: **0.026** (0.58)	M vs HI: 1.000 (0.06)
	HI		167.77 ± 117.58 (141.31–194.23)	200.59 ± 132.97 (170.37–230.81)	19.56	**0.000** (0.26)	**0.000** (0.25)	M vs C: 0.779 (0.57)	M vs C: 0.060 (0.55)
	C		113.31 ± 51.00 (78.85–147.76)	109.64 ± 52.32 (70.29–148.99)	-3.23	0.684 (0.07)	0.053 (0.14)	HI vs C: **0.001** (0.82)	HI vs C: **0.013** (0.31)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; P1NP: N-terminal propeptide of type1 procollagen; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); bALP: bone-specific alkaline phosphatase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

Table 38. *Intervention effects on bone health related variables at pre and post training period (32 weeks) from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
25OHD (ng/ml)	M	24.74	23.90 ± 8.53 (19.62–28.18)	26.80 ± 12.05 (22.28–31.32)	12.15	**0.032** (0.28)	**0.031** (0.28)	M vs HI: 0.836 (0.24)	M vs HI: 1.000 (0.01)
	HI		27.30 ± 14.88 (23.49–31.12)	30.12 ± 14.82 (26.09–34.15)	10.33	**0.019** (0.19)	**0.012** (0.21)	M vs C: 0.550 (0.43)	M vs C: 0.559 (0.25)
	C		21.52 ± 10.29 (16.55–26.48)	22.13 ± 8.86 (16.88–27.37)	2.83	0.694 (0.06)	0.887 (0.02)	HI vs C: 0.055 (0.62)	HI vs C: 0.459 (0.22)
Na (mEq/L)	M	140.89	141.03 ± 1.76 (140.35–141.71)	141.51 ± 1.38 (140.93–142.09)	0.34	0.109 (0.31)	**0.029** (0.35)	M vs HI: 0.182 (0.45)	M vs HI: 0.655 (0.25)
	HI		140.38 ± 2.03 (139.77–140.99)	140.76 ± 1.84 (140.24–141.28)	0.27	0.152 (0.2)	0.556 (0.07)	M vs C: 1.000 (0.29)	M vs C: 0.225 (0.46)
	C		141.56 ± 1.85 (140.77–142.35)	141.08 ± 1.56 (140.41–141.76)	-0.34	0.171 (0.28)	0.644 (0.08)	HI vs C: 1.000 (0.18)	HI vs C: 1.000 (0.15)
K (mEq/L)	M	4.57	4.65 ± 0.37 (4.52–4.77)	4.61 ± 0.34 (4.49–4.74)	-0.76	0.507 (0.1)	0.781 (0.04)	M vs HI: 1.000 (0.02)	M vs HI: 1.000 (0.14)
	HI		4.58 ± 0.31 (4.46–4.69)	4.60 ± 0.34 (4.49–4.72)	0.56	0.591 (0.08)	0.420 (0.11)	M vs C: 0.286 (0.45)	M vs C: 1.000 (0.05)
	C		4.43 ± 0.38 (4.29–4.58)	4.45 ± 0.37 (4.30–4.59)	0.29	0.834 (0.03)	0.571 (0.09)	HI vs C: 0.293 (0.44)	HI vs C: 1.000 (0.19)
Cl (mEq/L)	M	105.06	105.64 ± 1.95 (104.76–106.52)	106.70 ± 2.11 (105.81–107.60)	1.01	**0.003** (0.52)	**0.000** (0.6)	M vs HI: 0.101 (0.51)	M vs HI: 1.000 (0.14)
	HI		104.33 ± 2.72 (103.55–105.11)	105.41 ± 2.83 (104.61–106.20)	1.03	**0.001** (0.39)	**0.004** (0.31)	M vs C: 1.000 (0.2)	M vs C: 1.000 (0.16)
	C		105.52 ± 2.57 (104.50–106.54)	106.26 ± 2.37 (105.22–107.29)	0.70	0.068 (0.3)	**0.024** (0.35)	HI vs C: 0.599 (0.32)	HI vs C: 1.000 (0)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; 25OHD: 25-hydroxy-vitamin D; Na: sodium; K: potassium; Cl: chloride; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

V.VI.II. Project two

A. areal bone mineral density and T-score at lumbar spine

Changes in aBMD on the lumbar spine from the ITT analysis are displayed in Table 39. Repeated-measures ANOVA showed a main effect of time on L1 aBMD [$F(1, 132) = 12.12$, $p < 0.001$, $\eta^2p = 0.084$, $1-\beta = 0.933$], L1 T-score [$F(1, 132) = 8.18$, $p < 0.005$, $\eta^2p = 0.058$, $1-\beta = 0.811$], L2 aBMD [$F(1, 132) = 3.87$, $p < 0.050$, $\eta^2p = 0.029$, $1-\beta = 0.498$], L2 T-score [$F(1, 132) = 5.06$, $p < 0.026$, $\eta^2p = 0.037$, $1-\beta = 0.608$], and total lumbar spine aBMD [$F(1, 132) = 3.96$, $p < 0.049$, $\eta^2p = 0.029$, $1-\beta = 0.506$]. Pairwise comparisons revealed significant increases in L1, L2, and total lumbar spine aBMD and a significant decrease in the T-score values for the same parameters in the P group, with trivial ESs in all of them. In addition, the MT group achieved a significant increase in the aBMD and T-score of the L1 vertebra, with trivial ESs as well. No significant time × group interactions were found. After controlling for baseline values and age, repeated-measures ANCOVA showed the same significant effects by time and similar ESs, except for the appearance of a significant decrease of the L1 T-score in the P group and a lack of difference for the MT group in the same parameter. However, significant main effects of time × group interaction were found in the L4 aBMD [$F(3, 130) = 3.25$, $p < 0.024$, $\eta^2p = 0.070$, $1-\beta = 0.736$], L4 T-score [$F(3, 130) = 3.03$, $p < 0.032$, $\eta^2p = 0.065$, $1-\beta = 0.703$], total-lumbar-spine aBMD [$F(3, 130) = 2.8$, $p < 0.043$, $\eta^2p = 0.061$, $1-\beta = 0.663$], and total-lumbar-spine T-score [$F(3, 130) = 2.58$, $p < 0.046$, $\eta^2p = 0.056$, $1-\beta = 0.625$]. The differences were found between the P and C groups in these parameters (trivial and small ESs). The PPA results found almost the same significant differences as did the ITT analysis, with only a significant decrease in L1 T-score in the P group after applying the ANOVA as a difference between both analyses. The results from the PPA are presented in Supplementary Material D (Table D.1).

Table 39. *Intervention effects on BMD at lumbar spine from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L1vertebra aBMD (g/cm^2)	MT	0.82	0.80 ± 0.11 (0.76–0.84)	0.82 ± 0.11 (0.78–0.86)	2.70	**0.003** (0.18)	**0.010 (**0.16)	MT vs P: 0.706 (0.38)	MT vs P: 1.000 (0.03)
	P		0.85 ± 0.11 (0.81–0.89)	0.86 ± 0.11 (0.82–0.90)	1.73	**0.042 (**0.13)	**0.022** (0.14)	MT vs T: 1.000 (0.08)	MT vs T: 1.000 (0.05)
	T		0.82 ± 0.10 (0.78–0.86)	0.83 ± 0.11 (0.79–0.87)	1.52	0.085 (0.11)	0.064 (0.11)	MT vs C: 1.000 (0.06)	MT vs C: 0.462 (0.16)
	C		0.82 ±0.11 (0.79–0.86)	0.83 ± 0.11 (0.79–0.87)	0.15	0.861 (0.01)	0.893 (0.01)	P vs T: 1.000 (0.3)	P vs T: 1.000 (0.03)
								P vs C: 1.000 (0.32)	P vs C: 0.746 (0.13)
								T vs C: 1.000 (0.02)	T vs C: 1.000 (0.1)
L1 vertebra T-score (SD)	MT	-1.50	-1.71 ± 1.08 (-2.06 to -1.36)	-1.55 ± 1.09 (-1.91 to -1.19)	-9.11	**0.026** (0.14)	0.064 (0.12)	MT vs P: 0.748 (0.38)	MT vs P: 1.000 (0.02)
	P		-1.29 ± 1.00 (-1.64 to -0.94)	-1.16 ± 1.00 (-1.51 to -0.80)	-10.43	0.053 (0.13)	**0.031** (0.15)	MT vs T: 1.000 (0.12)	MT vs T: 1.000 (0.01)
	T		-1.53 ± 0.99 (-1.88 to -1.18)	-1.42 ± 1.06 (-1.78 to -1.07)	-6.72	0.140 (0.1)	0.100 (0.11)	MT vs C: 1.000 (0.09)	MT vs C: 1.000 (0.12)
	C		-1.45 ± 1.04 (-1.81 to -1.10)	-1.45 ± 1.04 (-1.81 to -1.09)	-0.20	0.966 (0)	0.991 (0)	P vs T: 1.000 (0.26)	P vs T: 1.000 (0.03)
								P vs C: 1.000 (0.26)	P vs C: 0.755 (0.15)
								T vs C: 1.000 (0.29)	T vs C: 1.000 (0.11)
L2 vertebra aBMD (g/cm^2)	MT	0.86	0.84 ± 0.13 (0.80–0.88)	0.85 ± 0.12 (0.81–0.89)	1.24	0.139 (0.08)	0.294 (0.06)	MT vs P: 1.000 (0.34)	MT vs P: 1.000 (0.1)
	P		0.87 ± 0.10 (0.83–0.91)	0.89 ± 0.09 (0.85–0.93)	2.01	**0.014** (0.17)	**0.006** (0.18)	MT vs T: 1.000 (0.23)	MT vs T: 1.000 (0)
	T		0.87 ± 0.12 (0.83–0.91)	0.88 ± 0.11 (0.84–0.92)	0.65	0.419 (0.05)	0.259 (0.07)	MT vs C: 1.000 (0.1)	MT vs C: 1.000 (0.11)
	C		0.87 ± 0.12 (0.83–0.91)	0.86 ± 0.11 (0.82–0.90)	-0.69	0.391 (0.05)	0.392 (0.04)	P vs T: 1.000 (0.1)	P vs T: 1.000 (0.1)
								P vs C: 1.000 (0.24)	P vs C: 0.065 (0.22)
								T vs C: 1.000 (0.14)	T vs C: 0.974 (0.11)
L2 vertebra T-score (SD)	MT	-1.46	-1.67 ± 1.21 (-2.05 to -1.29)	-1.56 ± 1.15 -(1.92 to -1.20)	-6.50	0.066 (0.09)	0.144 (0.07)	MT vs P: 1.000 (0.3)	MT vs P: 1.000 (0.07)
	P		-1.39 ± 0.97 (-1.76 to -1.01)	-1.24 ± 0.91 (-1.60 to -0.88)	-10.36	**0.016** (0.15)	**0.008** (0.16)	MT vs T: 1.000 (0.22)	MT vs T: 1.000 (0.01)
	T		-1.37 ± 1.13 (-1.75 to -0.99)	-1.32 ± 1.04 (-1.6 to -0.96)	-4.06	0.344 (0.05)	0.220 (0.07)	MT vs C: 1.000 (0.09)	MT vs C: 0.714 (0.11)
	C		-1.41 ± 1.12 (-1.79 to -1.04)	-1.46 ± 1.12 (-1.82 to -1.10)	3.11	0.454 (0.04)	0.461 (0.04)	P vs T: 1.000 (0.07)	P vs T: 1.000 (0.08)
								P vs C: 1.000 (0.07)	P vs C: 0.100 (0.19)
								T vs C: 1.000 (0.21)	T vs C: 0.998 (0.1)

Table 39. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L3 vertebra aBMD (g/cm^2)	MT	0.89	0.86 ± 0.13 (0.82–0.90)	0.86 ± 0.13 (0.82–0.91)	0.45	0.613 (0.03)	0.941 (0)	MT vs P: 0.383 (0.48) MT vs T: 1.000 (0.32)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.03)
	P		0.92 ± 0.09 (0.87–0.96)	0.92 ± 0.10 (0.88–0.96)	0.18	0.829 (0.02)	0.614 (0.03)	MT vs C: 1.000 (0.25)	MT vs C: 1.000 (0)
	T		0.90 ± 0.14 (0.86–0.95)	0.90 ± 0.12 (0.86–0.95)	0.36	0.671 (0.02)	0.563 (0.03)	P vs T: 1.000 (0.13)	P vs T: 1.000 (0.01)
	C		0.90 ± 0.13 (0.85–0.94)	0.90 ± 0.13 (0.85–0.94)	0.04	0.966 (0)	0.962 (0)	P vs C: 1.000 (0.2) T vs C: 1.000 (0.07)	P vs C: 1.000 (0.02) T vs C: 1.000 (0.03)
L3vertebra T-score (SD)	MT	-1.68	-2.00 ± 1.20 -(2.40 to -1.60)	-1.96 ± 1.22 (-2.35 to -1.57)	-2.06	0.542 (0.03)	0.826 (0.01)	MT vs P: 0.374 (0.48) MT vs T: 1.000 (0.31)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.02)
	P		-1.46 ± 0.89 (-1.85 to -1.06)	-1.43 ± 0.93 (-1.82 to -1.04)	-1.61	0.727 (0.03)	0.535 (0.05)	MT vs C: 1.000 (0.24)	MT vs C: 1.000 (0.01)
	T		-1.62 ± 1.34 (-2.01 to -1.22)	-1.58 ± 1.16 (-1.97 to -1.19)	-2.18	0.601 (0.03)	0.519 (0.03)	P vs T: 1.000 (0.14)	P vs T: 1.000 (0)
	C		-1.67 ± 1.20 (-2.06 to -1.27)	-1.67 ± 1.24 (-2.06 to -1.28)	0.00	1.000 (0)	0.995 (0)	P vs C: 1.000 (0.14) T vs C: 1.000 (0.21)	P vs C: 1.000 (0.04) T vs C: 1.000 (0.04)
L4 vertebra aBMD (g/cm^2)	MT	0.91	0.87 ± 0.14 (0.82–0.92)	0.87 ± 0.13 (0.82–0.92)	0.16	0.857 (0.01)	0.936 (0.01)	MT vs P: 0.251 (0.51) MT vs T: 0.990 (0.37)	MT vs P: 1.000 (0.11) MT vs T: 1.000 (0.02)
	P		0.93 ± 0.13 (0.88–0.97)	0.94 ± 0.13 (0.89–0.99)	1.39	0.087 (0.1)	0.065 (0.1)	MT vs C: 1.000 (0.17)	MT vs C: 0.518 (0.12)
	T		0.92 ± 0.13 (0.87–0.97)	0.92 ± 0.11 (0.87–0.96)	-0.30	0.713 (0.02)	0.776 (0.02)	P vs T: 1.000 (0.17)	P vs T: 0.789 (0.13)
	C		0.91 ± 0.15 (0.87–0.96)	0.89 ± 0.16 (0.85–0.94)	-2.11	**0.011** (0.12)	**0.012** (0.12)	P vs C: 1.000 (0.29) T vs C: 1.000 (0.15)	P vs C: **0.014** (0.22) T vs C: 0.704 (0.11)
L4 vertebra T-score (SD)	MT	-1.35	-1.71 ± 1.33 (-2.15 to -1.27)	-1.72 ± 1.23 (-2.16 to -1.29)	0.69	0.855 (0.01)	0.576 (0.03)	MT vs P: 0.228 (0.54) MT vs T: 0.960 (0.37)	MT vs P: 0.707 (0.12) MT vs T: 1.000 (0)
	P		-1.17 ± 1.20 (-1.61 to -0.73)	-1.07 ± 1.18 (-1.61 to -0.73)	-8.27	0.133 (0.08)	0.093 (0.09)	MT vs C: 1.000 (0.2)	MT vs C: 0.976 (0.09)
	T		-1.23 ± 1.23 (-1.67 to -0.79)	-1.28 ± 1.15 (-1.72 to 0-.85)	4.04	0.438 (0.04)	0.561 (0.03)	P vs T: 1.000 (0.18)	P vs T: 0.659 (0.12)
	C		-1.29 ± 1.39 (-1.73 to -0.85)	-1.45 ± 1.51 (-1.89 to -1.02)	12.78	**0.011** (0.11)	**0.011** (0.11)	P vs C: 1.000 (0.18) T vs C: 1.000 (0.28)	P vs C: **0.019** (0.2) T vs C: 1.000 (0.09)

Table 39. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total lumbar spine aBMD (g/cm^2)	MT	0.87	0.84 ± 0.12 (0.80–0.88)	0.85 ± 0.11 (0.81–0.89)	0.75	0.137 (0.05)	0.301 (0.04)	MT vs P: 0.331 (0.5)	MT vs P: 1.000 (0.07)
	P		0.89 ± 0.09 (0.85–0.93)	0.90 ± 0.09 (0.86–0.94)	1.28	**0.008 (0.12)**	**0.004** (0.13)	MT vs T: 1.000 (0.31)	MT vs T: 1.000 (0)
	T		0.88 ± 0.11 (0.84–0.92)	0.88 ± 0.11 (0.85–0.92)	0.43	0.366 (0.03)	0.243 (0.04)	MT vs C: 1.000 (0.2)	MT vs C: 0.737 (0.07)
	C		0.88 ± 0.12 (0.84–0.92)	0.87 ± 0.12 (0.84–0.91)	-0.54	0.264 (0.04)	0.251 (0.03)	P vs T: 1.000 (0.17)	P vs T: 1.000 (0.08)
								P vs C: 1.000 (0.26)	P vs C: **0.027** (0.15)
								T vs C: 1.000 (0.09)	T vs C: 0.625 (0.08)
Total lumbar spine T-score (SD)	MT	-1.53	-1.81 ± 1.09 (-2.17 to -1.45)	-1.76 ± 1.06 (-2.11 to -1.40)	-2.76	0.217 (0.05)	0.389 (0.03)	MT vs P: 0.296 (0.51)	MT vs P: 0.806 (0.09)
	P		-1.37 ± 0.90 (-1.73 to -1.01)	-1.26 ± 0.88 (-1.61 to -0.90)	-8.33	**0.005** (0.13)	**0.003** (0.14)	MT vs T: 1.000 (0.3)	MT vs T: 1.000 (0.01)
	T		-1.46 ± 1.07 (-1.82 to -1.10)	-1.44 ± 1.00 (-1.80 to -1.09)	-1.40	0.611 (0.02)	0.501 (0.03)	MT vs C: 1.000 (0.22)	MT vs C: 1.000 (0.06)
	C		-1.48 ± 1.12 (-1.84 to -1.12)	-1.51 ± 1.18 (-1.87 to -1.16)	2.38	0.383 (0.03)	0.391 (0.03)	P vs T: 1.000 (0.2)	P vs T: 0.588 (0.1)
								P vs C: 1.000 (0.20)	P vs C: **0.039** (0.15)
								T vs C: 1.000 (0.25)	T vs C: 1.000 (0.06)
L2-L4 lumbar spine segment aBMD (g/cm^2)	MT	0.89	0.86 ± 0.12 (0.82–0.90)	0.86 ± 0.12 (0.82–0.90)	0.62	0.308 (0.04)	0.541 (0.02)	MT vs P: 0.504 (0.45)	MT vs P: 1.000 (0.04)
	P		0.91 ± 0.10 (0.87–0.95)	0.91 ± 0.10 (0.87–0.95)	0.67	0.249 (0.06)	0.183 (0.07)	MT vs T: 1.000 (0.34)	MT vs T: 1.000 (0.01)
	T		0.90 ± 0.12 (0.86–0.94)	0.90 ± 0.11 (0.86–0.94)	0.24	0.676 (0.02)	0.517 (0.03)	MT vs C: 1.000 (0.21)	MT vs C: 1.000 (0.06)
	C		0.89 ± 0.12 (0.85–0.94)	0.89 ± 0.13 (0.85–0.93)	-0.62	0.287 (0.04)	0.283 (0.04)	P vs T: 1.000 (0.1)	P vs T: 1.000 (0.03)
								P vs C: 1.000 (0.19)	P vs C: 0.539 (0.1)
								T vs C: 1.000 (0.1)	T vs C: 1.000 (0.07)
L2-L4 lumbar spine segment T-score (SD)	MT	-1.65	-1.97 ± 1.15 (-2.36 to -1.59)	-1.91 ± 1.13 (-2.29 to -1.53)	-3.27	0.164 (0.06)	0.303 (0.04)	MT vs P: 0.296 (0.5)	MT vs P: 1.000 (0.01)
	P		-1.43 ± 0.97 (-1.81 to -1.05)	-1.38 ± 1.00 (-1.75 to -1.00)	-3.55	0.273 (0.05)	0.185 (0.06)	MT vs T: 1.000 (0.32)	MT vs T: 1.000 (0.01)
	T		-1.59 ± 1.16 (-1.97 to -1.21)	-1.56 ± 1.01 (-1.94 to -1.18)	-1.85	0.525 (0.03)	0.452 (0.03)	MT vs C: 1.000 (0.19)	MT vs C: 0.743 (0.08)
	C		-1.63 ± 1.18 (-2.01 to -1.25)	-1.68 ± 1.25 (-2.06 to -1.30)	3.24	0.254 (0.04)	0.252 (0.04)	P vs T: 1.000 (0.18)	P vs T: 1.000 (0.03)
								P vs C: 1.000 (0.18)	P vs C: 0.489 (0.1)
								T vs C: 1.000 (0.27)	T vs C: 1.000 (0.08)

Note. Data are expressed as mean ± SD and 95% CIs. Sample size of each group: n = 34. MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; aBMD: areal bone mineral density; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

B. areal bone mineral density at proximal femur and fracture risk

The aBMD at the proximal femur and the fracture risk outcomes from the ITT analysis are displayed in Table 40. Pairwise comparison after the repeated-measures ANOVA revealed a significant effect by time in the P group by increasing the intertrochanteric, Ward's triangle, and total hip aBMD and by decreasing the T-score of the Ward's triangle and total hip areas. At the same time, significant within-group effects were also found in the T group for Ward's triangle aBMD and total-hip T-score. The ESs of these changes were mostly trivial. No significant differences between groups were found in the aBMDs and T-scores of the analyzed variables. After applying the repeated-measures ANCOVA, a significant time × group interaction was found in the intertrochanteric aBMD [$F(3, 130) = 3.55$, $p < 0.016$, $\eta^2p = 0.076$, $1-\beta = 0.777$] and total hip aBMD [$F(3, 130) = 2.76$, $p < 0.045$, $\eta^2p = 0.060$, $1-\beta = 0.657$]. In both cases, the differences were found between the P and the C group. The magnitudes of change were considered trivial, and no additional differences by time were found after the corrections.

With regard to fracture risk, a main effect of time was revealed through the ANOVA on the 10-year probability of a major osteoporotic fracture [$F(1, 132) = 26.54$, $p < 0.000$, $\eta^2p = 0.167$, $1-\beta = 0.999$] and 10-year probability of hip fracture [$F(1, 132) = 13.84$, $p < 0.000$, $\eta^2p = 0.095$, $1-\beta = 0.958$]. Significant reductions were achieved by the three training modalities in the probability of osteoporotic fracture, while the MT and P groups also found significant decreases in the probability of hip fracture. The ESs ranged from trivial to moderate. After adjustments, the significant reduction by the MT group in the probability of osteoporotic fracture disappeared, while a significant reduction of hip-fracture risk was achieved by the T group. Significant time × group interactions were only found between the MT and the T group after ANCOVA in the 10-year probability of hip fracture, with a trivial ES.

The results of the PPA showed numerous differences between analyses. The repeated-measures ANOVA revealed no significant changes in the 10-year probability of a hip fracture within the M group after the training program, and a significant within-group effect in the intertrochanteric T-score of the P group. For the rest of the parameters, the same significant differences by time were found as in the ITT analysis. Moreover, the significant difference between the MT and T groups in the 10-year probability of a hip fracture disappeared. With the ANCOVA analysis, significant differences by time were found in intertrochanteric T-score, Ward's triangle aBMD, and 10-year probability of a major osteoporotic fracture in the P, T, and MT groups, respectively. Nevertheless, the significant difference of the MT group in the 10-year probability of a hip fracture disappeared. Finally, significant differences between the P and C groups were found in the intertrochanteric T-score and the 10-year probability of hip fracture following the ANCOVA statistical test. The rest of the changes were the same as in the ITT analysis. The ESs of the aforementioned changes in the PPA were similar as in the ITT analysis. The results from PPA are presented in Supplementary Material D (Table D.2).

Table 40. *Intervention effects on BMD at proximal femur from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Femoral neck aBMD (g/cm^2)	MT	0.68	0.68 ± 0.07 (0.65–0.71)	0.68 ± 0.07 (0.65–0.71)	0.28	0.695 (0.03)	0.617 (0.04)	MT vs P: 1.000 (0.24) MT vs T: 1.000 (0.11) MT vs C: 1.000 (0.2) P vs T: 1.000 (0.1) P vs C: 0.546 (0.4) T vs C: 1.000 (0.28)	MT vs P: 1.000 (0.05) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.07) P vs T: 1.000 (0.04) P vs C: 1.000 (0.11) T vs C: 1.000 (0.07)
	P		0.69 ± 0.07 (0.66–0.72)	0.70 ± 0.07 (0.67–0.73)	0.86	0.221 (0.08)	0.169 (0.09)		
	T		0.69 ± 0.08 (0.66–0.72)	0.69 ± 0.09 (0.66–0.72)	0.64	0.365 (0.05)	0.419 (0.04)		
	C		0.67 ± 0.10 (0.64–0.70)	0.66 ± 0.09 (0.64–0.69)	-0.31	0.668 (0.02)	0.564 (0.03)		
Femoral neck T-score (SD)	MT	-1.46	-1.48 ± 0.67 (-1.74 to -1.22)	-1.46 ± 0.64 (-1.72 to -1.2)	-1.39	0.602 (0.03)	0.465 (0.04)	MT vs P: 1.000 (0.22) MT vs T: 1.000 (0.11) MT vs C: 1.000 (0.16) P vs T: 1.000 (0.1) P vs C: 0.828 (0.1) T vs C: 1.000 (0.33)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.04) P vs T: 1.000 (0.02) P vs C: 1.000 (0.05) T vs C: 1.000 (0.03)
	P		-1.35 ± 0.64 (-1.61 to -1.08)	-1.31 ± 0.68 (-1.58 to -1.05)	-2.40	0.413 (0.05)	0.353 (0.05)		
	T		-1.42 ± 0.77 (-1.68 to -1.15)	-1.38 ± 0.74 (-1.65 to -1.12)	-2.28	0.413 (0.04)	0.568 (0.03)		
	C		-1.59 ± 0.95 (-1.85 to -1.33)	-1.59 ± 0.97 (-1.85 to -1.33)	0.37	0.882 (0.01)	0.838 (0.01)		
Trochanter aBMD (g/cm^2)	MT	0.66	0.64 ± 0.10 (0.61–0.68)	0.65 ± 0.10 (0.61–0.68)	0.34	0.449 (0.02)	0.387 (0.03)	MT vs P: 0.824 (0.36) MT vs T: 1.000 (0.07) MT vs C: 1.000 (0.18) P vs T: 1.000 (0.31) P vs C: 1.000 (0.18) T vs C: 1.000 (0.12)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.02) MT vs C: 0.511 (0.07) P vs T: 1.000 (0) P vs C: 1.000 (0.05) T vs C: 1.000 (0.05)
	P		0.68 ± 0.08 (0.65–0.71)	0.68 ± 0.08 (0.65–0.71)	0.12	0.782 (0.01)	0.804 (0.01)		
	T		0.65 ± 0.09 (0.62–0.68)	0.65 ± 0.09 (0.62–0.69)	0.09	0.838 (0.01)	0.952 (0.01)		
	C		0.67 ± 0.09 (0.64–0.70)	0.66 ± 0.09 (0.63–0.70)	-0.70	0.103 (0.05)	0.116 (0.04)		
Trochanter T-score (SD)	MT	-0.37	-0.54 ± 1.00 (-0.86 to -0.22)	-0.53 ± 1.00 (-0.85 to -0.22)	-1.08	0.850 (0.01)	0.815 (0.01)	MT vs P: 0.756 (0.37) MT vs T: 1.000 (0.08) MT vs C: 1.000 (0.21) P vs T: 1.000 (0.31) P vs C: 1.000 (0.31) T vs C: 1.000 (0.15)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.01) P vs C: 1.000 (0.02) T vs C: 1.000 (0.01)
	P		-0.18 ± 0.88 (-0.50 to 0.12)	-0.18 ± 0.87 (-0.50 to 0.13)	0.00	1.000 (0)	0.928 (0)		
	T		-0.46 ± 0.92 (-0.78 to -0.15)	-0.46 ± 0.90 (-0.78 to -0.14)	-0.63	0.925 (0)	0.883 (0.01)		
	C		-0.30 ± 0.92 (-0.62 to 0.00)	-0.32 ± 0.96 (-0.64 to -0.01)	6.67	0.509 (0.02)	0.580 (0.02)		

Table 40. Continued.

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Intertro-chanteric area aBMD (g/cm^2)	MT	0.99	0.98 ± 0.13 (0.94–1.03)	0.98 ± 0.13 (0.94–1.02)	-0.20	0.693 (0.01)	0.686 (0.01)	MT vs P: 1.000 (0.3) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.09) P vs T: 1.000 (0.34) P vs C: 1.000 (0.18) T vs C: 1.000 (0.11)	MT vs P: 0.153 (0.13) MT vs T: 1.000 (0.04) MT vs C: 1.000 (0.04) P vs T: 0.608 (0.1) P vs C: **0.011** (0.16) T vs C: 0.837 (0.08)
	P		1.00 ± 0.11 (0.96–1.05)	1.02 ± 0.12 (0.97–1.06)	1.38	**0.007** (0.12)	**0.006** (0.12)		
	T		0.98 ± 0.11 (0.93–1.02)	0.98 ± 0.10 (0.93–1.02)	0.29	0.577 (0.03)	0.656 (0.03)		
	C		1.00 ± 0.14 (0.96–1.05)	0.99 ± 0.15 (0.95–1.04)	-0.88	0.083 (0.06)	0.096 (0.05)		
Intertro-chanteric area T-score (SD)	MT	-0.67	-0.74 ± 0.87 -(1.02 to -0.45)	-0.67 ± 0.89 -(0.95 to -0.38)	-9.88	0.058 (0.08)	0.062 (0.08)	MT vs P: 1.000 (0.18) MT vs T: 1.000 (0.12) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.34) P vs C: 1.000 (0.34) T vs C: 1.000 (0.15)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.1) MT vs C: 0.184 (0.12) P vs T: 1.000 (0.11) P vs C: 0.192 (0.13) T vs C: 1.000 (0.05)
	P		-0.59 ± 0.74 (-0.87 to -0.30)	-0.52 ± 0.71 (-0.80 to -0.24)	-11.3	0.080 (0.09)	0.064 (0.1)		
	T		-0.76 ± 0.74 (-1.05 to -0.48)	-0.76 ± 0.67 (-1.04 to -0.48)	-0.38	0.939 (0)	0.926 (0.01)		
	C		-0.60 ± 0.97 (-0.88 to -0.31)	-0.65 ± 0.99 (-0.93 to -0.37)	8.29	0.195 (0.05)	0.233 (0.05)		
Ward's triangle aBMD (g/cm^2)	T	0.51	0.49 ± 0.09 (0.46–0.53)	0.51 ± 0.09 (0.47–0.55)	3.01	0.068 (0.16)	0.062 (0.16)	MT vs P: 0.840 (0.41) MT vs T: 1.000 (0.29) MT vs C: 1.000 (0.1) P vs T: 1.000 (0.1) P vs C: 0.352 (0.43) T vs C: 0.810 (0.33)	MT vs P: 1.000 (0.1) MT vs T: 1.000 (0) MT vs C: 1.000 (0.08) P vs T: 1.000 (0.09) P vs C: 0.452 (0.16) T vs C: 1.000 (0.08)
	P		0.53 ± 0.10 (0.49–0.57)	0.55 ± 0.10 (0.51–0.59)	4.66	**0.003** (0.23)	**0.002 (**0.24)		
	T		0.52 ± 0.11 (0.49–0.56)	0.54 ± 0.11 (0.50–0.58)	3.13	**0.045** (0.14)	0.058 (0.13)		
	C		0.49 ± 0.14 (0.45–0.53)	0.50 ± 0.14 (0.46–0.54)	1.10	0.504 (0.04)	0.540 (0.03)		
Ward's triangle T-score (SD)	MT	-1.85	-2.01 ± 0.77 (-2.36 to -1.65)	-1.87 ± 0.83 (-2.25 to -1.49)	-6.73	0.090 (0.17)	0.088 (0.17)	MT vs P: 0.721 (0.42) MT vs T: 1.000 (0.27) MT vs C: 1.000 (0.03) P vs T: 1.000 (0.12) P vs C: 0.594 (0.12) T vs C: 1.000 (0.38)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.03) P vs C: 1.000 (0.05) T vs C: 1.000 (0.02)
	P		-1.62 ± 1.11 (-1.97 to -1.27)	-1.45 ± 1.15 (-1.83 to -1.06)	-10.85	**0.027** (0.16)	**0.027** (0.16)		
	T		-1.74 ± 1.00 (-2.09 to -1.39)	-1.59 ± 1.23 (-1.97 to -1.21)	-8.43	0.065 (0.13)	0.081 (0.13)		
	C		-2.02 ± 1.21 (-2.37 to -1.67)	-1.90 ± 1.22 (-2.28 to -1.52)	-5.96	0.130 (0.1)	0.135 (0.1)		

Table 40. Continued.

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total hip aBMD (g/cm^2)	MT	0.84	0.83 ± 0.11 (0.79–0.86)	0.83 ± 0.10 (0.80–0.86)	0.38	0.380 (0.03)	0.372 (0.03)	MT vs P: 0.840 (0.32)	MT vs P: 1.000 (0.06)
	P		0.85 ± 0.09 (0.82–0.89)	0.86 ± 0.08 (0.83–0.90)	1.03	**0.016** (0.1)	**0.011** (0.1)	MT vs T: 1.000 (0.03)	MT vs T: 1.000 (0)
	T		0.83 ± 0.09 (0.79–0.86)	0.83 ± 0.08 (0.80–0.87)	0.55	0.202 (0.05)	0.334 (0.03)	MT vs C: 1.000 (0.14)	MT vs C: 0.604 (0.07)
	C		0.85 ± 0.11 (0.82–0.89)	0.85 ± 0.12 (0.81–0.88)	-0.68	0.110 (0.05)	0.152 (0.04)	P vs T: 1.000 (0.34)	P vs T: 1.000 (0.07)
								P vs C: 0.352 (0.16)	P vs C: **0.030** (0.13)
								T vs C: 0.810 (0.12)	T vs C: 0.560 (0.08)
Total hip T-score (SD)	MT	-0.79	-0.90 ± 0.91 (-1.19 to -0.61)	-0.86 ± 0.83 (-1.14 to -0.58)	-4.25	0.195 (0.04)	0.245 (0.04)	MT vs P: 0.721 (0.31)	MT vs P: 1.000 (0.04)
	P		-0.68 ± 0.76 (-0.97 to -0.39)	-0.62 ± 0.71 (-0.90 to -0.34)	-8.62	**0.047 (**0.08)	**0.024** (0.09)	MT vs T: 1.000 (0)	MT vs T: 1.000 (0.01)
	T		-0.89 ± 0.77 (-1.18 to -0.60)	-0.86 ± 0.73 (-1.14 to -0.58)	-3.62	0.272 (0.04)	0.377 (0.03)	MT vs C: 1.000 (0.15)	MT vs C: 1.000 (0.05)
	C		-0.70 ± 0.94 (-0.99 to -0.41)	-0.72 ± 0.98 (-1.00 to -0.44)	2.49	0.549 (0.02)	0.666 (0.01)	P vs T: 1.000 (0.33)	P vs T: 1.000 (0.06)
								P vs C: 0.594 (0.33)	P vs C: 0.342 (0.09)
								T vs C: 1.000 (0.12)	T vs C: 1.000 (0.04)
10-year probability of a major osteoporotic fracture (%)	MT	0.11	0.12 ± 0.04 (0.10–0.15)	0.11 ± 0.03 (0.09–0.13)	-9.66	**0.003** (0.28)	0.326 (0.07)	MT vs P: 1.000 (0.02)	MT vs P: 0.397 (0.23)
	P		0.13 ± 0.13 (0.10–0.16)	0.11 ± 0.13 (0.09–0.14)	-12.86	**0.000 (**0.13)	**0.000** (0.25)	MT vs T: 1.000 (0.67)	MT vs T: 0.594 (0.27)
	T		0.10 ± 0.03 (0.07–0.13)	0.09 ± 0.02 (0.06–0.11)	-11.39	**0.004** (0.37)	**0.001** (0.61)	MT vs C: 1.000 (0.44)	MT vs C: 1.000 (0.08)
	C		0.10 ± 0.01 (0.07–0.12)	0.10 ± 0.01 (0.07–0.12)	-0.17	0.965 (0.01)	0.095 (0.23)	P vs T: 0.902 (0.26)	P vs T: 1.000 (0)
								P vs C: 1.000 (0.16)	P vs C: 1.000 (0.2)
								T vs C: 1.000 (0.41)	T vs C: 1.000 (0.27)
10-year probability of a hip fracture (%)	MT	0.01	0.02 ± 0.01 (0.01–0.02)	0.02 ± 0.01 (0.01–0.02)	-11.69	**0.049** (0.19)	**0.005** (0.25)	MT vs P: 0.283 (0.4)	MT vs P: 1.000 (0.04)
	P		0.02 ± 0.01 (0.01–0.02)	0.01 ± 0.01 (0.01–0.02)	-22.25	**0.001** (0.28)	**0.000** (0.11)	MT vs T: **0.006** (0.77)	MT vs T: 1.000 (0.09)
	T		0.01 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.00–0.01)	-15.55	0.100 (0.36)	**0.000** (0.43)	MT vs C: 0.331 (0.42)	MT vs C: 0.578 (0.3)
	C		0.01 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.01–0.02)	-4.34	0.601 (0.08)	0.641 (0.11)	P vs T: 1.000 (0.38)	P vs T: 1.000 (0.01)
								P vs C: 1.000 (0.38)	P vs C: 0.079 (0.14)
								T vs C: 0.959 (0.02)	T vs C: 0.160 (0.52)

Note. Data are expressed as mean ± SD and 95% CIs. Sample size of each group: n = 34. MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; aBMD: areal bone mineral density; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

C. Bone turnover markers

Changes in BMTs from the ITT analysis are displayed in Table 41. Repeated-measures ANOVA showed a main effect of time on OC [$F(1, 99) = 56.76$, $p < 0.000$, $\eta^2p = 0.364$, $1-\beta = 1$] and β-CTx [$F(1, 97) = 8.48$, $p < 0.004$, $\eta^2p = 0.079$, $1-\beta = 0.823$]. Pairwise comparisons revealed significant increases in the bone-formation biomarker OC within both training groups and a significant decrease in the bone-resorption biomarker β-CTx also in both groups at the end of the training period. Indeed, the magnitude of the effect on the OC within the P group was considered large, while the MT achieved a moderate ES. The changes in β-CTx were considered small in both groups. No significant changes were found in the C group after the training period. Furthermore, a significant time × group interaction was found in β-CTx [$F(2, 97) = 5.29$, $p < 0.007$, $\eta^2p = 0.097$, $1-\beta = 0.826$] between the two training modalities vs the C group. The magnitude of these changes was considered moderate. After controlling for baseline values and age, repeated-measures ANCOVA showed the same significant effects by time and similar ESs. Nevertheless, along with the significant difference between groups in terms of β-CTx, a significant time × group interaction was found in OC [$F(2, 97) = 23.86$, $p < 0.000$, $\eta^2p = 0.330$, $1-\beta = 1$], again between both training modalities and the C group. The ESs of these changes were moderate (MT–C) and large (P–C). The results of the PPA were very similar to those of the ITT analysis. There were significant differences between P and C in OC from the ANOVA. The rest of the outcomes were the same as in the ITT analysis. The PPA results are presented in Supplementary Material D (Table D.3).

Table 41. *Intervention effects on bone biomarkers from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
OC (ng/mL)	MT	17.32	16.31 ± 4.87 (14.82–17.79)	18.98 ± 4.80 (17.35–20.61)	16.37	**0.000** (0.55)	**0.000** (0.56)	MT vs P: 0.475 (0.35)	MT vs P: 0.283 (0.26)
	P		16.52 ± 3.12 (15.04–18.01)	20.63 ± 4.51 (19.00–22.26)	24.82	**0.000** (1.06)	**0.000** (1)	MT vs C: 1.000 (0.12)	MT vs C: **0.000** (0.66)
	C		19.12 ± 4.86 (17.63–20.60)	18.39 ± 5.02 (16.76–20.02)	-3.81	0.118 (0.15)	0.259 (0.11)	P vs C: 0.169 (0.47)	P vs C: **0.000** (0.93)
β-CTx (ng/L)	MT	0.36	0.36 ± 0.14 (0.31–0.40)	0.32 ± 0.13 (0.28–0.37)	-9.05	**0.002** (0.23)	**0.001** (0.22)	MT vs P: 1.000 (0.11)	MT vs P: 1.000 (0.03)
	P		0.34 ± 0.11 (0.29–0.39)	0.31 ± 0.10 (0.27–0.35)	-8.76	**0.005** (0.27)	**0.000** (0.32)	MT vs C: **0.039** (0.57)	MT vs C: **0.002** (0.36)
	C		0.39 ± 0.13 (0.35–0.44)	0.40 ± 0.13 (0.36–0.44)	2.56	0.334 (0.08)	0.120 (0.12)	P vs C: **0.011** (0.76)	P vs C: **0.001** (0.43)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: $n = 34$. MT: multi-component training group; P: power strength training group; C: control group; OC: osteocalcin; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 68.48.

V.VII. DISCUSSION ON BONE HEALTH

To the best of our knowledge, the studies presented in this PhD dissertation are the first to investigate the effects of two key training parameters (intensity and modality training) using elastic resistance during a medium to long training period (16, 20, and 32 weeks) on bone health through the analysis of the aBMD and T-score of the lumbar spine (L1, L2, L3, L4, total lumbar spine, and L2-L4 segment) and proximal femur (femoral neck, trochanter, intertrochanteric area, Ward's triangle, and total hip), the fracture risk (10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture), and the BTMs of bone formation (P1NP, bALP, OC), bone resorption (β-CTx), its relation (ratio bALP/ β-CTx), and bone-related variables (25OHD, Na, K and Cl) in older women.

Regarding intensity, the first study's main and novel finding was that both training intensities are effective for increasing the aBMD of the lumbar spine and proximal femur, reducing the fracture risk, and improving the bone turnover rate after 8 months of resistance training with elastic bands. Although there are no significant differences between training intensities in most of the parameters analyzed, it seems that high intensity achieves better results in lumbar spine, some areas of proximal femur (trochanter and total hip), fracture risk, and BMTs at 16 and 32 weeks, particularly in the bALP. However, the progressive resistance training at moderate intensity results in a higher increase of aBMD at femoral neck and Ward's triangle than high intensity.

Furthermore, regarding the training modality, the main and novel finding of the second study was that although all training modalities – multi-component, power strength training, and high-intensity resistance training – achieved improvements in aBMD at the lumbar spine and proximal femur, only the power training group demonstrated changes that were statistically significant. The MT and T training groups, alongside the P group, also significantly improved the reduction of fracture risk by decreasing the 10-year probability of

a major osteoporotic fracture and 10-year probability of hip fracture. Additionally, both the MT and P group improved the bone turnover rate by increasing the concentrations of OC and decreasing the levels of β-CTx. Both training modalities achieved significant differences with the C group in these parameters. In all the parameters except the decrease of β-CTx, the P group accomplished the best results, being the most effective modality to improve bone health after the 5 months of the study period. In fact, only the P group reached significant differences with C group in some parameters of lumbar spine (L4 aBMD and T-score, total lumbar spine aBMD and T-score) and proximal femur (intertrochanteric and total hip aBMD). It is important to note that no significant effects between training modalities were found except in the 10-year probability of hip fracture between multi-component and traditional high-intensity resistance training exercise regimes.

We had hypothesized in H3 and H10 (Chapter III, Section III.I.III.) that a 32-week program of progressive resistance training with elastic bands at high intensity improves the bone remodeling circle by increasing the concentrations of P1NP and bALP and by reducing the values of β-CTx at the midpoint (16 weeks) and in the long term (32 weeks), while the moderate intensity produces a positive effect in the same parameters only over the long term, finding differences between the training intensities. Our findings partially confirmed this hypothesis, as we found that high intensity improved all the BTMs at 16 and 32 weeks, but the moderate intensity also achieved improvements in the P1NP and β-CTx at the midpoint, although not at bALP, and in all the parameters at the end of the training program. Differences between training intensities were only found in bALP at 16 and 32 weeks and in the ratio bALP/β-CTx at 16 weeks.

Next, we had hypothesized in H4 and H10 (Chapter III, Section III.I.III.) that both training intensities improve the aBMD and T-score of the lumbar spine and proximal femur areas, with no impact in the biochemical markers of 25OHD, Na, K, and Cl after a 32-week

program of progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity. Our findings largely confirmed this hypothesis, as we found that both training intensities significantly improved the aBMD and T-score of most of the parameters of the lumbar spine and proximal femur areas with no significant differences between the training intensities, although the HI group produced greater effects. However, some differences in the biochemical markers of Na, K, and Cl were found.

Furthermore, we had also hypothesized in H5 and H10 (Chapter III, Section III.I.III.) that both training intensities reduce the risk of major osteoporotic and hip fracture in the following 10 years after a 32-week program of progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity.These hypotheses were entirely confirmed, because we found that moderate- and high-intensity resistance training programs were effective at reducing the fracture risk through the reduction of the major osteoporotic and hip fracture probability in the following 10 years, with the HI group reaching the best results. Additionally, we found significant differences between the training intensities in both fracture risk parameters (10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture).

Regarding the influence of the training modality, we had hypothesized in H2 and H10 (Chapter III, Section III.II.III.) that both the multi-component and power strength training modalities improve the bone remodeling circle by increasing the concentrations of OC and reducing the values of β-CTx after an intervention period of 20 weeks using elastic resistance, probably with differences between the training modalities groups in the parameters analyzed. These hypotheses were partially refuted because we found that both training modalities significantly improved the bone remodeling cycle by increasing the bone

formation markers and decreasing the bone resorption markers, but no significant differences were found between the training groups.

Next, we had hypothesized in H3 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) improve the aBMD and T-score of the lumbar spine and proximal femur areas after an intervention period of 20 weeks using elastic resistance, with power training producing greater effects than multi-component and high-intensity resistance training in the analyzed bone regions. This hypothesis was confirmed; we found that although all the training modalities improved the aBMD and T-score of lumbar spine and proximal femur areas, only the power strength training modality achieved significant changes. However, regarding H10, no significant differences were found between training modalities at the end of the training period. Thus, the hypothesis was refuted.

Finally, we also hypothesized in the H4 and H10 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) reduce the risk of major osteoporotic and hip fracture in the following 10 years after an intervention period of 20 weeks using elastic resistance, with power training producing greater effects than multi-component and high-intensity resistance training, achieving significant differences between the groups. Our findings partially confirmed these hypotheses, as we found significant differences in all the groups after the training period in the reduction of the probability of major osteoporotic fractures and hip fracture, but in the latter only when values were adjusted by age and baseline scores. Additionally, we only found differences between the MT and T groups in the reduction of the 10-year probability risk of hip fracture.

V.VII.I. Specific discussion of the first project

Evidence regarding exercise's effects on bone health has been mostly based on premenopausal or menopausal women and single-stimulus exercise interventions; thus, fewer studies have focused on postmenopausal or elderly women comparing different stimuli – for example, different training intensities (Bembem et al., 2000, Bemben & Bemben, 2010; Bocalini et al., 2009; Humphries et al., 2000; Karaarslan et al., 2010; Kemmler et al., 2004; Kerr et al., 1996; Liu- Ambrose, Khan, Eng, Heinonen & Mckay, 2004; Maddalozzo et al., 2000; Nichols et al., 1995; Pruitt et al., 1995; Taaffe et al., 1996; Vincent & Braith et al., 2001).

Our first investigation was the first to examine the dose-response effect of 32 weeks of elastic resistance training on bone health (aBMD, BTMs and fracture risk) in older women. The training programs varied by intensity (moderate vs high) and utilized site-specific exercises to apply mechanical loads to the skeleton. The high- and moderate-intensity programs were designed to produce similar total workloads in the subjects. In contrast with previous studies (Beavers, Ambrosius et al., 2017; Bemben & Bemben, 2010; Bilek et al., 2016; Borba-pinheiro et al., 2016; Candow et al., 2019), we directly compared the effects of both intensities on the bone's adaptations to resistance exercise. The results indicated that regional BMD can be increased via supervised high- and moderate-intensity resistance training in 32 weeks, even in healthy older women, with both intensities being effective at improving bone health. The results also showed that both high and moderate intensity can positively change the biochemical indices of bone turnover and also reduce the probability risk of osteoporotic and hip fracture in the next 10 years. However, no significant differences were detected between the training groups for the change in the proximal femur areas or lumbar spine aBMD and BTMs, although they were found in fracture risk.

A limited number of studies in older adults have been designed to examine whether the training intensity in a resistance training program can impact the aBMD of the lumbar spine or proximal femur, with disparate findings reported (Bembem et al., 2000; Bemben & Bemben, 2010; Bocalini et al., 2009; Humphries et al., 2000; Karaarslan et al., 2010; Kemmler et al., 2004; Kerr et al., 1996; Liu- Ambrose, Khan, Eng, Janssen et al., 2004; Maddalozzo & Snow, 2000; Nichols et al., 1995; Pruitt et al., 1995; Taaffe et al., 1996; Vincent & Braith et al., 2001).

Our findings agree that no significant differences are found between the training intensities applied regarding their effects on aBMD (Bemben et al., 2000; Bemben & Bemben, 2010; Maddalozzo et al., 2000; Pruitt et al., 1995). For example, after 12 months, Maddalozzo and Snow (2000) reported that both moderate- (40–60% 1RM) and high-intensity (70–90% 1RM) resistance exercise protocols significantly increased trochanter aBMD in older men, but not in women, although the aBMD of the lumbar spine was only increased in the high-intensity group, a possible site-specific intensity effect (Maddalozzo & Snow, 2000). Pruit et al. (1995) examined the effects of 12 months of high-intensity (80% of 1RM, 3 sets) vs low-intensity (40% 1RM) resistance exercise, 3 days a week, on the lumbar spine, total hip, femoral neck, and Ward's triangle in 26 women between the ages of 65 and 79. Both high and low intensity improved the aBMD of the aforementioned sites without significant differences between intensities and with increases similar to our studies (high intensity: lumbar spine: + 0.70%, total hip: + 0.80%, femoral neck: -0.20%, Ward's triangle: +5.20%; low intensity: lumbar spine: + 0.50%, total hip: + 1.0%, femoral neck: + 1.80%, and Ward's triangle: + 7.20%). However, these improvements were not significant. The authors attributed the lack of significant aBMD changes to the fact that the subjects had normal BMD values before study participation.

Nevertheless, along with the higher basal values of the subjects, another possible reason our study found significant differences achieving similar absolute and relative improvements on aBMD in the same areas – and Pruit's study did not – was their small sample size with only 8, 7 and 11 subjects in the high, low and control groups, respectively. Additionally, Bemben and colleagues studied several times the effects of the training intensities on the aBMD by applying different resistance training programs. Firstly, Bemben et al. (2000) studied bone response to high-load (80% 1RM, 8 repetitions) or high-repetition (40% 1RM, 16 repetitions) training protocols, 3 days a week for 6 months in 25 estrogen-deficient postmenopausal women (mean + SD, 51.4 + 5.5 yrs). Authors found no group differences in absolute change or in percent change from pre- to post-training for any BMD site after 6 months, but they also did not find significant differences by time in any group at any skeletal site. In this case, the initial levels of aBMD were also higher than in our study. Additionally, the number of sets per exercise and the number of exercises were also lower than in our study.

However, 10 years later, Bemben and colleagues (Bemben & Bemben, 2010) again found no significant differences between training intensities (high intensity: 80% 1RM; low intensity: 40% 1RM) in the lumbar spine, total hip, trochanter and femoral neck after 40 weeks of resistance training in older adults, with around 60% of the sample being classified with normal BMD. On this occasion, the authors found significand improvements in the lumbar spine, trochanter, and total hip with low and high intensities and performing the training program 2 or 3 days a week, but not at femoral neck. The improvements ranged between 0.4% and 1.5%, percentages similar to those achieved in our study. Discrepancies between studies regarding the significant improvements achieved in the aBMD in some but not in others are not clear, but they may be related to factors such as the initial aBMD values

of the sample, the length of the training program, the number and type of exercises involved, and the total volume performed.

In general, our outcomes in the first study align with the findings from the reviews and meta-analyses of controlled trials, which indicate that the majority of resistance training studies seem to show beneficial effects to BMD during aging, having potentially modest beneficial effects for reducing postmenopausal bone loss at the femoral neck and lumbar spine regions (Benedetti et al., 2018; Bonaiuti et al., 2002; Gómez-Cabello et al., 2012; Guadalupe-Grau et al., 2009; Howe , Shea et al., 2011;Kelley, 1998; Kim et al 2016; Marques et al., 2012; Martyn-St James & Carroll, 2006; Mcmillan et al., 2017; Nordstrom & Hogstrom 2011; Sañudo et al., 2017; Shojaa et al., 2020; Souza et al., 2020; Rutherford, 1999;; Wallace et al., 2000; Xu et al., 2016; Zehnacker et al., 2007; Zhao et al., 2015; Zhao, Zhang & Zhang, 2017). Particularly, our results concur with two recent meta-analyses published on this topic. Souza and colleagues (Souza et al., 2020) demonstrated that both low-to-moderate (< 70 of 1RM) and high-load (≥ 70 of 1RM) resistance training protocols seem to be effective, providing similar results in femoral neck (WMD: 0.00 g/cm²; 95% CI = -0.01 to 0.01; p = 0.63; I^2 = 47%) and lumbar spine (MD: 0.01 g/cm²; 95% CI, -0.00 to 0.02; p = 0.12; I^2 = 59%) BMD in older people, with no significant differences between both intensities.

Additionally, Shojaa and colleagues (Shojaa et al., 2020) examined the effects of dynamic resistance exercise on BMD in postmenopausal women, categorizing the relative exercise intensity according to percentage of 1RM in low (< 65%), moderate (65–< 80%) and high (≥ 80%). Alongside Souza et al. (2020) and our results, the subgroup analysis did not reveal significant differences between at any of the skeletal sites analyzed: lumbar spine, femoral neck and total hip. It is important to note that, although Souza and colleagues (Souza et al., 2020) reported no significant differences between low and high intensities, they

realized that half of the included studies found superior results for high intensity in at least one measure of BMD, while no study found superior results for low-intensity resistance training. Although our study compared high intensity with moderate intensity and not low intensity, the behavior in our results followed the same pattern, with the high intensity achieving higher improvements in all the skeletal sites except the femoral neck and Ward´s triangle. In the case of short- (≤ 6 months) or moderate-term (6 to 12 months) interventions, it seems that high-intensity resistance training could provide better results than lower intensities, even in people with higher BMD values at baseline in the lumbar spine or some areas of the proximal femur. It seems that higher intensities produce more rapid results than lower intensities, maybe due to the discomfort caused by low loads performed at or near muscle failure (Fisher et al., 2017; Fisher & Steele, 2017), which might prevent reaching high efforts, thus impairing BMD adaptations, especially in a short-term intervention.

Conversely, our results from the first study contrast with previous studies that reported significantly higher benefits for high intensity than moderate or low intensity (Kerr et al., 1996; Vincent & Braith, 2002). Vincent and Braith (2002) compared the effects of a 24-week resistance training program, performed 3 days a week at 50% 1RM (1 set of 13 repetitions) or 80% 1RM (1 set of 8 repetitions) using weight machines in older men and women (60 to 83 years old). The authors found that high intensity was a sufficient stimulus to significantly increase the BMD of the femoral neck (1.96%), whereas the low-intensity program had no significant effect on BMD. Additionally, no significant differences were found for lumbar spine and whole body aBMD for high or low intensities. Comparing the results with those found in our study, the higher initial BMD values of the sample, the shorter length of the training period (8 weeks less) and the number of sets per exercise performed (1 vs 3–4) in the study of Vincent and Braith could explain the difference in the final results between studies. Similarly, Kerr et al. (1996) compared the effects of low (20 RM) and high

(8 RM) intensities in a 12-month resistance training program (3 sets, 3 days/week) on hip and forearm aBMD in estrogen-depleted postmenopausal women. They reported that training intensity was an important factor, as aBMD significantly increased by 2.4% at the ultradistal radius, 1.7% at the trochanter, and 1.5% at the intertrochanteric sites only in the high-intensity group. Moreover, the findings of the Cochrane meta-analysis by Howe and colleagues (Howe, Shea et al., 2011) suggest a positive response of femoral neck (MD: 1.03; CI 95% = 0.24 to 1.82) and spine (MD: 0.86; 95% CI = 0.58 to 1.13) BMD to high-intensity resistance training (> 60% 1RM) but not at total hip (MD: 0.11%; 95% CI = − 0.06 to –0.29), while no effects at any site were reported for low-intensity protocols (≤ 60% 1RM). However, it appears that this subgroup analysis was limited, because it only included eight clinical trials. The intensities applied in our study were both above the 70% 1RM, which could explain how both cases obtained significant improvements.

The impact of high-intensity resistance training (≥ 70% or 80% 1 RM, depending on the authors) performed alone or in combination with another exercise modality on bone adaptation has been investigated by a large number of studies in older adults and postmenopausal women (Ayalon et al., 1987; Bembem et al., 2000, 2010; Bemben & Bemben, 2010; Bilek et al., 2016; Bocalini et al., 2009; Brentano et al., 2008; Chilibeck et al., 2002, 2013, 2015; Cussler et al., 2004; Daly et al., 2005; Hartard et al., 1996; Hawkins et al., 2002; Humphries et al., 2000; Karaarslan et al., 2010; Kemmler et al., 2003, 2004; Kemmler, von Stengel, Engelke, Häberle & Kalender, 2010; Kerr et al., 1996, 2001; Kohrt et al., 1997; ; Liu- Ambrose, Khan, Eng, Janssen et al., 2004; Maddalozzo et al., 2000; Marques, Mota, Machado et al., 2011; Miliken et al., 2003; Nelson et al., 1994; Nichols et al., 1995; Pruitt et al., 1995; Rhodes et al., 2000; Ryan et al., 1998; Smidt et al., 1992; Stengel et al., 2005; Taaffe et al., 1996, 1999; Verschueren et al., 2004; Villareal et al., 2003, 2004; Vincent & Braith et al., 2001; Watson et al., 2015, 2018). Overall, the results align with our first study

since this kind of modality has been shown to have positive effects on bone health in older people, increasing or preserving bone mass at the lumbar, femoral neck and hip sites. It is important to highlight the results of the meta-analysis from Martyn-St James and Carroll (2006), which, to date, has been the only one to focus specifically on analyzing the effects of high-intensity resistance training in postmenopausal women. They found a statistically significant benefit of 0.006 g/cm^2 in lumbar spine aBMD and a nonsignificant benefit of 0.010 g/cm^2 in femoral neck aBMD. Thus, based on these results, high-intensity resistance exercise is only effective in preserving postmenopausal bone loss at the lumbar spine. However, this conclusion was based on an analysis including studies that enrolled participants receiving antiresorptive agents or HRT (14 and 11 RCTs included, respectively). When a subgroup analysis that excluded studies with participants receiving HRT was performed (11 and 17 RCTs included, respectively), the results suggested that high-intensity resistance training did not significantly affect either spine or hip aBMD.

Comparing these findings with our results in the first study, the M group obtained a significant benefit of 0.007 g/cm^2 (pre: 0.830 g/cm^2, post: 0.837 g/cm^2; Δ%: + 0.89%) in the total lumbar spine (L1-L4) and a nonsignificant improvement of 0.011 g/cm^2 (pre: 0.844 g/cm^2, post: 0.855 g/cm^2; Δ%: + 0.78%) in the L2-L4 segment. On the other hand, the HI group obtained significant increase in both areas, with an improvement of 0.010 g/cm^2 (pre: 0.874 g/cm^2, post: 0.884 g/cm^2; Δ%: + 1.12%) in total lumbar spine and a benefit of 0.009 g/cm^2 (pre: 0.904 g/cm^2, post: 0.913 g/cm^2; Δ%: + 1.03%) in the L2-L4 segment. As we can observe, both training intensities achieved higher improvements (from 0.007 to 0.011 g/cm^2) than those reported by Martyn-St James and Carroll (2006) for the lumbar spine (0.006 g/cm^2). In our study, the lack of significant differences in the M group in the L2-L4 segment – despite their improvement and the significant effects of the HI group with lower absolute changes – could be related to differences in the sample size of the groups.

Our results for the aBMD of lumbar spine support the wide body of evidence that found that resistance training performed alone is an effective method to increase or maintain the aBMD at this site in postmenopausal and older women (Benedetti et al., 2018; Bonaiuti et al., 2002, Howe, Shea et al., 2011; Martyn-St James & Carroll, 2006; Rutherford, 1999; Sañudo et al., 2017; Shojaa et al., 2020; Wallace et al., 2000; Zehnacker et al., 2007, Zhao et al., 2015), achieving significant but low-to-moderate effects (Shojaa et al., 2020). In general, lumbar spine aBMD can be increased by 1–2% following resistance training (Nikander et al., 2010). In our case, the improvements for the M group were close to the 1%, while for the HI group, there were above 1%.

Regarding the results of the aBMD at the proximal femur, the M group obtained a significant benefit of 0.011 g/cm^2 (pre: 0.667 g/cm^2, post: 0.678 g/cm^2; Δ%: + 1.57%), 0.013 g/cm^2 (pre: 0.516 g/cm^2, post: 0.529 g/cm^2; Δ%: + 2.59%), and 0.010 g/cm^2 (pre: 0.844 g/cm^2, post: 0.854 g/cm^2; Δ%: + 1.13%) in the femoral neck, Ward's triangle, and total hip, respectively. Additionally, the M group found a nonsignificant improvement of 0.005 g/cm^2 (pre: 0.665 g/cm^2, post: 0.670 g/cm^2; Δ%: + 0.73%) and 0.004 g/cm^2 (pre: 0.985 g/cm^2, post: 0.989 g/cm^2; Δ%: + 0.49%) in the trochanter and intertrochanteric areas, respectively. However, the HI group obtained significant increases in all the sites except for the intertrochanteric area, with a benefit of 0.009 g/cm^2 (pre: 0.663 g/cm^2, post: 0.672 g/cm^2; Δ%: + 1.39%), 0.009 g/cm^2 (pre: 0.644 g/cm^2, post: 0.653 g/cm^2; Δ%: + 1.38%), 0.012 g/cm^2 (pre: 0.488 g/cm^2, post: 0.500 g/cm^2; Δ%: + 2.47%), and 0.010 g/cm^2 (pre: 0.832 g/cm^2, post: 0.842 g/cm^2; Δ%: + 1.21%) for femoral neck, trochanter, Ward's triangle, and total hip, respectively. In the intertrochanteric area, the HI group achieved a nonsignificant benefit of 0.006 g/cm^2 (pre: 0.986 g/cm^2, post: 0.992 g/cm^2; Δ%: + 0.68%).

If we compare the results from Martyn-St James and Carroll (2006) in the aBMD of the femoral neck, which reported a nonsignificant improvement of 0.010 g/cm^2, we can see

that in our study, the benefits reached by both groups were similar, 0.011 g/cm^2 for moderate intensity and 0.009 g/cm^2 for high intensity, but these differences were statistically significant. Our results also contradict those reported by Marques, Mota & Carvalho (2011), who found no significant effects at femoral neck aBMD (0.023 g/cm^2; 95% CI = -0.009to 0.054; p = 0.157; Marques, Mota & Carvalho, 2011), or Rutherford (1999), Wallace et al. (2000), and Rahimi et al. (2020), who also found no significant effects after analyzing the RCTs that applied a solely resistance training program. Again, on the basis that the absolute differences are similar to other studies, the sample size and type of analysis performed might explain the differences between the previous evidence and our results.

In the rest of the areas analyzed from the proximal femur, conflicting results have been found. Some reviews and meta-analyses reported that resistance training alone or combined resistance training has a significant effect on total hip in postmenopausal and older women with or without osteopenia/osteoporosis (Cheung & Giangregorio, 2012; Shojaa et al., 2020; Zhao et al., 2015; Zhao, Zhang & Zhang, 2017; Zehnacker et al., 2007). However, other reviews and meta-analyses found no significant effect in this skeletal site after resistance training (Bonaiuti et al., 2002; Howe, Shea et al., 2011). Additionally, Kim et al. (2016) and Zhao, Zhang & Zhang (2017) showed that combined exercise improve total body and trochanter aBMD. However, Howe, Shea et al. (2011) found that resistance exercise did not improve aBMD at total body (0.55%; 95% CI = -0.51 to 1.62), Ward's triangle (-1.77%; 95% CI = -3.87 to 0.33), or trochanter (0.40%; 95% CI = -1.36 to 2.17). Additionally, Martyn-St James and Carroll (2006) also found no effect for resistance exercise on total hip aBMD (0.002 g/cm^2; 95% CI = -0.001 to 0.005; p = 0.20).

Although progressive resistance training is perhaps the most widely researched exercise modality targeting the preservation of aBMD in older adults and postmenopausal women, as we can see, there are still inconclusive results at different skeletal sites. This

heterogeneity can likely be attributed to a number of factors, such as the wide variance in exercise protocols [methods of exercise progression, frequency, intensity, numbers of sets and repetitions, modes of delivery (e.g., group or individual; at home or a gym), supervision, devices, combined exercise or resistance training along, duration of training period], study populations (inadequate samples sizes, healthy postmenopausal women with normal BMD or at risk of osteoporosis development, older adults with functional deficits, compliance of subjects), or the methods and sites of aBMD assessment applied.

As can be observed, overall, the results achieved in most of the skeletal areas in our first study have been positive, since both intensities increased significantly or at least maintained the aBMD of most of the areas. As documented in previous studies and also happened in our first study, the size of the improvement differs between the skeletal sites analyzed. Furthermore, it was not possible to significantly improve all the areas studied. In both groups, there was a small ES but significant increase in aBMD of the total lumbar spine (L_1-L_4), femoral neck, Ward's triangle, and total hip, while the HI group also achieved significant differences after the training period in the L_2-L_4 lumbar spine segment and trochanter. These areas (spine and hip) were specifically targeted in both exercise regimens. Thus, the threshold strain magnitude for osteogenesis in specific areas (trochanter and some vertebral segments) may be higher than for the rest of the skeletal zones analyzed, because moderate intensity had no the same benefit than the high intensity in these areas.

The positive effects of both exercise regimens at the spine in our first study are consistent with a number of intervention studies and meta-analyses in older women, which have reported a significant beneficial effect for resistance training, especially at high intensity, on the lumbar spine aBMD (Martyn-St James &Carroll, 2006; Nelson et al., 1994). As mentioned in the literature review, one of the major mechanisms to produce an osteogenic response at any skeletal site is via the action of muscle contraction and the forces generated at

the tendon attachment to the bone through resistance training. Because the bone adaptations are site-specific, our findings in lumbar spine aBMD could be partly explained by the selected exercises. Our exercise program was specifically designed to increase the activity of the extensor muscles of the spine and the muscles that originate from or insert on the lumbar vertebra (psoas major, quadratus lumborum, and the back extensor muscles) through exercises such as upright and incline rowing, narrow stance squat and lunge. Even standing elbow curl and hip abduction exercises suppose a higher stimulus for the spine muscles than a static standing position. Especially in older adults, the erector spinae muscles are loaded in a lengthened position excessively to counteract the advancing kyphosis of the thoracic spine and trunk inclination at old ages, reducing their moment arms and force-generating capacity and requiring greater activation to counterbalance the increased flexion moment. Thus, it is extremely important to design exercises to reduce the risk of vertebral fracture through the increase of aBMD at this RoI.

In general, greater skeletal benefits in response to progressive resistance training have been observed at the lumbar spine than at the femoral neck or total hip, which could be attributed to the fact that resistance exercises may not produce enough strain across the proximal femur to elicit a positive skeletal response (Pellikaan et al., 2018) due to the high level of stress that this site suffers from everyday activities (e.g., weight-bearing loads in one-legged standing situations such as walking result in high tension of the abductor muscles and high stresses, especially at the femoral neck region) (Shojaa et al., 2020). However, the results of our first study showed similar improvements between lumbar spine and most of the RoI of the proximal femur analyzed (femoral neck, trochanter, Ward's triangle, and total hip), all with improvements around 0.010 g/cm^2 ($\Delta\%$: ~ +1%). The positive effect observed in these parameters is probably related, at least partially, with the inclusion of exercises that involve hip extensor muscles (gluteus maximus, semimebranous, semitendinous, and biceps

femoris long head) such as the narrow stance squat and lunge, which are especially effective for increasing the bone activity of the femoral neck; hip abductor (gluteus medius and minimus) and adductor muscles such as the standing hip abduction, which are particularly effective for the trochanteric area due to the insertions of the muscles involved in this movement; hip flexor (iliopsoas) such as the narrow stance squat, lunge, and the multidirectional aerobic and coordination exercises performed at the active pauses, which are more effective for the lesser trochanter; and finally exercises that involve both the hip adductor and hip extensor muscles, such as the narrow stance squat, lunge, and standing hip abduction to increase the activity on the Ward's triangle RoI (Daly, Dalla Via et al., 2019; Dali Gianoudis, 2019; Kelley et al., 2001; Kerr et al. 1996; Lang et al., 2014; Martelli et al., 2017).

However, it is difficult to quantify exactly the bone response in front of different exercises because DXA examinations may not provide an accurate representation of highly localized femoral neck changes and also because the different muscles normally active during an activity may induce different, spatially heterogeneous mechanical stimuli for bone tissue adaptation (Lang et al., 2014). Additionally, is not easy to measure bone strain in vivo (Martelli et al., 2014). Is important to note that although it is widely thought that in a single individual, there exists a single mechanostat threshold, this view is flawed, as different bones require a specific strain magnitude to maintain bone mass. Therefore, different bones and bone tissues (cortical vs trabecular) respond differently to decreases or increases in loading depending on the sensibility of the mechanostat (Pivonka, 2018).

This phenomenon is clearly reflected in our study, as the response in each analyzed site was different. What seems clear is that the MES loading threshold is different for each RoI. This notion of a variable MES threshold is supported by the results of a study by Hsieh, Robling et al. (2001), which showed that the strain threshold for osteogenesis was variable at

different bone sites. The proximal femur mechanoresponse is variable and the distribution of strain varied across the proximal femur for different exercises, leading to different bone adaptations, ranging from no response to a significant increase in bone mass (Bailey & Brooke-Wavell, 2010; Guadalupe-Grau et al., 2009; Kohrt et al., 1997; Lang et al., 2014). It seems that some areas have a lower threshold level for adaptation while others need greater or different stimuli to produce bone adaptations. It is likely that our loading program generated enough magnitude stresses and strains at the total lumbar spine and at the femoral neck, trochanter, Ward's triangle and total hip (mostly in the high-intensity group), and it is possible that there is a higher threshold at the intertrochanteric site, which may have contributed to the lack of significant aBMD changes in this RoI in our first study. Thus, the exercise program planned did not provide sufficient stimulus to induce an osteogenic response at this site.

Especially interesting are the results obtained in the femoral neck, as it is a site that does not have muscle attachments and is closely related to hip fracture. Additionally, the area along with the lumbar spine is used for the classification of osteoporosis condition. However, the designed exercise program generated the necessary stimulus to increase the aBMD at this key site. Considering the length of our study along with the use of a feasible, safe, acceptable, and cost-effective training equipment such as elastic bands, the results obtained not only in the femoral neck if not in the lumbar spine and most of the RoI of the proximal femur by the moderate- and, especially, the high-intensity group are particularly relevant. Interestingly, the bone loss in the C group was around 0.6% in the lumbar spine and 0.3% in the proximal femur areas. These data are in accordance with those provided by previous studies, which found a bone loss of between 0.2% and 0.8% per year (Dennison et al., 1999; Jones et al., 1994; Nguyen, Center et al., 2007).

In postmenopausal and older women, there is an increase in bone turnover and a high rate of loss of trabecular bone, particularly in the vertebrae, due to estrogen deficiency after menopause. In fact, after menopause, bone resorption increases by 90%, whereas bone formation also increases, but only by 45%, as assessed by the markers of bone resorption and formation (Garnero et al., 1996). Lower circulating levels of serum 17β-estradiol, primarily in the early years after menopause (decrease by 85–90% from the mean premenopausal level; Khosla et al., 1997), are related to the loss of the estrogen-mediated inhibition of bone resorption without a fully compensatory increase in bone formation (Riggs et al., 1998). Therefore, one of the main objectives of the first study was to analyze the effects of the elastic resistance programs on a series of BMTs of bone formation and resorption in the population with higher rates of bone turnover: the elderly women. In an attempt to examine the biochemical alterations underlying aBMD changes with resistance training, several serum markers of bone metabolism were measured. In fact, P1NP and β-CTX biomarkers – which are the reference BTMs for the current European guidance for the diagnosis and management of osteoporosis in postmenopausal women (Kanis et al., 2013) and for the consensus statement on the use of BTMs in the Asia-Pacific region, published in 2019 (Wu et al., 2019) – were analyzed together with bALP in the first study.

One of the main advantages of the BMTs is that they are noninvasive and can detect changes in bone status earlier than DXA, because they have the capability to detect changes in bone turnover rates after 3–6 months (approximately the length of the bone remodeling cycle of cortical and trabecular bone, respectively) of the therapy applied (therapies as physical exercise, antiresorptive or anabolic drugs), and in some cases, after just 2 weeks (Delmas et al., 2006; De Papp et al 2007; Garnero et al., 1994; Kalaiselvi et al., 2013; Park et al., 2019; Pivonka, 2018; Shetty et al., 2016). Thus, we decided to measure them not only at

the end of the program but also at 16 weeks to observe if relevant changes were already taking place at the cellular level in this period of time.

Our results revealed that after 16 weeks of resistance training, both training intensities were effective in improving bone health, achieving significant increases in at least one formation marker (P1NP or bALP) and a significant decrease in the bone resorption marker (β-CTx). In these first 4 months, the high intensity seems to be more effective than moderate intensity in the bALP and β-CTx, while for the P1NP, the changes were greater in the M group. In fact, only the HI group found significant differences in the bone formation marker of bALP, with significant differences in this biomarker between the training groups. Furthermore, our results obtained at the end of the training program, after 8 months – with significant positive changes in all the bone formation and resorption biomarkers for both groups – support those found in the aBMD of the RoI analyzed by DXA. At 32 weeks of training, the HI group reached higher improvements in the P1NP than M group. It seems that the increase in this biomarker occurs later in response to high intensity than bALP and β-CTx, where the percentage of increment were higher in the first 4 months than in the later 4. Conversely, the response of the biomarker bALP to moderate intensity occurred to a greater extent in the second 4 months, while high intensity produces similar responses in the first 16 weeks (+ 4.68%) than in the second 16 weeks (+ 5.27%).

Our findings support the hypotheses that the mechanical load and strain produced by the resistance training at moderate-high and high intensities may induce positive results in the bone remodeling cycle by increasing the bone formation biomarkers and decreasing the bone resorption biomarkers. To date, only a few studies have compared the effects of different training intensities on the BTMs in the same RCT in elderly populations (Bemben et al., 2000; Karaarslan et al., 2010; Pruitt et al., 1995; Vincent & Brait 2002). However, their results are contradictory. Benben et al. (2000) examined the response of a 6-month resistance

training program involving high (80% 1 RM, 8 reps) and low (40% 1RM, 16 reps) intensity on OC and β-CTx in early postmenopausal women. After 6 months of training, no changes in BMD at the spine and hip or β-CTx levels were seen in any group. Nevertheless, there was a trend (p = 0.008) in both intensity groups for increasing OC levels [7.0 ± 0.2 ng/ml to 9.0 ± 0.2 ng/ml in the high-intensity group (n = 10); 5.0 ± 3.0 ng/ml to 6.0 ± 0.1 ng/ml in the low-intensity group (n = 7)].

Similar to Bemben et al. (2000), Vincent and Braith (2002) investigated the aBMD, OC, BAP, and PYD responses to 6 months of resistance training at high intensity (80% 1 RM, 8 reps) or low intensity (50% 1RM, 13 reps) in men and women over 60 years of age. At the end of the study, only the high-intensity group significantly increased aBMD at the femoral neck (1.96%). Additionally, the results showed significant increases in OC in both groups (low-intensity group: 25.1%; high-intensity group: 39.0%) with only the high-intensity group significantly increasing the BAP (7.1%) and BAP/PYD ratio, which indicates that the formation rate of bone is dominating the resorption and could result in increased BMD over time. In line with the results reported by Vincent regarding BAP, our study confirms that bALP and BAP seems to be more receptive to high intensity than moderate intensity. The results of these two articles are similar to those found in our study, although the improvements showed in our study are higher, especially in the bone resorption biomarker. Most likely, the longer duration of our study, along with the larger sample size and greater volume and intensity of training, favored the results obtained in our first study. Conversely, some authors did not find significant improvements in any BTMs after applying a resistance training program. For example, Pruit et al. (1995) found no significant changes in serum OC after 12 months of high- and low-intensity resistance training.

In an attempt to shed light on how the biochemical markers relate to each other and how they may serve as indicators of possible anabolism or catabolism, we calculated ratio

scores of bALP to β-CTx. Since bALP is an anabolic marker, and β-CTx is a catabolic marker, an increase in the bALP/ β-CTx ratio could indicate a state of bone turnover favoring increased bone formation. We observed significant increases in this ratio in both training groups at 16 and 32 weeks. These changes appear to be in accordance with the aBMD changes we observed.

Additionally, some studies have analyzed only the high-intensity resistance training effects in older adults and postmenopausal women (Bemben et al., 2010; Hawkins et al., 2002; Humphries et al., 2000; Huovinen et al., 2016; Kemmler et al., 2004; Marques et al., 2013; Nelson et al., 1994; Ryan et al., 1998). Nelson et al. (1994) studied the effects of a 12-month high-intensity resistance training (80% 1 RM, 3 sets x 8 reps) intervention, 2 days a week, in 39 postmenopausal women. Upon completion of the study, lumbar spine and femoral neck aBMD increased 1.0% and 0.9%, respectively, with no changes in the control group. The OC in the resistance training group increased significantly at 14%,d while the OC levels of the controls decreased by 5%. Conversely, Hawkins et al. (2002) examine the effects of a 4-month resistance training program performed at 70–90% 1RM 3 days a week in postmenopausal women. The subjects performed 3 sets of 9 resistance exercises. The results showed significant increases in aBMD at the trochanter and total hip; however, there were no changes in OC and urinary β-CTX. It is important to note that, to date, there are no studies that have analyzed the effects of different training intensities on the P1NP formation biomarker in older women, although it is the reference biomarker for bone formation. Only OC, BALP, and β-CTX were usually analyzed. It is also remarkable the small number of studies that measured the PINP after applying resistance training protocol in postmenopausal women or older adults (Beavers et al., 2018; Huovinen et al., 2016; Judge et al., 2005). For example, Huovinen et al. (2016) found a significant increase in OC but not in P1NP and β-CTX after 16 weeks of resistance training performed 3 days a week in 37 elderly women

(mean age 71.9 ± 3.1 years). Most of the exercise-based studies on bone metabolism were short term, lasting commonly 16 weeks or less, as bone marker responses to training are more rapid than aBMD responses. The length of our first study could be decisive in the results finally obtained, although at 16 weeks, our subjects also achieved significant improvements in most of the BTMs analyzed. Thus, adequate power achieved by a higher sample size coupled with resistance training design in terms of training principles and load applied could explain our findings.

It is important to note that BTMs are defined as nonspecific biomarkers of bone because they provide information of the whole body skeletal turnover process as opposed to site-specific information on a particular bone region, as other measurements provided (Pivonka 2018). Moreover, BTMs' thresholds to prevent bone loss in menopausal and elderly subjects have not yet been defined, as the usefulness of BTMs in this sense still debatable. Thus, BTMs are not more widely used in clinical practice due to the wide variation of the reference values and the lack of consensus on normal reference intervals (Cho et al., 2020; Hu et al., 2013; Rathnayake et al., 2020), particularly for postmenopausal and elderly population, where the reports of the optimal BTM thresholds to date are controversial (Cho et al., 2020; Fisher et al., 2018; Hu et al., 2013; Rathnayake et al., 2020).

Currently, only one study reported RIs for serum β-CTx and PINP concentrations in Spanish postmenopausal women. This study included 1,080 postmenopausal Spanish women aged 44–93 years (63 ± 9) and reported RIs of 0.112–1.018 ng/mL for serum β-CTx and 19–100 ng/mL for serum PINP (Martinez et al., 2009). More specifically, the authors found that the mean value for the β-CTx for the entire sample was 0.387 ng/ml (63 ± 9 age range), while, for 75-year-old individuals, it was 0.353 ng/ml, and for those older 80 years, 0.435 ng/ml. Our entire sample in the first study showed values that are located in the RIs reported by Martinez et al. (2009), which demonstrate that the sample analyzed is representative of the

target population. The baseline values of all the groups were slightly lower than the mean value reported for the β-CTx (M: 312.22 ng/ml; HI: 294.20 ng/ml; C: 348.65) but closer to those reported for the individuals of 75 years. It is reasonable considering that the mean age of the sample is close to 70 years (69.93 ± 6.27). Regarding the P1NP values, Martinez et al. (2009) also reported the mean values for the entire sample at 47.7 ng/ml for individuals with normal aBMD and 50.5 ng/ml for subjects with osteoporosis. In our first study, the entire sample again is representative of healthy elderly women, as the values are located in the RIs reported by Martinez et al. (2009). The baseline values of all the groups were also slightly lower than the mean values reported for individuals with or without osteoporosis (M: 35.28 ng/ml; HI: 34.75 ng/ml; C: 40.62). No RIs for bALP have been found for postmenopausal or elderly Spanish women. It is important to note that one of the greatest challenges for the adoption of BTMs within the clinical setting is their potentially high variability, especially for the bone resorption biomarkers. For this reason, to avoid or at least reduce the pre-analytical variability, the blood and urine samples were collected at the same time of the day (morning) and in the fasting state (after the overnight fast) for their optimal clinical use.

Regarding the fracture risk, the use of exercise as a possible prevention strategy for the prevention of fractures in elderly people has previously been hypothesized. However, the results have been discordant, depending on the intensity, type, and duration of exercise and the participants' characteristics. In our first study, we detected a significant reduction in the 10-year probability of a major osteoporotic fracture (spine, forearm, hip, or shoulder) or hip fracture in both training groups, with significant differences between groups, with the high intensity the most effective strategy to reduce the fracture risk in older women. Comparing the baseline 10-year probability values of a major osteoporotic fracture of the sample of the first study with those reported by Hernlund et al. (2013) in a sample of women with previous fracture from the countries with more elderly population in Europe (Spain, Italy, Germany,

France), we can observe that the values are similar due to the 10-year probability (%) of a major osteoporotic fracture in women in Spain is 9%, 13%, 18%, and 24% for women aged 67, 72, 77, and 82 years, respectively. In our study, the mean percentage is 10%.

From a clinical perspective, a decrease of 0.110 g/cm^2 in femoral neck aBMD in older women was associated with a 2.6-fold increase in relative risk for hip fracture (Cummings et al., 1993). Additionally, prospective studies have indicated that a decrease of one SD in the T-score represents a 10% to 12% decrease in BMD, and the risk for fracture increases by a factor of 1.5 to 3.0 for each SD decrease. For example, at the hip, the fracture risk increases 2.6-fold for each SD decrease in age-adjusted BMD at hip (Cummings et al., 2006; Kanis & Gluer, 2000; Marshall et al., 1996), while the risk for spine fracture increases 2.3-fold for each SD decrease in age-adjusted BMD at lumbar spine (Kanis & Gluer, 2000). Additionally, the T-score BMD value of total hip can predict the risk to suffer any fracture, with an increase of 1.6-fold for each SD decrease at the hip (Bonnick et al., 2010). In our first study, the improvements of the T-score values in the lumbar spine, femoral neck, and hip in both groups ranged between 0.06 to 0.10 SD.

The results obtained are highly relevant, because the risk of hip fracture has been shown to increase exponentially with age, mostly above age 70, and especially in women, who are two times more likely than men to fracture their hips after age 50 (Joseph et al., 1988). Additionally, the vast majority of major osteoporotic fractures occur in elderly women (Hernlund et al., 2013). It is estimated that a 50-year-old white woman has a 50% lifetime risk of any osteoporotic fracture and 15–20% risk of hip fracture (Black, & Rosen, 2016), about twice as high a risk of sustaining any fracture than men (Hernlund et al., 2013), although there are variations between different fracture sites (x 5 higher risk at forearm and x 2 higher risk at spine than men). Indeed, these kinds of fractures, especially in the hip, have serious and devastating effects in terms of morbidity, disability, and mortality (Melton &

Cooper, 2001), as up to 20–25% of patients die in the first year following a hip fracture (Harvey et al., 2010). But even if the person survives, 50% have some long-term loss of mobility, which can finally result in a dependent living situation with a poor quality of life and a decrease in the healthspan (Black, & Rosen, 2016). Therefore, and considering the results obtained in the first study, it seems that a resistance training program performed with elastic resistance at moderate or high intensities represents a relevant strategy to reduce the 10-year risk of hip and major osteoporotic fracture in older women.

It is important to highlight that low BMD (osteoporotic and osteopenic conditions) alone accounts for a maximum 44% of the fracture risk (Stone et al., 2003). Thus, although the gold standard method DXA has been the most widely used clinical tool to assess bone strength by measuring BMD, it only provides partial information about bone strength because it does not capture the other main component of bone strength: bone quality (Bouxsein, 2003; Burr, 2004). In fact, though aBMD is a good predictor of population fracture risk (Kanis et al., 2008), an osteoporosis diagnosis based on bone density alone seems to miss a large proportion of individuals with low bone strength, and as example, up to 80% of all low-trauma fractures occur in individuals who are not osteoporotic but have normal or reduced BMD (osteopenia) (Jarvinen et al., 1999; Jarvinen et al., 2005; Sievanen, 2000), reaching 50% only in women (Nguyen, Eisman et al., 2007). In relation, it is important to note that although the bone responses to resistance training were significant in most of the parameters, the magnitudes of the ES were trivial or small in most of them However, exercise interventions may also cause changes in other bone strength parameters, such as bone geometry, not measured by DXA, which translate to large gains in bone strength. The use of sophisticated techniques such as quantitative CT or high-resolution MRI would provide more information about bone geometry changes and volumetric BMD.

Finally, although the exact mechanisms by which the resistance training protocols conducted in the first study lead to bone health improvement are not fully understood, we can speculate on several possibilities. There are several factors that may account for the beneficial effect on bone health in older women in our study. First, the attendance and compliance rates of the study sample were high; 91.4% and 82.8% of the women completed the study at 16 and 32 weeks, respectively, and exercise compliance averaged 75% at the end of the study period and 83% at the midpoint. In this context, Bemben and Bemben (2010) did not observe frequency-induced differences (2 vs 3 sessions per week) in BMD in older adults after applied high-intensity resistance training for 9 months, and Shoja et al. (2020) arrived at the same conclusion in their meta-analysis. It is important consider that the authors analyzed the net training frequency, which could be one of the reasons for their results because in the RCTs, authors usually reported general frequency but lower rates of compliance for the participants, producing a decrease in the "real" or net exercise frequency. Thus, the "real" or net exercise frequency in our first study was close to the theoretical compliance, and most of the subjects performed at least three-quarters of the training sessions. The ITT may confound the results due to underestimating the participants that exercised less than required. However, we found similar findings from the PPA. Second, the significant changes in lean mass and muscle strength reported by both groups suggest that it can be precursors to the improvement of aBMD and BTMs, as reported previously (Beverly et al., 1989; Dalsky et al., 1988).

Third, the magnitude of the weight loss was small and nonsignificant in the case of the M group, and no loss of total body weight was registered in the HI group. Greater weight loss has been shown to be related with greater bone loss (Jensen et al., 1994; Ramsdale & Bassey, 1994; Van Loan et al., 1998). In the M group, the significant loss of fat mass was compensated with the gains in fat-free mass. Several mechanisms have been proposed to explain the loss in aBMD due to weight loss. It seems that a reduction in body weight leads to

a decline in the mechanical loads imparted to the skeleton, increasing the bone remodeling and, subsequently, bone loss (Jensen et al., 1994; Ricci et al., 1998; Salamone et al., 1999).

Four, the training program was designed to incorporate the key loading characteristics shown to be osteogenic in animal models and human studies. As such, the strength training exercises were dynamic, not static. The load mobilized induced moderate- to high-magnitude strains, as the intensity in both group was above the 70% 1RM. The load was applied in short bouts separated by periods of rest and during a moderate-long training period. The exercises involved the most relevant muscles in the most common skeletal fracture sites or with a higher BMD loss rate, such as the hips and spine (site-specific exercises). Furthermore, the load was unusual, not customary, s the resistance training was progressive in terms of loads and the exercises included in the active rest (multidirectional weight-bearing exercises). All these characteristics or principles of mechanical bone adaptation to exercise were considered when the training programs were designed with the objective to prevent bone loss. As we can see in the results of different reviews and meta-analyses mentioned above, not all doses or types of exercise training are equally effective for eliciting a positive bone response, because the application of the osteogenic exercises principles obtained from animal studies to human beings is not a trivial task, and sometimes the principles were not correctly applied or many confounding variables affected the results.

Five, the exercise program was designed not only considering the key osteogenic rules, but we also considered the basic training principles to improve bone health. The principle of specificity (related with the site-specific and type of strain characteristic of bone loading) and the principle of progressive overload (related with the bone loading characteristics of magnitude, rate, frequency, duration, rest periods, and strain distribution). The exercise program in our study was designed to be progressive, which is important because the adaptive skeletal response to loading only occurs when a given load (strain)

exceeds a certain threshold, the minimum effective strain. Once bone adapts to this given level of strain, progressively greater loads are required to stimulate further bone adaptation. We designed a periodized exercise program where the perceived exertion, the number of sets, the rest period, and the load were progressively changing, becoming more challenging to gradually overload the musculoskeletal system. Importantly, both training resistance training programs were well tolerated by the women, as no major injuries or adverse events were associated with the training programs.

It is also necessary to consider another possible factor that could explain partially our results in the first study – the principle of initial values, which inform that the greatest changes in BMD in response to exercise loading will usually occur in the individuals with the lowest level of BMD at the beginning of the training program. In this case, the prevalence rate of low BMD (osteopenia or osteoporosis) in the entire sample was 77.41% (72 of 93 subjects) and by groups as follows: 76.92% in HI (30 of 39 subjects), 80.64% in M (25 of 31 subjects), and 73.91% in C group (17 of 23 subjects). The higher prevalence of subjects with low BMD compared to subjects with normal BMD has likely favored our findings because bone tissue with less aBMD is more receptive to the stimuli – in this case, exercise stimulus – than bone tissue with higher aBMD. In fact, if we observe the T-score of the RoI analyzed, all the groups presented osteopenic values in the total lumbar spine, L2-L4 lumbar spine segment, femoral neck, and Ward's triangle, the areas with the highest rates of improvement, while in the trochanter, intertrochanteric area, and in total, the subjects showed values corresponding with normal BMD, showing particularly in trochanter and intertrochanteric areas the lowest improvements. Therefore, we can confirm that the behavior based in the principle of the initial values happened in our first study. Additionally, the average age of the overall sample was close to 70 years, which means that it is older than other study groups

with a higher proportion of peri-menopausal or postmenopausal women, another possible factor that could indirectly explain our findings.

Additionally, the bone adaptive response also depends on other systemic factors, such as the levels of vitamin D. Vitamin D is recognized as an important component that is essential in the physiologic regulation of calcium and phosphorus, because it stimulates their intestinal absorption, which enables normal mineralization of the bone (Heaney, 2009; Harrison et al., 1991; Rizzoli et al., 2014; Veldurthy et al., 2016). The overall vitamin D status in the first study was assessed through the specific form 25OHD, considered the best biomarker to assess vitamin D status (Agostini et al., 2018). While the level of dietary 25OHD necessary to optimize BMD in the presence of exercise is not known, the mean baseline 25-OHD levels of the women in our study ranged from 21.52 ng/ml (C group) to 27.30 mg/day (HI group) a day. Although the optimal 25OHD level still remains controversial, according to the current indications of plasma 25OHD levels from the AACE and US Endocrine Society, all the groups in the first study showed levels of insufficiency (20-30 ng/ml). Based on the US Institute of Medicine classification, all the groups presented adequate levels of concentrations of 25OHD (above 20 ng/ml) (Francis et al., 2015; Ross et al., 2011). Permanent vitamin D deficiency is associated with increased bone turnover and bone loss due to a decrease in intestinal calcium absorption, which lowers serum calcium and consequently leads to increased PTH (Dobnig et al., 2008; Ginde et al., 2009; Girgis et al., 2013). Thus, this situation may exacerbate osteoporosis in postmenopausal women and older adults. Since the study subjects did not show a deficiency of this vitamin and their values were framed within ranges of insufficiency or normality, there is no reason to suggest that the circulating levels of 25OHD have affected the results obtained.

Finally, we cannot forget that the type of the training devices used – the elastic bands, which provides a variable elastic resistance – may also be an important factor. Only a few

articles used this device to apply variable resistance loads with the objective to improve the bone health of postmenopausal and older women (Bravo et al., 1996; Duckham et al., 2015; Going et al., 2003; Kemmler et al., 2004, Kemmler, von Stengel, Engelke, Häberle & Kalender, 2010; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Preisinger et al., 1995; Stengel et al., 2005; Tolomio et al., 2009; Woo, 2007), finding mixed results. All of them, except the study from Woo et al. (2007), combined resistance training with other training components such as aerobic, balance, or flexibility sections. Only Woo et al. (2007) performed a basic resistance training protocol, comparing it with the effectiveness of Tai Chi on bone health in older men and women. The study consisted of 12 months of resistance training, 3 days a week, performing 1 set of 30 repetitions at an intensity "of medium strength" (no more information given) of 6 exercises (arm lifting, hip abduction, heel raise, hip flexion, hip extension, and squat). The authors found no significant changes in the lumbar spine (L2-L4) and total hip. The low volume and probably also the low intensity could explain the lack of significant changes. Regarding the BTMs, only the studies from Judge et al. (2005) and Banitalebi et al. (2020) analyzed the effect of resistance training programs performed with elastic bands, with mixed findings. Judge et al. (2005) found significant improvements in the bone resorption markers after 2 years of intervention, while no significant changes were found by Banitalebi et al. (2020) after 12 weeks. As we can see, our first study is the first to analyze an entirely strength program using elastic bands and designed following the key osteogenic loading characteristics and training principles in a population of elderly women.

Along with the intensity, to optimize bone health throughout the lifespan, it is necessary to engage in correct physical activity that produces appropriate levels of mechanical strains. Different strain levels have been reported from different types of physical activities to maintain or strengthen bone, such as walking (393–557 με), zigzag running

(1147–1226 με), sprinting (2104 με), forward jumping (1600–3450 με), or vigorous exercise (~ 2000 με), which support the mechanostat theory (Frost, 1987, 2003; Rosa et al., 2015). It is now well-accepted that bone cells modulate their responses to dynamic mechanical stimuli through not only the load magnitude but also through various parameters such as the pattern (distribution/site-specific), rate, number, and frequency of loading (Daly, Dalla Via et al., 2019; Duncan & Turner, 1995; Kunnel et al., 2002). Thus, in conjunction with resistance training, new training strategies like multi-component and power strength training have been tested regarding their effects on the bone health in older adults, although there are not many studies on the matter (Chuin et al., 2009; Cusser et al., 2003; Daly, Gianoudis et al., 2019; Deng, 2013; Duckham et al., 2015; Englund et al., 2005; Gianoudis et al., 2014; Going et al., 2003; Hamaguchi et al., 2017; Jessup et al., 2003; Karinkanta et al., 2007; Kemmler et al., 2005, 2015; Korpelainen et al., 2006; Lord et al., 1996; Marín-Cascales et al., 2017; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Metcalfe et al., 2001; Mosti et al., 2013; Papaionnau., 2003; Park et al., 2008; Preisinger et al., 1995; Snow et al., 2000; Tolomio et al., 2009; Tolomio et al., 2010; Von Stengel et al., 2005, 2007, 2009, 2011).

V.VII.II. Specific discussion of the second project

Our second investigation was the first to examine the modality-response effect of 20 weeks of a multi-component, power strength, or traditional high-intensity elastic resistance training program on bone health (aBMD, BTMs, and fracture risk) in older women. In contrast with the previous studies mentioned above, we directly compared the three modalities' effects on bone adaptations in older women. The results indicated that aBMD can be increased in the lumbar spine and the proximal femur regions via supervised power strength training in 20 weeks, even in healthy older women, and also that the aBMD can be maintained in the same skeletal sites by the multi-component and traditional high-intensity resistance training in the same training period. The results also showed that both multi-

component and power strength modalities can positively change the biochemical indices of bone turnover and that the three training strategies can reduce the probability risk of osteoporotic and hip fracture in the next 10 years. However, no significant differences were detected between the training groups for the changes in proximal femur areas or lumbar spine aBMD and BTMs, although they were found in fracture risk.

To our knowledge, this is the first RCT addressing the effects of these three different training modalities on parameters of bone health in older women. Because of the novelty of our analysis, it is difficult to make direct comparisons with the current literature, which lacks such studies. Much of the research on resistance exercise and bone health in postmenopausal and older adults has been performed using a traditional strength training strategy, which focuses primarily on strain magnitude. However, strain rate, defined as the alteration in strain magnitude per second during the acceleration or deceleration of loading (μΣ/s), corresponding to movement velocity, has been rarely studied (Maddalozzo et al., 2007), and the time under load or velocity at the different phases of the movement (concentric–isometric–eccentric) have also been rarely mentioned in the studies (Hartard et al., 1996; Maddalozzo et al., 2007; Rhodes et al., 2000).

In this sense, our results align with the only two studies previously conducted that compare the traditional resistance training with power training in older adults, in which it was reported that high-velocity resistance training was more effective than conventional strength training for preventing osteoporosis in this population (Von Stengel et al., 2005, 2007). Stengel et al. (2005) confirmed that 12 months of periodized power training, performed twice weekly (60 min each), designed such that 12 weeks of high-load training (70–90% 1 RM) were interleaved by 4–5 weeks of low-load training (50% 1 RM), was more effective in reducing bone loss in osteopenic postmenopausal women at lumbar spine and hip than traditional strength training. The only difference between groups was the movement velocity.

The training protocol specified a 4-second concentric, 4-second eccentric sequence in the strength training and concentric fast/explosive, 4-second eccentric sequence in the power training group and consisted of a 20-min warm-up (running, low-/high-impact aerobics at 70–85% maximum heart rate), followed by a jumping sequence and resistance training with machines for the following exercises: horizontal leg press, leg curls, bench press, rowing, leg adduction and abduction, abdominal flexion, back extension, lat pulley, hyperextension, leg extension, shoulder raises, and hip flexion. Additionally, both groups also performed 1 session per week of "gymnastics" (coordination, endurance, and flexibility training) and 1 session per week of home training consisting of 25 min of isometric exercises, stretching, rope skipping, and exercise with rubber bands. All subjects were supplemented with Ca and vitamin D.

The authors found that the traditional strength training group experienced a significant decrease at the total hip (-1.2%), femoral neck (-1.6%), trochanter (-0.9%), and intertrochanter area (-1.4%) and a nonsignificant change in the lumbar spine (-0.9%), whereas the power training group maintained the aBMD in all the skeletal sites [lumbar spine (+0.7%), total hip (+0%), femoral neck (-0.4%), trochanter (+0.2%), and intertrochanter (+0.1%), except at the total forearm, -1.0% (p<0.01)]. In this case, the differences between the groups were observed for aBMD at the lumbar spine and total hip. These benefits persisted at the spine after 2 years (Von Stengel et al., 2007). However, interestingly, the 2-year results were slightly different from the 1-year, showing a habituation effect in the power training group, as in the 2-year results, the authors found a decrease of 0.8% and 0.4% in the total hip and lumbar spine. This behavior supports the model by Schriefer et al. (2005), wherein bone adapts mainly to changes in its mechanical environment based on the principle of cellular accommodation. It seems that in the second year, the women had become accustomed to the new training stimulus produced by the power training and it lost its

superiority over the traditional resistance training. We can confirm, as a result of our findings, that in a short duration interventions (< 6 months), the power modality seems more osteogenic than the traditional high resistance training in all the skeletal sites analyzed. However, unlike previous studies, we did not find significant differences between both modalities in any RoI.

As we can see, the P and T groups of our study achieved greater results than those found by Von Stengel et al. (2005, 2007). Despite the shorter duration of our study, the sample population (postmenopausal vs older women), the loads used (high vs low-moderate), and the training program design parameters applied (the number of sets and repetitions and the rest between sets and exercises were not defined, but due to the high number of exercises, it is highly probable that the subjects performed 1 set of 8–15 repetitions vs 3–4 sets of 10 repetitions) are factors that have been able to influence the response between the studies.

Additionally, some studies have shown the benefits of these three training regimens individually in the elderly population. Some authors arrived at the same conclusion as Von Stengel years later, and the same one that we have reached, when analyzing the effect of power training alone on bone health in women with osteoporosis or osteopenia. The authors found that a 12-week power training program, performed twice weekly, based on high-load and low repetition (4 sets of 3–5 repetitions at 85–90% of RM) performing a hack squat exercise, was effective in preserving aBMD in postmenopausal women with osteoporosis or osteopenia by increasing the aBMD of the lumbar spine and femoral neck by 2.9% and 4.9%, respectively (Mosti et al., 2013). However, the significant increases in aBMD in this study must be interpreted with caution in light of the small sample (8 women in the strength training group completed the study) and the very short duration of the training program, which is not normally considered long enough to detect BMD change from densitometry.

However, similar results to ours in the P group have been reported in other studies. Gianoudis and colleagues (Gianoudis et al., 2014) in the Osteo-cise program reported modest but statistically significant gains in BMD at the femoral neck and lumbar spine (1.0 to 1.1 %, $p < 0.05$) after 12 months of multi-component high-velocity progressive resistance training (power training + moderate loading weight-bearing impact exercises + balance training) three times a week in older adults (men and women) without osteoporosis or low-trauma fractures. This training program was also effective for improving functional muscle power (timed stair climb), muscle strength, and dynamic balance compared to the usual care controls (Gianoudis et al., 2014), as also observed in our study, with both multi-component and power training improving the physical function parameters. Furthermore, Hamaguchi et al. (2017) found significant improvements in pelvis aBMD (+1.6%), but no significance changes in the lumbar spine after 6 weeks of low-repetition and light-load power training (8 sets of 3 repetitions with a 15-second rest between each set) in postmenopausal women with sarcopenia. The training exercise comprised five kinds of exercises (squats, front lunges, side lunges, calf raises, and toe raises).

As we can observe, there are very few intervention studies using the power strength training modality for improving bone health in older people. This may be one reason why the overall benefits of power training in this age group are still controversial. Older people are generally advised to perform weightlifting exercises with low movement velocity because it is often believed that performing an exercise movement at maximum speed results in a higher incidence of injury. However, in our study, there were no increased adverse events or lower compliance and attendance rates in the P group than in the rest of the training modality groups. Therefore, the number and grade of adverse events are not necessarily associated with movement velocity. Thus, power strength training is a safe modality and, as we can see through the results of our study, the most effective in the short term.

In contrast with some of the previously reported power training studies – which found only a maintenance, not increase, of the aBMD at most of the skeletal sites analyzed (Stengel eta l., 2005; Mosti et al., 2013) – we found a significant within-group increase in the total lumbar spine, intertrochanteric area, Wards's triangle, and total hip aBMD in the P group and relative to the control group in the total lumbar spine and total hip. One of the main reasons behind these findings is that most of the previous studies employed high-load power training (>70% 1RM) while we used a light load, equivalent to 40–60% 1RM (low-to-moderate intensity), because the current evidence indicates that maximal power output is achieved with light and moderate loads, specifically at 30–70% of 1RM (Cuoco et al., 2004; Mohamad et al., 2012; Sleivert et al., 2004). It seems that the lighter load allows subjects to move more quickly, resulting in greater power output, even though the generated force output is smaller (Mohamad et al., 2012). In fact, a previous study found that peak power during low-load (35% of 1RM) is comparable to or even larger than that of high-load (70% of 1RM) (Mohamad et al., 2012). Such a difference in peak power output may have led to the variation observed in BMD outcomes.

In this way, Snow et al. (2000) demonstrated that light-load power training with a weighted vest in older postmenopausal women was effective for increasing hip aBMD and, therefore, preventing the bone loss in this population. Additionally, Hamaguchi et al. (2017) found significant changes in pelvis aBMD after a very short training period (12 weeks) using light loads. Light-load power training may have helped our subjects generate greater power output than that generated by higher-load power training, thereby facilitating an increase in aBMD. Additionally, the rest intervals between sets and exercises may have also contributed to the increases in BMD, as the bone tissue needs to restore the mechanosensitivity of bone cells and enhance the osteogenic effects of exercise (Robling, Burr & Turner, 2001). Considered collectively, it could be possible that light-to-moderate loads were a better choice

than higher loads for preventing bone loss in older adults and postmenopausal women, achieving higher increases in the aBMD in a very short period of time (3–6 months). It is also important to note that there are no previous studies implementing a power strength program using elastic bands, and therefore, the training device is also an important factor to consider when interpreting the results obtained.

Regarding the effects on the BTMs, our results revealed that after 20 weeks, the power strength training program was an effective strategy for improving bone health by achieving significant increases in the bone formation marker (OC) and significant decreases in the bone resorption marker (β-CTX). It is necessary to highlight that the ES achieved in the bone formation biomarkers was large, even greater than the ES obtained in the bone resorption marker, which was small. Previously, only one study had examined the effects of high-velocity resistance training on BTMs in postmenopausal or older women. Mosti and colleagues (Mosti et al., 2013) found that after 12 weeks of power strength training performed 3 days a week of the squat exercise (4 sets of 3–5 repetitions at 85–90% of 1RM), no significant changes were shown in the serum levels of P1NP and β-CTx, even though the ratio of serum P1NP/CTX tended to increase ($p = 0.09$), indicating the stimulation of bone formation. In fact, the P1NP tended to increase, but not significantly, while the levels of β-CTx were similar at the end of the intervention. The short duration of the training program and the small sample size (10 and 11 subjects in the exercise and control group), along with the low volume prescribed in terms of the number of exercises performed (only one), the number of repetitions, and the high load, could explain the lack of significant changes achieved in this study.

By comparing the values of the BTMs presented by the P group with the RI values reported by (Martinez et al., 2009) for the serum β-CTx in Spanish postmenopausal women, we found that the values of our sample are located in the RIs reported by Martinez et al.

(2009), with the mean value being similar to the mean value of the Spanish population (0.360 ng/ml vs 387 ng/ml). However, the OC values are slightly lower than the reference values reported by Gossiel et al. (2014) from a sample of 343 women, 55 to 79 years old, collected from the UK, Germany, and France (17.32 ng/ml vs 24.5). Nevertheless, other authors such as Cho et al. (2020) and Iki et al. (2004) have reported reference values of 20.25 ng/ml and 8.4 ng/ml, respectively, from Korean and Japanese populations. Probably the lowest initial level in this biomarker favored a greater response to exercise, in the same way that occurs with low levels of aBMD.

Furthermore, the P group was also the group with the greatest improvements in the evaluated fracture risk parameters: the 10-year probability of a major osteoporotic fracture and the 10-year probability of a hip fracture. Although 10 risk factors are considered to calculate the fracture risk with the FRAX tool, it seems that the improvements in the aBMD of the femoral neck, despite not being significant, along with the rest of the improvements in the RoI analyzed, were associated with a higher reduction of fracture risk in this group. Comparing the baseline 10-year probability values of major osteoporotic fracture for the sample of the second study with those reported by Hernlund et al. (2013), we can observe that the values are similar because the 10-year probability (%) of a major osteoporotic fracture in women in Spain is 9%, 13%, 18%, and 24% for women aged 67, 72, 77, and 82 year, respectively, while in our study, the mean percentage is 11%. In this case, in the P group, the improvements of the T-score values in the lumbar spine, femoral neck, and hip ranged between 0.04 and 0.11 SD.

It is important to note that despite the significant responses obtained by the P group in most of the bone health parameters, the magnitudes of the ES were trivial or small in most of them, achieving only large ES in OC. As mentioned previously, DXA only provides partial information about bone strength. The use of techniques to measure bone quality could

generate a more complete understanding of the impact of exercise on bone strength. It is well-known that, along with the ground-reaction forces produced by the weight-bearing activities, the joint-reaction forces generated in the bone tissue through the action of muscle contraction is one of the major osteogenic mechanisms by which power training contributes an osteogenic response.

Several factors may account for the beneficial effect on bone health in older women achieved by this training modality in our study. Along with the light load and rest intervals previously mentioned, the most important factor is the high rate and high velocity at which the load was mobilized and, therefore, the strain was applied. It is well-known through animal studies that osteogenesis is evocated if mechanical loading is applied rapidly (Hert et al., 1971; Lanyon & Rubin, 1984; Robling, Duijvelaar et al., 2001; O'Connor et al., 1982; Rubin & Layon, 1985; Turner & Robling, 2003). Thus, strain rate plays an important role in the adaptive remodeling bone response (Hsieh & Turner, 2001), being one of the major contributors to the adaptive osteogenic response. In fact, it is demonstrated that increasing the strain rate (from -0.018 to -0.100 s-1) increases bone formation (Mosley & Lanyon, 1998; Turner et al., 1995) and also that the formation of new bone tissue is directly proportional to the rate of strain on bone tissue (Turner et al., 1995). The effect of applied high strain rates are able to stimulate the formation of both cortical and trabecular bone (Meakin et al., 2013; Meakin et al., 2014; Rubin, Turner et al., 2001; Rubin et al., 2002; Saxon et al., 2011; Sugiyama et al., 2012). Consequently, exercises that involve high-impact weight-bearing activities such as jumping or resistance training at high velocities (power training) are better for increasing bone formation, as these activities produce higher strain rates than isometric, normal velocity isotonic resistance exercise or walking. Unfortunately, high-impact exercises in some clinical circumstances – such as osteoarthritis or in frail elderly subjects – are

difficult to apply; the better alternative – strength training performed at maximal velocity in the concentric phase –was carried out in our second study.

Additionally, it is necessary to mention that shear stresses are proportional to the rate of fluid flow. Thus, as bone is loaded at a higher strain rate, fluid velocity and the consequent shear stresses increase (Burr, et al., 2002). In fact, some authors have shown that high levels of shear stress and fluid velocities are present at simulations of vigorous activity, wherein this stimulus is closely linked with the mechanosensitivity of the osteocyte (Jacobs et al, 1998; Verbruggen et al, 2013). Additionally, as with the first study, we further attributed these results in the P group to the following factors: the high compliance and attendance rate of the sample; the significant changes in lean mass, muscle strength, and muscle power, with the increase in the bone health likely attributable to structural and neural adaptations; the small loss of fat mass and total weight, despite the latter being significant; the training program design, which was composed following the key loading characteristics and training principles regarding the type of exercise (site-specific), the intensity (magnitude of the load), the volume (number of sets, repetitions, rest intervals, training days a week), and the progression of the load.

To optimize bone health throughout the lifespan, it is necessary to engage in physical activity that produces appropriate levels of mechanical strains. Different strain levels have been reported from different types of physical activities to maintain or strengthen bone, such as walking (393–557 με), zigzag running (1147–1226 με), sprinting (2104 με), forward jumping (1600–3450 με), or vigorous exercise (~ 2000 με), which support the mechanostat theory (Frost, 1987, 2003; Rosa et al., 2015). It is now well-accepted that bone cells modulate their responses to dynamic mechanical stimuli through not only the load magnitude if not also through various parameters such as the pattern (distribution/site-specific), rate, number, and

frequency of loading (Daly, Dalla Via et al., 2019; Duncan & Turner, 1995; Kunnel et al., 2002).

Based on this body of evidence, our second study tested the efficacy of a multi-component training program composed by resistance exercises, aerobic weight-bearing activities (running, skipping, stepping, hopping, dancing, and others low-to-moderate-impact aerobic activities), balance, mobility/flexibility, and coordination exercises on bone health. The findings reached in our second study agree with the body of evidence that has shown that multi-component training is an effective method for maintaining the aBMD at the lumbar spine and different proximal femur areas (Benedetti et al., 2018; De Kam et al., 2009; Giangregorio et al., 2016; Gomez-Cabello et al., 2012; Howe, Shea et al., 2011; Korpelainen et al., 2010; Martyn-St James & Carroll, 2008a; Nuti et al., 2019; Xu et al., 2016; Zhao et al., 2015), as the participants in the MT group were able to enhance, although insignificantly, the aBMD at the lumbar spine (+0.78%), femoral neck (+0.28%), trochanter (+0.34%), Ward's triangle (+3.01%), and total hip (+0.38%).

Not many authors have conducted multi-component training programs in older adults and postmenopausal women to analyze their effect on aBMD (Chuin et al., 2009; Cusser et al., 2003; Daly, Gianoudis et al., 2019; Deng, 2013; Duckham et al., 2015; Englund et al., 2005; Gianoudis et al., 2014; Going et al., 2003; Jessup et al., 2003; Karinkanta et al., 2007; Kemmler et al., 2005, 2015; Korpelainen et al., 2006; Lord et al., 1996; Marín-Cascales et al., 2017; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Metcalfe et al., 2001; Papaionnau., 2003; Park et al., 2008; Preisinger et al., 1995; Tolomio et al., 2009, 2010;Von Stengel et al., 2009, 2011). Generally, as we can also observe in our second study, the results indicated that multi-component exercise programs may help to increase or at least prevent bone mass decline with aging, especially in postmenopausal women at the trochanter, femoral neck, and lumbar spine, especially (Benedetti et al., 2018; De Kam et al., 2009; Giangregorio

et al., 2016; Gomez-Cabello et al., 2012; Howe, Shea et al., 2011; Korpelainen et al., 2010; Martyn-St James & Carroll, 2008a; Nuti et al., 2019; Xu et al., 2016; Zhao et al., 2015). They combine the effects of the resistance exercises, which provide muscular loading to bone with the effects of the weight-bearing aerobic exercise, which also provides an additional mechanical loading to the bone above gravity (Hong & Kim, 2018).

The superior effect reported in previous studies in the lumbar spine area compared with the RoI of the proximal femur after the multi-component training program was also observed in our study, with the exception of the Ward's triangle zone. We observed that the MT group obtained nonsignificant benefits in all the skeletal sites except the intertrochanteric area. The absolute changes in the lumbar spine were 0.006 g/cm^2 (pre: 0.848 g/cm^2, post: 0.854 g/cm^2; Δ%: + 0.78%) and 0.005 g/cm^2 (pre: 0.861 g/cm^2, post: 0.885 g/cm^2; Δ%: + 0.62%) for the total lumbar spine and L_2-L_4 lumbar spine segment, respectively. However, the absolute changes in the proximal femur areas were as follows: 0.002 g/cm^2 (pre: 0.684 g/cm^2, post: 0.686 g/cm^2; Δ%: + 0.28%), 0.002 g/cm^2 (pre: 0.648 g/cm^2, post: 0.650 g/cm^2; Δ%: + 0.34%), -0.002 g/cm^2 (pre: 0.986 g/cm^2, post: 0.984 g/cm^2; Δ%: - 0.20%), 0.015 g/cm^2 (pre: 0.499 g/cm^2, post: 0.514 g/cm^2; Δ%: + 3.01%), and 0.003 g/cm^2 (pre: 0.831 g/cm^2, post: 0.834 g/cm^2; Δ%: + 0.38%) for the femoral neck, trochanter, intertrochanteric area, Ward's triangle, and total hip. As we can see, if we set aside the improvement obtained in the Ward's triangle, the bone formation in the lumbar spine doubles the rest of the areas of the proximal femur.

Studies similar to ours – in terms of duration and exercise programs performed – found mixed results. Tolomio et al. (2008) demonstrated that a 20-week exercise program with strength, aerobic, and balance exercises was able to improve all bone parameters assessed by phalangeal quantitative osteosonography in osteoporotic and osteopenic postmenopausal women. Similarly, another study conducted by the same group found that an

11-monts multi-component exercise program composed of strength, aerobic, balance, and joint mobility exercises three times a week in dual-modality (on ground and in water; alternating group and home-based exercise periods) was able to improve the femoral neck T-score in the same specific population (Tolomio et al., 2010). In another 20-week program, Hourigan et al. (2008) also reported no significant alterations in BMD at the proximal femur or lumbar spine after balance and weight-bearing exercises. Similarly, Stewart et al. (2005) showed that a combined program including aerobic and resistance exercises performed three times per week for 24 weeks had no effect on aBMD among men and reduced aBMD among women. Additionally, although some studies found significant positive responses to multi-component training at the femoral neck (Kohr et al., 1997; Nelson et al., 1994; Wesh & Rutherford, 1996), others previous studies are more consistent with our results, indicating no such effect (Lord et al., 1996; Kerr et al., 2001; Uusi-Rasi et al., 2003). For example, Karikanta et al. (2017) did not find any exercise effect on aBMD of the femoral neck, and the same result was found by Villareal et al. (2004) in frail elderly subjects.

On the other hand, some investigations observed significant improvements in some of the RoI analyzed. For instance, Marques, Mota, Machado et al. (2011) showed a significant increase of aBMD at femoral the neck [0.018 ± 0.028 g/cm^2 (2.8% ± 4.6%)] with a nonsignificant trend of increased aBMD at all other sites (trochanter: +0.007 g/cm^2, intertrochanter: +0.003 g/cm^2, total hip: +0.004 g/cm^2, lumbar spine: +0.011 g/cm^2) after 8 months of multi-component training (10 min of warm-up, 15 min of weight-bearing activities, 10 min of muscular endurance, 10 min of balance training, 10 min of agility training, and 5 min of stretching), 2 days a week (60 min each session) in a similar population than ours (older women over 70 years of age) and with similar sample size (30 subjects in each group: multi-component and control). As we can observe, the results revealed by Marques, Mota, Machado et al., (2011) are slightly better than ours in all parameters,

probably due to its longer duration. However, the authors do not report the intensity and volume of the aerobic and strength components, which makes comparison between studies difficult, as these key parameters are that can alter the final result. In fact, some authors found positive effects on aBMD in multi-component training programs that used high intensities in the aerobic or strength components (Cusser et al., 2003; Jessup et al., 2003; Marques et al., 2013), while others found no improvements (Deng et al., 2013; Karikanta et al., 2007). As well, very recently, Daly, Gianoudis et al. (2019) found a significant net beneficial effect for an 18-month multi-component training program on the lumbar spine and femoral neck, with improvements of 1% and 1.1%, respectively. The exercise regimen consisted of progressive resistance, weight-bearing impact, and balance training (3 days/week) performed at community leisure centers in adults aged ≥ 60 years with osteopenia or at an increased fall risk.

Comparing the results achieved by the MT group in our study with those reported by a wide range of reviews and meta-analyses in combined training (aerobic plus strength or impact weight-bearing plus strength exercises), because there are no specific reviews or meta-analyses of multi-component training and bone health, our findings align with those that found the combination of aerobic plus resistance training to be effective for improving the aBMD at the femoral neck (Kim et al., 2016) or that nonsignificant aBMD changes at the femoral neck occur when low-impact activities and resistance exercises are applied in the same session (Marques, Mota & Carvalho, 2011; Rahimi et al., 2020). Unlike our study, some meta-analyses showed that integrating different physical activities in the same session significantly increased the femoral neck (Zhao, Zhang & Zhang, 2017) or that the combination of different types of exercise has a significant effect on aBMD at the lumbar spine, femoral neck, and trochanter (Howe, Shea et al., 2011).

Regarding the lumbar spine, a recent meta-analysis reported that progressive resistance training combined with high-impact or weight-bearing exercise significantly increased aBMD at the lumbar spine (Zhao et al., 2015). Another systematic review and meta-analysis focused on impact exercise combined with resistance exercise in postmenopausal women arrived at the same conclusion, a reduction in postmenopausal bone loss in the intervention groups for lumbar spine (0.016 g/cm^2; 95% CI = 0.005 to 0.027; p = 0.02) when compared to the controls (Martyn-St James & Carroll, 2008a). Additionally, combined exercise programs were found to significantly increase aBMD at the lumbar spine (3.22%, 95% CI = 1.80 to 4.64) when compared to a control group in the review of Howe and colleagues (Howe, Shea et al, 2011).

In a more recent systematic review and meta-analysis, combined loading also improved the lumbar spine segment (0.016 g/cm^2, 95% CI = 0.002 to 0.030; p = 0.028) (Marques, Mota & Carvalho, 2011). Furthermore, in the overview of the systematic review and meta-analysis of Xu and colleagues (Xu et al., 2016), the authors likewise advocated for the use of odd/high-impact exercise in combination with resistance exercise for the preservation of BMD levels in pre- and postmenopausal women. Bonaiuti et al. (2002), Kim et al. (2016), Zhao, Zhang & Zhang (2017) (SMD: 0.170; 95% CI = 0.027 to 0.313; p = 0.019) and Benedetti et al. (2018) also found positive effects for the combined training on lumbar spine BMD in postmenopausal and older women. In contrast, other evidence did not find positive effects or revealed negative outcomes (Chilibeck et al., 2013; Going et al., 2003; Miliken et al., 2003) after combined resistance training interventions. For example, the meta-analysis from Rahimi et al. (2020) found no significant effects on lumbar spine BMD after applying combined training (MD: 0.03; 95% CI = − 0.01 to 0.08; p = 0.13).

As we can see, the reported effects of progressive resistance training in combination with other exercise protocols in the same session (combined exercise), commonly including

weight-bearing activities, balance training, jogging, low-impact loading, high magnitude exercise, or simulated functional tasks, are heterogeneous and may result from the variation that exists in the sample size, population age, and exercise interventions. However, it seems, as in our study, that most of the evidence confirm the positive effects of the progressive resistance training whether applied in combination with other exercises at lumbar spine aBMD in postmenopausal and older women, suggesting that combined training could produce even more benefits in this region than resistance training alone (Giangregorio et al., 2016; Howe, Shea et al., 2011; Zhao et al., 2015; Zhao, Zhang & Zhang, 2017), as seen in our study.

Regarding the findings in the fracture risk parameters, the MT group showed significant improvements in the10-year probability of a major osteoporotic fracture and the 10-year probability of hip fracture parameters. However, between the three training modalities analyzed, the multi-component training regimen showed the lowest improvements, probably because the net gain of aBMD in the femoral neck was also smaller than the P and T modalities (MT: 0.002 g/cm^2, P: 0.006 g/cm^2, T: 0.004 g/cm^2). In fact, a significant difference between the MT and T groups in favor of the T group was found in the 10-year probability of a hip fracture.

Focusing on the effects of the multi-component training on BTMs, our study showed it is an effective exercise regimen, as it significantly increased the bone formation marker OC and also significantly decreased the bone resorption biomarker β-CTX. Previously, only four studies analyzed the effects of this modality on different BTMs (Bilek et al., 2016, Marques et al., 2013; Miliken et al., 2003; Villareal et al., 2008). In contrast with our findings, most of the studies did not find any significant change in BTMs. For example, Marques et al. (2013) reported no changes in OC and CTX after 32 weeks of multi-component training in healthy older men and women. However, Villareal et al. (2008) found significant increases in OC and

CTX after 6 and 12 months of multi-component training in obese older adults. Although the reasons for these contradictory results are not readily apparent, we can speculate that these findings may be related to the characteristics of the participants and/or the methodological differences in the study design (training intensity, training volume, duration of intervention, etc.). The small number of studies conducted to date and the heterogeneity of the sample population studied, as well as the training parameters applied in each study, make it difficult to draw a clear conclusion. As happened with the P group, the magnitude of the ES obtained by the MT group in most of the bone health parameters analyzed was trivial or small, with only moderate ES in OC.

Several factors may account for the beneficial effect on bone health in older women achieved by the multi-component training in our study. Along with the correct prescription of the strength component in terms of strain magnitude, volume, and the site-specific selected exercises, to achieve the gain or maintenance of bone mass in older people it is necessary to find the correct exercise prescription of all the training components that compose the multi-component training program. In this sense, one of the most important factors is the prescription of the weight-bearing activities performed at the aerobic, balance, and coordination sections due to these kinds of activities are the most bone-osteogenic exercises along with the resistance activities, and it is especially important to prescribe them properly. In this sense, the correct prescription of the weight-bearing activities in our study could be one of the most important factors for explaining the findings achieved by the MT group. In fact, the balance block was composed of dynamic balance exercises (walking on a straight line or line walking, heel-toe walking, changes in distance and directions of the walking displacement, heel and toe walking, walking backward and sideways, and heel-to-toe forwards and back) while the aerobic block participants performed stationary impact aerobic exercises (weight-bearing activities) with a small, moderate, and high impact, including the

following: stomping, stepping, marching in place, skipping, heel-drops (consists of raising the body weight onto the toes and then letting it drop to the floor, keeping the knees locked and hips extended), knee bends, small hops in place, jumps opening and closing the legs and arms at the same time, and activities with similar ground-reaction forces (Bergmann et al., 1993; Nilsson & Thorstensson, 1989). Furthermore, this block included aerobic exercises with displacements (in different combinations, directions and pace), such as forward, backward, lateral and multidirectional walking, jogging, dance, step choreographies, introducing changes of direction exercises (such as acceleration and deceleration back and forth, and sideways walking with stops and turns), changing the speed of the execution (i.e. walking as quickly as possible without running), and walking with longer steps and coordinated arms movements. The 100 impacts per session were always exceeded and the peak vertical ground-reaction forces of most of these activities reached, at minimum, 1.5 times the body weight.

These activities were designed keeping in mind that, in older women, the skeletal response to high-impact activities is less consistent than in premenopausal women, and some, but not all, trials reported positive effects (Bassey et al., 1998; Snow et al., 2000). It appears that mixed-impact loading programs including low-to-moderate impact exercises – such as walking, jogging, walking, and stair-climbing – are most effective for preserving aBMD at the femoral neck and lumbar spine when combined with resistance training rather than high-impact activities (Martyn-St James & Carroll, 2008a). In this population, intensity is important, but novel or diverse loading patterns performed in different directions (odd-impact exercises) may be particularly important for the effective stimulation of bone in older adults unable to tolerate high-impact loads (Marques, Mota & Carvalho, 2011).

Furthermore, although several meta-analyses showed that walking appears to have little or no effect on either femoral neck or lumbar spine BMD (Kelley et al., 2013a, 2013b),

it is currently well-known that it depends on the intensity, controlled via the walking speed. Fast walking (5-6 km/h), hopping, and running (5-9 km/h) result in higher compressive and tensile strains than walking at 4 km/h for the femoral neck in postmenopausal women, which was considered the minimal level to induce an osteogenic response (only for bone preservation) (Pellikaan et al., 2018). Additionally, Hatori et al. (1993) found that walking at high intensity improves the lumbar spine aBMD, while the low-intensity group showed a similar loss of bone to the controls. For these reasons, high-impact exercises were not prescribed, but a wide range of low-to-moderate impact exercises performed in numerous directions to produce different loading patters and with velocity were performed by the subjects, which could be behind the positive effects on aBMD, BMTs and fracture risk in this training group.

As an inherent mechanosensitive organ, the exercises and doses proposed for the multi-component training regimen could have produced changes in the bone cells, changing their dimensions or indirectly impacting intralacunar pressure, shear stresses, or fluid flow within the lacunar–canalicular network to stimulate bone formation. Additionally, in the present study, the three rules for bone adaptation proposed by Turner and the Beam theory were considered when designing the multi-component exercise program. Furthermore, we further attribute these results in the MT group to the following factors: the high compliance and attendance rate of the sample; the significant changes in lean mass and muscle strength, with the increase in the bone health likely attributable to structural and neural adaptations; and the training program design, which was composed following the key loading characteristics and the training principles regarding type of exercise (site-specific), intensity (magnitude of the load), volume (number of sets, repetitions, rest intervals, training days a week) and progression of the load.

It is also important to highlight that most of the multi-component training programs performed previously were conducted in frail older adults or with low bone mass, reduced physical function, or previous falls and fractures. Additionally, most of these studies were moderate to long intervention (≥ 6 months). Moreover, it is important to highlight that only five studies used elastic bands in their multi-component training programs applied to older adults (Marques, Mota, Machado et al., 2011; Marques et al., 2013; Preisinger et al., 1995; Tolomio et al., 2009; Duckham et al., 2015). But none of them used it alone, if not in combination with other training devices such as free weights or machines. Therefore, the results of our second study illuminate the field of multi-component training on bone health, since it is the first that showed positive effects on aBMD, BMTs, and fracture risk in healthy older adults after a short intervention and, importantly, by using a training device as portable and useful as elastic bands.

It has been argued that one bone remodeling cycle takes 3 to 4 months to complete the sequence of bone resorption, formation, and mineralization, and to achieve a new steady state bone mass that is measurable, a minimum of 6 to 8 months is required (Kohr et al., 1996). Therefore, it is suggested that interventions must last a minimum of 6 to 9 months (preferably 12 to 24 months) to detect any measurable physiological skeletal changes beyond the normal bone remodeling transient. However, many short-term studies and measurements made before 6 months of intervention in long-term studies have confirmed positive changes in bone tissue (Beverly et al., 1989; Dornemann et al., 1997; Lohman, Going et al., 2009; Pruitt et al., 1992). Additionally, due to the principle of cellular accommodation of the bone cells, several exercise interventions over 12 to 18 months reported the greatest changes in aBMD during the initial 5–6 months (Bassey & Ramsdale, 1994; Lohman, Going et al., 2009). Furthermore, although a longer exercise intervention would produce greater changes, it would also increase dropout rates due to participants' difficulties in managing the vacation period and continuing

to attend training sessions. At the end, the results may be influenced by a wide range of factors, not only by length of the training period, such as the frequency of the training sessions, intensity of loading, specificity of skeletal loading, hormonal status, baseline values of aBMD of the subjects, type of BMD scans performed, or whether the exercise program followed the progressive overload principle. Additionally, the use of BTMs, which can effectively detect changes within a shorter period of time (after 3 to 6 months), could be a good alternative to DXA to detect early changes in bone status. Based on this evidence, we decided to design a short-term intervention.

Particularly, the studies in postmenopausal women indicate that progressive resistance training can produce modest gains in BMD (1–3% per year) (Asikainen et al, 2004; Bonaiuti et al., 2002; Karikanta et al., 2007) or at least attenuate age-related losses in BMD at the hip and spine following resistance training programs of 16 to 104 weeks (Guadalupe-Grau et al., 2009; Kelley et al., 2012). Furthermore, some studies also showed positive effects on BTMs after training interventions that lasted less than 6 months (Fujimura et al., 1997; Hawkins et al., 2002; Lester et al., 2009; Menkes et al., 1993; Ryan et al., 1994; Vincent & Braith, 2002). These interventions are usually based on traditional resistance training protocols, but there is also one that analyzed the effects of the power strength training (Mosti et al., 2013).

In accordance with those previous studies that found positive effects after applying a traditional resistance training program for a short period, as we can observe in our study, the T group showed positive improvements in all the RoI analyzed. Focusing on the net gain, the T group achieved a significant improvement of 0.016 g/cm^2 (pre: 0.529 g/cm^2, post: 0.545 g/cm^2; Δ%: + 0.016%) in the Ward's triangle. In the rest, a nonsignificant improvements were found of 0.004 g/cm^2 (pre: 0.885 g/cm^2, post: 0.889 g/cm^2; Δ%: + 0.43%), 0.002 g/cm^2 (pre: 0.904 g/cm^2, post: 0.906 g/cm^2; Δ%: + 0.24%), 0.004 g/cm^2 (pre: 0.691 g/cm^2, post: 0.695 g/cm^2; Δ%: + 0.64), 0.000 g/cm^2 (pre: 0.656 g/cm^2, post: 0.656 g/cm^2; Δ%: + 0.09),

0.003 g/cm^2 (pre: 0.980 g/cm^2, post: 0.983 g/cm^2; Δ%: + 0.29), and 0.004 g/cm^2 (pre: 0.833 g/cm^2, post: 0.837 g/cm^2; Δ%: + 0.55) at the total lumbar spine, L_2-L_4 lumbar spine segment, femoral neck, trochanter, intertrochanteric area, and total hip. As in the first study, similar improvements were found at the lumbar spine and most of the proximal femur areas. At the same time, the Ward's triangle was again the skeletal site where the greatest changes occurred.

Comparing these changes with the values reported by the meta-analysis of Martyn-St James and Carroll (2006), who found that the high-intensity resistance training in postmenopausal women achieved a statistically significant benefit of 0.006 g/cm^2 in lumbar spine aBMD and a nonsignificant benefit of 0.010 g/cm^2 in femoral neck aBMD, our results also found a nonsignificant benefit in the femoral neck aBMD (0.004 g/cm^2) and lumbar spine (0.004 g/cm^2). As we can see, the values reached by the T group were slightly lower than those reported by Martyn-St James and Carroll (2006). Surely, with a longer duration of the study, significant differences would have appeared, as we observed in our first study. Nevertheless, our results reveal that with just 5 months of high-intensity traditional resistance training, the aBMD of the lumbar spine and proximal femur can be maintained in older women. The possible factors by which these results have been reached are the same as those listed in the first study, because the training program implemented was very similar (same intensity and similar exercises).

If we compare these data with the values reported by the P group, the subjects of this group accomplished higher improvements in all the skeletal sites analyzed. We found that the subjects of the P group obtained a significant benefit of 0.011 g/cm^2 (pre: 0.896 g/cm^2, post: 0.907 g/cm^2; Δ%: + 1.28%), 0.013 g/cm^2 (pre: 1.009 g/cm^2, post: 1.022 g/cm^2; Δ%: + 1.38%), 0.025 g/cm^2 (pre: 0.532 g/cm^2, post: 0.557 g/cm^2; Δ%: + 4.66%), and 0.009 g/cm^2 (pre: 0.858 g/cm^2, post: 0.867 g/cm^2; Δ%: + 1.03%) in the total lumbar spine,

intertrochanteric area, Ward's triangle, and total hip, respectively. The same group achieved nonsignificant improvements of 0.006 g/cm^2 (pre: 0.911 g/cm^2, post: 0.917 g/cm^2; Δ%: + 0.67%), 0.006 g/cm^2 (pre: 0.698 g/cm^2, post: 0.704 g/cm^2; Δ%: + 0.86%), and 0.001 g/cm^2 (pre: 0.684 g/cm^2, post: 0.885 g/cm^2; Δ%: + 0.01%) in the L_2-L_4 spine segment, femoral neck, and trochanter.

Regarding the fracture risk parameters, as the multi-component and power strength modalities, the T group also significantly improved the 10-year probability of a major osteoporotic fracture and the 10-year probability of a hip fracture, as the group with the greatest improvements after the P group. Additionally, the ES achieved after the adjustment by age and baseline values were moderate and small for the 10-year probability of a major osteoporotic fracture and the 10-year probability of a hip fracture parameters. Despite these ES, in the rest of the variables, the magnitude of the changes was trivial.

Focusing on the changes of the C group, the bone loss in this group was around 0.57% in the lumbar spine and 0.3% in the proximal femur areas; these values are very similar to those of the first study. Thus, these data again align with those provided by previous studies, which found a bone loss of between 0.2% and 0.8% per year (Jones et al., 1994; Dennison et al., 1999; Nguyen et al., 2007).

As previously stated, the baseline value of aBMD of the sample is a relevant factor when analyzing the effects obtained. In this case, the prevalence rate of low BMD (osteopenia or osteoporosis) in the entire sample was 71.32% (97 of 136 subjects). By groups, the prevalence rate was 73.5% in the MT group (25 of 34 subjects) and 70.58% (24 of 34 subjects) in the P, T and C groups. As in the first study, the higher prevalence of subjects with low aBMD compared to subjects with normal BMD probably favored our findings, as bone tissue with less aBMD is more receptive to the stimulus produced by

exercise. In fact, if we observe the T-score of the RoI analyzed, all the groups presented osteopenic values in the total lumbar spine, L2-L4 lumbar spine segment, femoral neck, and Ward's triangle, the areas with the highest rates of improvement, while in the trochanter and intertrochanteric area and in total hip, the subjects showed values corresponding with normal BMD, showing the lowest improvements in the trochanter and intertrochanteric areas. Therefore, we can confirm that the behavior based in the principle of the initial values also occurred in our second study. In this second study, the average age of the overall sample was close to 68 years, 2 years younger than the first study. However, the sample is still older than other study groups with a higher proportion of perimenopausal or postmenopausal women, another possible factor that could indirectly explain our findings.

Finally, a significant improvement in the second study compared to the first was the control of confounding variables, such as nutrition intake and physical activity, which can affect bone health outcomes. Nutritional variables such as protein, calcium, and vitamin D intake were recorded, as they can independently affect bone material properties (Bass et al., 2005). Our results revealed nonsignificant changes in every group in diet patterns between the baseline and post-training values. Only in the P group, after adjusting for age and baseline values, a significant decrease in the protein intake was found. In general, this lack of change emphasizes the leading exercise osteogenic potential.

The mean baseline calcium intakes of the women in our study ranged from 603.78 to 711.11 mg/day across the four groups. These levels are approximately half of what is recommended, more similar to older adults and postmenopausal women from places with less hours of natural light per day, such as Canada or the United States (Alaimo et al., 1988; Ervin et al., 2004; Statistics Canada, 2004). Most organizations (the AACE, NOF, Endocrine Society) recommend that women aged 51 years or older consume 1,200 mg of calcium per day (Ross et al., 2011), with no extra benefit from the consumption of amounts in excess of

1,500 mg/day (Bauer, 2013; Bonnick et al., 2010; Bolland et al., 2011; Moyer, 2013; Prentice et al., 2013; Reid & Bolland, 2012). The calcium deficiency showed by the subjects in our second study may have compromised the skeletal response to loading, since calcium plays an important role in the effects of exercise on bone in older adults. Findings from different studies prove that insufficient intakes of calcium can compromise the skeletal response to loading, while exceeding daily calcium requirements seems not result in greater exercise-induced skeletal gains (Lanyon et al., 1996; Prince et al., 1995). The threshold level of calcium required to optimize the osteogenic responses to exercise has been reported at least in 1,000 mg/d (Daly et al., 2014). However, more evidence is needed to support this cut-point. Therefore, based on the current evidence, it would appear that the effect of the three training modalities could have been greater than obtained if calcium intake had been within normal values.

In the past, it was reported that a high dietary protein intake may adversely affect bone health because it may result in increased urinary calcium excretion and increased acid production (calciuric effect) (Kerstetter, 1990). However, there is now evidence indicating that increased dietary protein intake has favorable effects on minimize bone loss in the elderly population, particularly when calcium intake is adequate (Darling et al., 2009; Hannan et al., 2000; Mangano et al., 2014; Rapuri et al., 2003), and also on the reduction of risk of hip fracture in both genders in patients with inadequate intake (Nuti et al., 2019). These effects of a higher protein intake on bone health can be attributed to multiple factors such as enhanced intestinal calcium absorption, suppressed PTH levels, increased IGF-1 concentrations, and improved strength and muscle mass, which may improve the osteogenic effect via increased loading on bone (Calvez et al., 2012). The recommendation for dietary protein intake in general population is 0.8 g/kg/d (Joint WHO/FAO/UNU Expert Consultation; 2007). However, the elderly population usually intakes lower levels; thus, the

European Society for Clinical Nutrition and Metabolism has proposed a daily recommended amount of 1.0–1.2 g/kg/d as optimal for a healthy older individual (Deutz et al., 2014; Volpi et al., 2013). All four groups showed baseline values of protein intake above the 0.8 g/kg/d recommended, and the three training groups also between the daily recommended values from the European Society for Clinical Nutrition and Metabolism (MT: 1.09 g/kg/d; P: 1.15 g/kg/d, T: 1.04 g/kg/d).

Based on the present results, if the purpose is to promote positive changes in aBMD and BTMs and prevent the risk fracture without dietary modifications in older women, both moderate and high-intensity elastic resistance training seems to be effective, as well as the power strength and multi-component training modalities. Furthermore, it is only necessary for a short-to-moderate period of time to achieve significant changes in these parameters. Additionally, the use of higher loads (high intensity) or light-to-moderate loads at high speed seem to promote superior effects regarding the aBMD of most of the skeletal sites analyzed, as well as BMTs and fracture risk prevention in comparison with moderate loads, high loads at normal velocity, or multi-component regimens, in older women with normal and low initial aBMD values. Additionally, these two training programs (high-intensity resistance training and power strength training) seem to be most effective when the interventions last less than 6 months (short interventions), because they achieved the best results at 16 and 20 weeks, which might be of practical importance when seeking more rapid results.

It is important to highlight that none of the studies performed reported serious adverse events like an increase of injury risk or pain related to the training programs. Therefore, both power strength training and high-intensity resistance training, despite beliefs that they produce a higher incidence of injuries, are also safe exercise modalities to enhance bone health in this population. Our results suggest that there should be no increase in pain and injury if sufficient adaptation to these training modalities is allowed. Additionally, it is very

important to promote this type of training, as individuals with osteoporosis have been shown to have diffuse and preferential type II muscle fiber atrophy, which has been related to the degree of bone loss in older women (Terracciano et al., 2013).

In the case of power strength training, considering the importance of this parameter (stain rate or fast movement velocity) to improve bone strength and the safe and easy applicability of them in older adults, more exercise studies should focus on this type of training and in their application with variable resistance, because none have used this type of load to date. Because this training program does not require high-load exercise and is, therefore, easily implementable as daily exercise, it could be an effective form of exercise for sedentary adults at risk for osteoporosis who are fearful of heavy loads and/or training that could cause fatigue.

From a practical standpoint, in view of the results obtained, the choice of the training modality and training regimen might be more related to individual and logistical aspects than training factors because all the training programs analyzed achieved positive effects on bone health status in older women.

V.VIII. RESULTS ON ANTHROPOMETRY AND BODY COMPOSITION

V.VIII.I. Project one

Changes in body composition from the ITT analysis are displayed in Table 42. Repeated-measures ANOVA showed a main effect of time on total fat mass [$F(1, 90) = 8.35$, $p < 0.005$, $\eta^2p = 0.085$, $1-\beta = 0.816$], total fat-free mass [$F(1, 90) = 32.55$, $p < 0.000$, $\eta^2p = 0.266$, $1-\beta = 1$], and total body fat percentage [$F(1, 90) = 27.22$, $p < 0.000$, $\eta^2p = 0.232$, $1-\beta = 0.999$]. Pairwise comparisons revealed significant decreases in total fat mass and total body fat percentage in the M group with small ESs, along with a significant increase in total fat-free mass within the same group (small ES). At the same time, a significant increase (trivial ES) in total fat-free mass was also found in the HI group, along with a significant decrease in total body fat percentage (small ES). No significant differences by time were found in total body mass for any group. Furthermore, no significant time × group interactions appeared after the training intervention. The ANCOVA showed a main effect of time on the same parameters with similar magnitudes of change. No significant changes were found in total body mass. However, after adjustments, the ANCOVA revealed significant group × time interactions in total fat mass [$F(2, 130) = 4.10$, $p < 0.020$, $\eta^2p = 0.085$, $1-\beta = 0.713$], total fat-free mass [$F(2, 88) = 10.58$, $p < 0.000$, $\eta^2p = 0.194$, $1-\beta = 0.987$], and total body fat percentage [$F(2, 88) = 9.75$, $p < 0.000$, $\eta^2p = 0.181$, $1-\beta = 0.980$]. The differences were found in total fat mass between M and C (small ES), and in total fat-free mass and total body fat percentage between the training groups and the C group (ESs ranged from trivial to small). The results of the PPA were similar to those from the ITT analysis, with the same changes except for a significant improvement in the HI group in terms of total body fat (after ANOVA and ANCOVA), as well as significant group × time interactions between HI and C in total body fat and between M and HI in total fat-free mass (in both cases following the ANCOVA). The results from PPA are presented in Supplementary Material E (Table E).

Table 42. *Intervention effects on body composition from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total body mass (Kg)	M	66.11	67.35 ± 10.68 (63.79–70.91)	67.15 ± 10.44 (63.63–70.68)	-0.29	0.354 (0.02)	0.403 (0.02)	M vs HI: 1.000 (0.2)	M vs HI: 0.708 (0.03)
	HI		64.89 ± 10.08 (61.72–68.07)	65.08 ± 10.09 (61.93–68.22)	0.28	0.335 (0.02)	0.389 (0.02)	M vs C: 1.000 (0.03)	M vs C: 0.284 (0.06)
	C		66.50 ± 8.75 (62.37–70.64)	66.87 ± 8.65 (62.77–70.96)	0.55	0.142 (0.04)	0.136 (0.04)	HI vs C: 1.000 (0.19)	HI vs C: 1.000 (0.02)
Total fat mass (Kg)	M	29.34	30.26 ± 7.14 (27.98–32.53)	27.82 ± 8.04 (25.44–30.21)	-8.04	**0.000** (0.32)	**0.000** (0.31)	M vs HI: 1.000 (0.02)	M vs HI: 0.355 (0.19)
	HI		28.61 ± 5.87 (26.58–30.64)	27.66± 5.70 (25.53–29.79)	-3.33	0.079 (0.16)	0.058 (0.18)	M vs C: 0.996 (0.25)	M vs C: **0.016** (0.36)
	C		29.31 ± 6.11 (26.67–31.96)	29.62 ± 6.18 (26.85–32.39)	1.04	0.665 (0.05)	0.662 (0.05)	HI vs C: 0.806 (0.33)	HI vs C: 0.394 (0.23)
Total fat-free mas (Kg)	M	35.91	35.32 ± 4.26 (33.80–36.83)	36.37 ± 4.75 (34.80–37.94)	2.98	**0.000** (0.23)	**0.000** (0.25)	M vs HI: 0.947 (0.24)	M vs HI: 0.293 (0.09)
	HI		36.67 ± 4.30 (35.32–38.02)	37.44 ± 4.25 (36.04–38.84)	2.10	**0.000** (0.18)	**0.000** (0.17)	M vs C: 1.000 (0.23)	M vs C: **0.000** (0.26)
	C		35.41 ± 4.11 (33.65–37.17)	35.32 ± 4.15 (33.49–37.14)	-0.26	0.645 (0.02)	0.702 (0.02)	HI vs C: 0.210 (0.5)	HI vs C: **0.006** (0.19)
Total body fat percentage (%)	M	43.61	44.47 ± 4.38 (42.86 –46.08)	43.18 ± 4.26 (41.55–44.81)	-2.90	**0.000** (0.3)	**0.000** (0.31)	M vs HI: 0.724 (0.29)	M vs HI: 0.594 (0.09)
	HI		42.83 ± 4.48 (41.40–44.27)	41.88 ± 4.70 (40.43–43.34)	-2.21	**0.000** (0.21)	**0.000** (0.2)	M vs C: 1.000 (0.17)	M vs C: **0.000** (0.33)
	C		43.76 ± 4.71 (41.90–45.63)	43.93 ± 4.74 (42.03–45.82)	0.37	0.538 (0.03)	0.544 (0.03)	HI vs C: 0.279 (0.43)	HI vs C: **0.004** (0.23)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

V.VIII.II. Project two

The anthropometry and body composition outcomes from ITT analysis are presented in Tables 43 and 44. Repeated measures ANOVA showed a main effect of time in WC [F(1, 132) = 29.40, p < 0.000, η^2p = 0.182, 1-β = 1], HC [F(1, 132) = 33.58, p < 0.000, η^2p = 0.203, 1-β = 1], WHtR [F(1, 132) = 29.79, p < 0.000, η^2p = 0.184, 1-β = 1], total fat mass [F(1, 132) = 28.40, p < 0.000, η^2p = 0.177, 1-β = 1], total fat-free mass [F(1, 132) = 7.23, p < 0.008, η^2p = 0.052, 1-β = 0.761] and total body fat percentage [F(1, 132) = 70.80, p < 0.000, η^2p = 0.349, 1-β = 2]. Pairwise comparisons revealed significant declines in all the training groups in the WC, HC, WHtR, total fat mass and total body fat percentage, with ES ranged between trivial and small. In addition, a significant increase was found in all the training groups in the total fat-free mass parameter, with trivial ES in all the groups. The C group increased significantly their values in the WC, HC, WHtR, total fat mass and total body fat percentage while also showed significant decreases intotal fat-free mass. A significant time × group interaction was found between all the training groups and the C group in the WC [F(3, 132) = 12.46, p < 0.000, η^2p = 0.221, 1-β = 1] (moderate ES), between the P and C group in HC [F(3, 132) = 15, p < 0.000, η^2p = 0.254, 1-β = 1] (small ES), between MT and C group in WHtR [F(3, 132) = 12.50, p < 0.000, η^2p = 0.221, 1-β = 1] (large ES) and between MT and P groups with C group in total body fat percentage [F(3, 132) = 30.26, p < 0.000, η^2p = 0.408, 1-β = 1] (small and moderate ES).

After controlling for baseline values and age, repeteated measures ANCOVA showed the same significant effects by time and similar ES. However, along with the significant main effects of time × group interaction that was found with the ANOVA, the ANCOVA also revelaled the following between groups interactions: HC [F(3, 130) = 16.89, p < 0.000, η^2p=0.280, 1-β = 1], [F(3, 130) = 15.23, p < 0.000, η^2p=0.259, 1-β = 1], total fat mass [F(3, 130) = 16.13, p < 0.000, η^2p = 0.271, 1-β = 1], total fat-free mass [F(3, 130) = 11.67, p <

0.000, $\eta^2p = 0.212$, 1-β = 0.999] and total body fat percentage: [$F(3, 130) = 30.59$, $p < 0.000$, $\eta^2p = 0.414$, 1-β = 1]. The new differences between groups were found between MT and C groups in HC (small ES), total fat mass (trivial ES) and total fat-free mass (small ES); between MT and T groups in HC (trivial ES); between P and C groups in total fat mass (trivial ES) and total fat-free mass (small ES); and between T and C groups in HC (small ES) and total body fat percentage (small ES).

Results of the PPA for the anthropometric parameters found similar changes than ITT analysis but with some differences. After applied ANOVA test, the same significant changes by time were found while the significant differences between groups in the WC (MT vs C, P vs C and T vsC) and HC (P vs C) disappeared. After the ANCOVA analysis, there are significant changes by time in WC in the MT and C groups while the the significant differences between MT and T groups in the HC disappeared. Regarding the body composition variables, the PPA analysis showed the same significant differences and similar ES except that a significant difference between MT and C groups in total body mass appeared. Results from PPA are presented in Supplementary Material F (Table F.1 and F.2).

Table 43. *Intervention effects on anthropometric measurements from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
WC (cm)	MT	98.73	97.50 ± 11.63 (93.81–101.18)	94.82 ± 10.69 (91.29–98.35)	-2.75	**0.000** (0.24)	**0.000** (0.32)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.11)	MT vs P: 1.000 (0.06) MT vs T: 0.248 (0.17)
	P		98.02 ± 11.49 (94.34–101.71)	95.82 ± 11.01 (92.29–99.35)	-2.25	**0.000** (0.2)	**0.000** (0.3)	MT vs C: **0.006** (0.79)	MT vs C: **0.000** (0.5)
	T		97.14 ± 8.16 (93.46–100.83)	95.86 ± 8.99 (92.33–99.40)	-1.32	**0.007** (0.15)	**0.003** (0.18)	P vs T: 1.000 (0)	P vs T: 1.000 (0.11)
	C		102.26 ± 11.73 (98.58–105.94)	103.32 ± 10.81 (99.79–106.85)	1.04	**0.026** (0.09)	**0.005** (0.16)	P vs C: **0.021** (0.69) T vs C: **0.022** (0.75)	P vs C**: 0.000** (0.11) T vs C**: 0.000** (0.46)
HC (cm)	MT	105.81	105.44 ± 8.86 (102.64–108.23)	102.94 ± 8.08 (100.23–105.64)	-2.37	**0.000** (0.29)	**0.000** (0.23)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.27)	MT vs P: 1.000 (0.04) MT vs T: **0.035** (0.16)
	P		104.67 ± 7.71 (101.88–107.47)	102.61 ± 7.24 (99.91–105.32)	-1.97	**0.000** (0.28)	**0.000** (0.19)	MT vs C: 0.065 (0.61)	MT vs C: **0.000** (0.33)
	T		106.14 ± 7.65 (103.35–108.94)	105.17 ± 8.26 (102.4–107.88)	-0.91	**0.016** (0.12)	**0.016** (0.11)	P vs T: 1.000 (0.33)	P vs T: 0.200 (0.12)
	C		107.00 ± 8.65 (104.20–109.79)	107.94 ± 8.27 (105.23–110.64)	0.88	**0.019** (0.11)	**0.009** (0.09)	P vs C: **0.041** (0.33) T vs C: 0.933 (0.68)	P vs C: **0.000** (0.29) T vs C: **0.003** (0.2)

Table 43. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
WHR	MT	0.933	0.924 ± 0.07 (0.900–0.948)	0.920 ± 0.07 (0.897–0.944)	-0.38	0.412 (0.05)	0.326 (0.05)	MT vs P: 1.000 (0.16)	MT vs P: 1.000 (0.03)
	P		0.935 ± 0.07 (0.912–0.960)	0.933 ± 0.07 (0.910–0.947)	-0.26	0.576 (0.03)	0.607 (0.03)	MT vs T: 1.000 (0.12)	MT vs T: 1.000 (0.01)
	T		0.916 ± 0.06 (0.893–0.941)	0.912 ± 0.06 (0.889–0.936)	-0.43	0.358 (0.06)	0.229 (0.07)	MT vs C: 0.249 (0.54)	MT vs C: 1.000 (0.09)
	C		0.954 ± 0.06 (0.931–0.979)	0.955 ± 0.05 (0.932–0.979)	0.10	0.831 (0.02)	0.543 (0.03)	P vs T: 1.000 (0.28)	P vs T: 1.000 (0.04)
								P vs C: 1.000 (0.32)	P vs C: 1.000 (0.06)
								T vs C: 0.072 (0.69)	T vs C: 1.000 (0.11)
WHtR	MT	0.635	0.614 ± 0.06 (0.589–0.639)	0.597 ± 0.05 (0.573–0.621)	-2.73	**0.000** (0.27)	**0.000** (0.29)	MT vs P: 0.365 (0.47)	MT vs P: 1.000 (0.06)
	P		0.644 ± 0.08 (0.619–0.669)	0.629 ± 0.07 (0.606–0.654)	-2.26	**0.000** (0.18)	**0.000** (0.17)	MT vs T: 0.987 (0.39)	MT vs T: 0.171 (0.16)
	T		0.629 ± 0.05 (0.605–0.655)	0.621 ± 0.06 (0.597–0.645)	-1.32	**0.006** (0.14)	**0.004** (0.13)	MT vs C: **0.002** (0.9)	MT vs C: **0.000** (0.37)
	C		0.654 ± 0.08 (0.629–0.679)	0.660 ± 0.07 (0.637–0.685)	1.04	**0.025** (0.08)	**0.007** (0.1)	P vs T: 1.000 (0.9)	P vs T: 1.000 (0.08)
								P vs C: 0.441 (0.12)	P vs C: **0.000** (0.08)
								T vs C: 0.139 (0.39)	T vs C: **0.001** (0.28)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: *n* = 34. MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; BMD: WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio. CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

Table 44. *Intervention effects on body composition from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total body mass (Kg)	MT	68.91	69.64 ± 13.39 (65.96–73.31)	69.23 ± 13.31 (65.57–72.89)	-0.58	**0.025** (0.03)	**0.026** (0.03)	MT vs P: 1.000 (0.28)	MT vs P: 1.000 (0)
								MT vs T: 1.000 (0.06)	MT vs T: 0.606 (0.04)
	P		66.32 ± 10.14 (62.65–69.99)	65.94 ± 10.20 (62.28–69.60)	-0.58	**0.032** (0.04)	**0.026** (0.04)	MT vs C: 1.000 (0.2)	MT vs C: 0.051 (0.06)
	T		68.50 ± 10.26 (64.83–72.17)	68.52 ± 10.27 (64.86–72.18)	0.02	0.933 (0)	0.910 (0)	P vs T: 1.000 (0.25)	P vs T: 0.581 (0.04)
								P vs C: 0.222 (0.58)	P vs C: 0.055 (0.07)
	C		71.19 ± 8.99 (67.52–74.87)	71.45 ± 8.85 (67.79–75.11)	0.36	0.152 (0.03)	0.134 (0.03)	T vs C: 1.000 (0.31)	T vs C: 1.000 (0.03)
Total fat mass (Kg)	MT	30.11	30.47 ± 8.92 (28.01–32.92)	29.18 ± 8.71 (26.75–31.61)	-4.24	**0.000** (0.15)	**0.000** (0)	MT vs P: 1.000 (0.19)	MT vs P: 0.832 (0)
								MT vs T: 1.000 (0.06)	MT vs T: 0.571 (0)
	P		28.49 ± 6.33 (26.04–30.95)	27.71 ± 6.40 (25.28–30.14)	-2.75	**0.000** (0.12)	**0.000** (0)	MT vs C: 0.919 (0.33)	MT vs C: **0.000** (0)
	T		30.41 ± 7.26 (27.96–32.87)	29.67 ± 7.21 (27.24–32.10)	-2.44	**0.000** (0.1)	**0.000** (0)	P vs T: 1.000 (0.29)	P vs T: 1.000 (0)
								P vs C: 0.145 (0.29)	P vs C: **0.000** (0)
	C		31.06 ± 6.09 (28.61–33.52)	31.67 ± 6.01 (29.24–34.10)	1.97	**0.004** (0.1)	**0.000** (0)	T vs C: 1.000 (0.64)	T vs C: **0.000** (0)
Total fat-free mas (Kg)	MT	36.99	37.33 ± 4.98 (35.84–38.82)	37.90 ± 5.23 (36.37–39.43)	1.52	**0.000** (0.11)	**0.001** (0.1)	MT vs P: 0.823 (0.34)	MT vs P: 1.000 (0.06)
								MT vs T: 1.000 (0.22)	MT vs T: 1.000 (0.02)
	P		36.03 ± 4.16 (34.54–37.52)	36.26 ± 4.27 (34.73–37.79)	0.66	0.131 (0.06)	0.116 (0.06)	MT vs C: 1.000 (0.02)	MT vs C: **0.000** (0.24)
	T		36.26 ± 4.37 (34.77–37.75)	36.83 ± 4.55 (35.30–38.36)	1.58	**0.000** (0.13)	**0.000** (0.14)	P vs T: 1.000 (0.13)	P vs T: 0.571 (0.08)
								P vs C: 0.980 (0.38)	P vs C: **0.003** (0.2)
	C		38.33 ± 3.97 (36.85–39.82)	37.80 ± 3.85 (36.27–39.33)	-1.40	**0.001** (0.14)	**0.000** (0.14)	T vs C: 1.000 (0.23)	T vs C: **0.000** (0.28)
Total body fat percentage (%)	MT	43.13	42.76 ± 4.36 (41.22–44.30)	40.82 ± 4.37 (39.26–42.39)	-4.53	**0.000** (0.44)	**0.000** (0.44)	MT vs P: 1.000 (0.03)	MT vs P: 1.000 (0.07)
								MT vs T: 0.450 (0.40)	MT vs T: 0.084 (0.16)
	P		42.53 ± 3.91 (40.99–44.07)	40.96 ± 4.24 (39.39–42.53)	-3.69	**0.000** (0.38)	**0.000** (0.39)	MT vs C: **0.022** (0.79)	MT vs C: **0.000** (0.65)
	T		43.91 ± 5.54 (42.37–45.45)	42.84 ± 5.64 (41.27–44.40)	-2.44	**0.000** (0.19)	**0.000** (0.2)	P vs T: 0.579 (0.38)	P vs T: 0.778 (0.1)
								P vs C: **0.032** (0.38)	P vs C: **0.000** (0.59)
	C		43.31 ± 4.17 (41.77–44.85)	44.14 ± 4.04 (42.57–45.70)	1.90	**0.000** (0.2)	**0.000** (0.21)	T vs C: 1.000 (0.77)	T vs C: **0.000** (0.4)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: n = 34.MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

V.IX. DISCUSSION ON ANTHROPOMETRY AND BODY COMPOSITION

To the best of our knowledge, the studies presented in this Ph.D. dissertation are the first to investigate the effects of two key training parameters (i.e., intensity and modality training) using an elastic variable resistance during a medium-to-long training period (i.e., 20 and 32 weeks) on anthropometry and body composition state throughout the analysis of WC, HC, WHR, WHtR, total body mass, total fat mass, total fat-free mass and total body fat percentage parameters in older women. In regard to intensity, the main and novel finding of the first study was that both training intensities are able to produce significant changes in body composition after an eight-month resistance training program by increasing the total fat-free mass and by decreasing the total body fat percentage. Although there were no significant differences between the two training intensities in any parameter, progressive elastic resistance training performed at moderate intensity results in greater changes in both fat and skeletal muscle body components. In fact, only the M group significantly decreased in total fat mass.

Furthermore, regarding the training modality, the main and novel finding of the second study was that all training modalities (i.e., multi-component, power strength training and traditional high-intensity resistance training) achieved improvements in anthropometry and body composition by significantly decreasing the values of the anthropometric parameters (i.e., WC, HC and WHtR) and the body composition variables (i.e., total fat and total body fat percentage). In addition, the MT and T groups significantly increased in total fat-free mass after the five-month training period. Although significant differences between training modalities were only found in the HC between MT and T groups, the multi-component exercise regimen may be the most effective training strategy to improve body composition and achieve anthropometric changes in older women since the MT group accomplished the greatest changes in most of the parameters analyzed.

We hypothesized in H6 (Chapter III, Section III.I.III.) that both training intensities improve body composition by decreasing body fat and by increasing muscle mass after a 32-week program of progressive resistance training with elastic bands, with the moderate intensity producing greater effects than the high intensity in all the body composition parameters. Our findings largely confirmed this hypothesis, as we found that both training intensities significantly improved the body fat and fat-free mass body composition components, with no significant differences between the training intensities, although the M group produced greater effects.

Regarding the influence of the training modality, we hypothesized in H5 and H10 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) reduce cardiovascular risk by reducing the WC, HC, WHR, and WHtR after an intervention period of 20 weeks using elastic resistance, with multi-component training producing greater effects than power and high-intensity resistance training. Our findings partially confirmed this hypothesis, as all training modalities reduced cardiovascular risk by significantly reducing the WC, HC and WHtR, but no significant differences were found in the WHR at the end of the training program. In addition, the findings confirmed that the MT group achieved the greatest effects in these parameters, although no significant changes were found between training strategies, except in the HC of the MT and T groups.

Finally, we hypothesized in H6 and H10 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) improve body composition by decreasing body fat and increasing fat-free mass after an intervention period of 20 weeks using elastic resistance, with multi-component training achieving greater effects than power and high-intensity resistance training in fat mass and high-intensity resistance training producing better results in fat-free mass than the other

training modalities. Our findings partially confirmed this hypothesis, as all training modalities significantly improved body composition by decreasing total body fat and the total body fat percentage, but only the MT and T groups significantly improved in the total fat-free mass component. In addition, although no significant differences between the training intensities were found, H6 is also confirmed because the MT group achieved the greatest changes in fat mass parameters, while the T group accomplished the greatest changes in the fat-free mass component.

V.IX.I. Specific discussion of the first project

Our findings in the first study are aligned with a wide and growing range of literature that has confirmed (Beckwée et al., 2019) the effectiveness of resistance training in improving skeletal muscle mass among older adults, and specifically in elderly women, with high-quality evidence (Beckwée et al., 2019; Borde et al., 2015; Buch et al., 2017; Csapo & Alegre, 2015; Johnston et al., 2008; Morley, 2007: Peterson et al., 2011; Theodorakopoulos et al., 2017; Yoshimura et al., 2017). The muscle tissue adaptations produced by both strength training programs in the first study are consistent with specific scientific evidence, which indicates that most resistance training protocols lasting longer than 12 weeks and with intensities greater than 40% of 1RM produce improvements in muscle mass, increasing the size of the CSA of the trained muscles and producing hypertrophy adaptations in both Type I and Type II fibers (Aagaard et al., 2010; Cassilhas et al., 2007; Hakkinen et al., 2007; Kalapotharakos et al., 2004; Hanson et al., 2009; Kosek et al., 2006; Petrella & Chudyk, 2008; Pyka et al., 1994; Reeves et al., 2004; Taafe et al., 1996; Trappe et al., 2000; Wallerstein, et al., 2012).

In fact, several studies and meta-analyses support these recommendations and confirmed that older adults training at moderate-to-high intensities, similar to those applied in our first study, is associated with relatively greater gains in muscle mass (Bemben et al.,

2000; Campbell, 1994; Cassilhas et al., 2007; Csapo & Alegre, 2016; Fatouros et al., 2005; Fiatarone et al., 1990; Frontera et al., 1988; Kalapotharakos et al., 2004; Kemmler, von Stengel, Engelke, Häberle & Kalender, 2010; Nickols et al., 1993; Onambélé-Pearson et al., 2010; Peterson et al., 2010; Steib et al., 2010; Silva et al., 2014; Treuth et al., 1994; Van Roie et al., 2013; Vincent et al., 2002); muscle CSA (Fiatarone et al., 1994; Hurley et al., 1995; Roth et al., 2001); and muscle fiber area (Charette et al., 1991; Frontera et al., 1991; Fry, 2004; Roth et al., 2001)than lower intensities.

Our findings in the first study in relation to fat-free mass are in accordance with the conclusions reported by the only meta-analysis to date that compares the efficacy of different training intensities in resistance training programs in older adults. Csapo and Alegre (2016) reported that both heavy (~80% 1RM) and light-to-moderate loads (~45–60% 1RM) provoke minor increases in muscle size, with increases of 11% and 9%, respectively, which indicates that muscle hypertrophy can be achieved with low, moderate and high intensities (Csapo & Alegre, 2016) although the potential of skeletal muscles to be hypertrophied is blunded at older ages. Although our study did not compare high and low intensities, but rather moderate-to-high (70% 1RM) and high intensities (85% 1RM), our results confirmed the lack of significant differences between intensities due to the total mechanical work and training-index fatigue being matched.

The absolute gain of fat-free mass reported by the M group was 1.05 kg, which supposed an increase of 2.98% from the initial values. Meanwhile, the HI group achieved an absolute increase of 0.770 kg, which represents an increase of 2.10% compared to the baseline values. Despite the differences between groups in the total amount of fat-free mass gained (i.e., 0.260 kg in favor of the M group), no significant differences between the training programs were found. Although progressive traditional or low-velocity (i.e., at least 2 s per movement phase) resistance training, especially at high intensities, has been recommended

for older adults to improve lean mass in recent decades (Binder et al., 2005; Fiatarone et al., 1990; Kalapotharakos et al., 2004; Chalé et al., 2012), and there is consistent evidence that higher intensities lead to greater improvements in muscle mass in the elderly population (Csapo & Alegre, 2016), our results are in agreement with the position statement from the NCSA (Fragala et al., 2019), which states that that moderate intensities of 51–69% of 1RM yield greater effects than either lower or higher intensities on muscle morphology based on the results found in the meta-analysis by Borde et al. (2015). Borde and colleagues also reported that the most effective dose-response characteristics of the resistance training program for improving muscle morphology in healthy older adults were composed of a training period of 50–53 weeks; training frequency of three sessions per week; training volume of two to three sets per exercise, seven to nine repetitions per set; 6.0 s of total time under tension; a 120-s rest between sets; and a 2.5-s rest between repetitions. Moreover, the meta-regression revealed that none of the examined training variables of volume (i.e., period, frequency, number of sets, and number of repetitions) predicted the effects of resistance training on measures of muscle morphology.

However, prior to the meta-analysis by Borde et al. (2015), to produce the desirable training adaptations in the skeletal muscle mass, narrative reviews by Mayer et al. (2011) and Petrella and Chudyk (2008) recommended a training period of eight to 12 weeks, three training sessions per week, training intensities of 60–80% of the 1RM, three to four sets and eight to 12 repetitions per exercise. In addition, world-leading organizations in exercise-related research such as ACSM and AHA (Chodzko-Zajko et al., 2009; Peterson & Gordon, 2011) have recommended that older adults engage in progressive muscle strengthening activities at moderate to vigorous intensity at least twice a week (Chodzko-Zajko et al., 2009; Peterson & Gordon, 2011), with eight to 10 exercises and one to three sets of eight to 15 repetitions, to prevent loss of muscle mass and avoid sarcopenia in the elderly population.

Such intensities coincide with subjective intensity at a scale or perceived exertion of 5–6 to 7 –9 on a scale of 0 to 10, or with objective loads equivalents to approximately 60–80% to > 80% of the individual 1RM with a wide range of repetitions per set based on the load selected (Chodzko-Zajko et al., 2009). We confirm, based on the results obtained in our first study where these recommendations were followed, that the doses in terms of intensity proposed by the ACSM and AHA are effective, not only to maintain but also to improve fat-free mass in older women.

We observe a lack of consensus in the guidelines with regard to the most effective doses to produce muscle mass in older adults since we found differences in the recommendations for all training parameters (e.g., duration, frequency, volume and intensity). Comparing the training programs designed in the first study with the overall recommendations mentioned above, we counteract the lower frequency in the number of sessions and the lower number of exercises per session with a higher volume of series performed per exercise and adequate intensities. What seems clear, contrary to what was previously believed and what many guidelines still include, is that muscle mass increase in older adults can be achieved by a wide range of intensities, not only at moderate intensities, although these seem to be the most effective. This spectrum of loading ranges where muscle hypertrophy can be equally achieved is called "hypertrophy continuum" and was postulated in a recent meta-analysis by Schoenfeld et al. (2017).

The total amount of fat-free mass reached by both training groups, but especially by the M group (i.e., M: +1.05 kg, $\Delta\%$: 2.98%; HI: 0.770 kg, $\Delta\%$: 2.98%), are in accordance with the data reported by the meta-analysis by Peterson et al. (2011), derived from 49 studies and 81 cohorts, which revealed that after an average of 20.5 weeks of resistance training, three training sessions per week, with an intensity of 75 % of the 1RM, two to three sets and 10 repetitions with a 110-s rest between sets, aging men and women experienced a significant

main effect equal to a 1.1 kg increase in lean body mass. Despite the lower training frequency, the M group achieved similar results to those reported by Peterson et al. (2011), which is likely due to the higher volume in terms of sets and repetitions and the longer duration of the training period. The HI group was close to reaching the same amount of profit, but in this case, the lowest frequency and volume in terms of the number of repetitions could be determining factors. In addition, our findings for both groups align with the results of previous meta-analyses which examined the effects of resistance training on muscle size (Stewart et al., 2014) in healthy as well as disabled and/or frail middle-aged and/or older adults (range 50–95 years) and reported increases in muscle size of 1.5–16% (Peterson et al., 2011; Raymon et al., 2013; Steib et al., 2010). It is also important to note that resistance training in the first study is associated with a 0.680 kg to 0.915 kg greater increase in fat-free mass than in the C group.

One of the most important reasons that could be behind the improvements obtained by both training groups is the high number of sets per sessions performed by the subjects in both groups. A higher volume of sets has been associated with greater increases in lean body mass in older adults (Petersen et al., 2011). In fact, in the meta-analysis by Petersen et al. (2011), the authors did not find any significant relationships between program duration, intensity or frequency after the meta-regression, but they suggested that the volume, and particularly higher volume, is related to greater improvements in lean body mass. In our first study, the subjects of the M and HI groups performed 24 sets per session during the first eight weeks, 32 sets per session in the subsequent 16 weeks and 28 sets per session (in supersets) in the last eight weeks. This volume is within the range reported by the studies involved in the meta-analysis of Petersen et al. (2011), which ranged from seven to 39 total sets per session.

The results obtained in the first study, although in terms of the magnitude of the ES are trivial and small, are especially relevant because these gains in fat-free mass can

counteract the nearly 0.2 kg annual decline that may occur that may occur due to sedentary lifestyles in individuals over 50 (Delmonico et al., 2009), allowing a greater preservation of muscle function and independence. Even more important is to have achieved this gain in older women, who suffer a decline of 0.6% per year of muscle mass after the menopause period (Rolland et al., 2007) and in whom it has been observed that the gain of fat-free mass may be attenuated relative to the change in younger women after six months of resistance training (i.e., 0.7 kg vs 1.2 kg, respectively; Dionne et al., 2004; Lemmer et al., 2001).

Moreover, several studies revealed that muscle mass tends to decrease more in the lower body muscles between the fourth and seventh decade than in the upper body (Janssen et al., 2000) or the whole-body muscle mass (Francis, McCormack et al. 2016; Francis, Toomey et al., 2016; Janssen et al., 2000; Lynch et al., 1999), with women showing a greater rate of decline in lower limbs than men (i.e., 4.9% to 5.75% vs 2.6% to 3.5% per decade; Francis, McCormack et al. 2016; Francis, Toomey et al., 2016; Janssen et al., 2000; Lynch et al., 1999). The knee extensor muscles have been reported as those which suffer a higher decrease (Frontera et al., 2008; Maden-Wilkinson et al., 2013; Ogawa et al., 2012). Although it has not been reported by regions in this case, we imagine that, as with the losses, the gains in muscle mass will have been produced mainly in the lower limbs, and probably in the knee extensor muscles, with the consequent improvements for the functionality of this population. If we take into account that muscle atrophy occurs to a greater extent in Type II fibers (i.e., fast fibers) than in Type I fibers (i.e., low fibers; Clarkson et al., 1981; Klitgaard et al., 1990; Lexell et al., 1988), the improvements achieved by both training groups are highly relevant for the improvement of the physical function and mobility of the population studied.

In addition, it is important to highlight that approximately 25% of the sample (i.e., 23.6% or 22 of 93 subjects) was identified as sarcopenic in terms of muscle mass, based on the classification of sarcopenia by Cruz-Jentoft et al. (2019) and Baumgartner et al. (1999)

where the ASM, which is the sum of arm and leg muscle mass adjusted by squared height, has to be lower than < 5.45 or 5.50 kg/m² in women (Baumgartner et al.,1999; Cruz-Jentoft et al., 2019). This prevalence was higher in the M group (i.e., 29% or 9 of 31 subjects) than in the HI (i.e., 25.6% or 10 of 39 subjects) and C (i.e., 13% or 3 of 23 subjects) groups. Although there was no difference between groups at the baseline in this parameter, the lower values of fat-free mass along with the higher prevalence of the sarcopenic condition in the M group could have influenced the greater gains obtained in this group. The prevalence of sarcopenic subjects found in our first study aligns with those studies that reported a prevalence of 13% and 24% in those aged 65 to 70 years when a cutoff point of two SD for the ASM index was used (Baumgartner et al., 1998), as was the case in our study.

One of the limitations of the first study was the lack of nutrition intake registration. It is well-known that achieving fat-free mass gains is essential for the correct intake of proteins. The recommended dietary allowance (RDA) for protein in older adults is a modest 0.8 grams of protein per kilogram of body weight. However, about 10–25% of older adults consume less than this recommendation (Fulgoni 2008). To increase muscle mass through resistance training, at least 0.8 g/kg/day of protein must be ingested, although higher amounts are recommended (i.e., 1.0 to 1.3 g/kg/day). Due to the improvements obtained, we assume that the majority of subjects ingested at least the RDA of protein.

Over the last 30 years, numerous studies have examined the effects of resistance training on measures of muscle hypertrophy and morphology in older adults, which is likely the most widely recognized training strategy to combat age-related muscle atrophy in this population (Borde et al., 2015; Csapo & Alegre, 2016; Lavin et al., 2019; Peterson et al., 2011; Sueta et al., 2008). Nevertheless, our study is the first to compare two different resistance training strategies based on the use of different intensities in older women. In addition, most of the studies performed to date used weight machines and free weights as a

training device, and little is known about the effects of the use of variable resistance (i.e., elastic bands) on muscle hypertrophy in older adults.

Our findings from the first study align with previous studies which demonstrated that resistance training programs composed of resistance exercises involving elastic bands are effective for increasing lean mass in older people (Aniansson et al., 1984; Colado & Triplett, 2008; Colado et al., 2009; Egaña et al., 2010; Fritz et al., 2018; Kraemer et al., 2001; Liao et al., 2018; McNee et al., 2009; Morse et al., 2005; So et al., 2013; Yasuda et al., 2015; Yasuda et al., 2016; Park et al., 2016).

Among the studies that found positive results, we highlight the study by Fritz et al. (2018), where after eight weeks of elastic resistance training (twice a week, six overall body exercises, and three to four sets of 10 repetitions at RPE of 7–9 on the OMNI-RES) with traditional elastic bands or with elastic handle devices in overweight older women (aged 60–85 years), both training groups significantly increased fat-free mass in the upper limbs while the traditional elastic band group also improved the trunk lean mass. In addition, 72.72% of the participants in the traditional group and 66.66% of the participants in the elastic handle group showed clinically significant increases in the fat-free mass (Fritz et al., 2018), whose cutoff point is located at an increase of 1.6% of lean mass (Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017). In our study, both training groups (M: +2.98%; HI: +2.10%) reached this clinically significant increase of 1.6%.

Our results are also consistent with those of Colado and Triplett (2008), who studied a group of middle-aged women (54.14 ±2.87) performing elastic band training for 10 weeks, twice a week, and showed that their subjects had a mild increase in fat-free mass that was similar to the increase we obtained in the present study (+1.2%), although the body composition was measured by eight-polar bioelectrical impedance analysis. The training

program consisted of six exercises with 20 repetitions performed at an intensity of five on the OMNI-RES scale for the first four weeks and seven for the next six weeks. In the first four weeks, two sets were performed for the lower limbs and one set for the upper extremities, while from weeks five to eight, they were equalized for the upper and lower body and for weeks nine and 10, the number of sets was three. Additionally, in another short-term study performed by the same group in postmenopausal women (54.14 ± 0.63) where the effects of a supervised strength training program using three devices (weight machines, elastic bands, and aquatic devices) were analyzed, the authors found a significant increase of 1.15% in the elastic band group at the end of the training period (Colado, Garcia-Masso, Rogers et al., 2012). Likewise, Egaña et al. (2010) performed a 12-week elastic resistance training program, twice a week, at a moderate-high RPE in elderly women and reported significant improvement in fat-free mass similar to the results we obtained in the present study (1 kg). As was the case for Egaña et al. (2010), the programs designed by Liao et al. (2018) and So et al. (2013) also found significant improvements in fat-free mass after a 12-week elastic resistance training program performed at moderate (60–70% of 1RM) and low intensities, respectively. The improvements reported were +0.720 gr by Liao et al. (2018) and +2.7% by So et al. (2013).

Contrary to our results, some investigations failed to note a significant effect of elastic resistance training on fat-free mass (Coelho-Júnior et al., 2019; Kraemer et al., 2001; Lubans et al., 2013; Martins, Safons et al., 2015; Oh et al., 2016; Skelton et al., 1995; Thiebaud et al., 2013). For instance, in the only previous study in which training intensities using variable resistance have been compared in older women, Fritz et al. (2015) conducted a short period (i.e., eight weeks) of resistance training at three different intensities (i.e., moderate [15 RM], moderate-high [10RM] and high [6RM]) with a RPE of 6–7 during the first three weeks and 8–9 in the last five. In general, the same methodology as in our study was used, as well as the

same type of exercises, except the open squat, which was substituted in our study for a standing hip abduction exercise. However, the authors did not find significant improvements in fat-free mass.

Likewise, Martins, Safons et al. (2015) conducted a short-term study in older adults of similar ages, although their participants were not obese, applying the same methods for monitoring the intensity of an elastic resistance training program that we employed in the first study. The training program lasted eight weeks, was performed twice a week and was composed of seven exercises, four for the lower limbs and three for the upper limbs. The older adults worked at an intensity of 5–7 on the OMNI-RES scale during the first four weeks and 8–10 during the last four weeks, performing two sets of 15 repetitions the first four weeks and increasing to three sets during the last four weeks. The authors arrived at the same conclusion as Fritz et al. (2015) since they did not find significant differences in whole or regional fat-free mass after the training period. These findings are likely due to the fact that they did not use multi-joint exercises for the lower extremities, which decreased the total muscle volume implicated during each exercise session, and they used a smaller number of sets for each exercise during half of the training program. Both the increased volume of muscle involvement and the greater number of sets are necessary for stimulating hypertrophic changes (Gentil et al., 2017; Helms et al., 2015; Paulsen et al., 2003). Straigth et al. (2012) and Thiebaud et al. (2013) found the same results after applied elastic resistance training programs for eight weeks.

The lack of significant changes in fat-free mass in these studies could be associated with the fact that they were all short training programs, lasting only eight weeks. It seems that a longer stimulus is necessary to generate significant changes in the fat-free mass of older adults, whether using moderate or high intensities. In fact, there is evidence that significant muscle mass improvement starts after nine weeks of training (Hunter et al., 2004). In

addition, the heterogeneity in the results may be due to the fact that the effectiveness of resistance training on muscle size in the elderly population could be influenced by the muscles analyzed (Häkkinen et al., 2001); the muscle length (Häkkinen et al., 2001; Reeves et al., 2004); the type of technique used (Reeves et al., 2004); and the sex and age of the participants (Peterson et al., 2011). In fact, in most of the studies cited above, body composition was not analyzed by DXA but rather by bioimpedance. In this sense, the use of DXA for the evaluation of body composition, along with the longer length of the prescribed training programs, represents an increase in the quality of the results obtained in our first study in comparison to previous studies and simultaneously brings new knowledge about the effects of progressive elastic resistance training in the medium to long term on the body composition of older women.

Regarding the mechanisms by which resistance training performed at low-moderate velocities (i.e., two to three seconds per phase) can produce adaptations in fat-free mass in older adults, several studies have attempted to elucidate this question. It is well-known that mechanical, metabolic and hormonal factors are involved in muscle hypertrophy (Schoenfield, 2013; Zanchi & Lancha, 2008). During aging, skeletal muscle mass undergoes numerous changes, but the most relevant are the loss of muscle size and the loss of muscle fibers. Changes in muscle size and volume are predominantly due to an increase in the muscle CSA (Roth et al., 2001; Treuth et al., 1995) through the size and number of myofibrils, with the fast-twitching fibers (i.e., Types IIa and IIx) being responsible for the greatest increase in muscle size (Suetta et al., 2008), which otherwise are more affected by aging-induced atrophy than slow-twitching ones. In addition, the mechanical loading offered by resistance training induces greater myofibrillar packing density of muscle fibers (Penman, 1970); elicits the activation of anabolic signaling pathways (Damas et al., 2015); improves myofibrillar protein synthesis (Kang & Krauss, 2010); and leads to a series of intracellular

events that ultimately regulates gene expression involved with myogenesis (Kosek et al., 2006; Roth et al., 2003). Others factors such as the endocrine responses of growth hormone, testosterone, insulin, cortisol and insulin-like growth factor I contribute to the magnitude of hypertrophy (Kraemer & Ratamess, 2005). In addition, changes in the nervous system (Aagaard et al., 2010); in muscle satellite cells (Kadi et al., 2004); in muscle structure (Narici et al., 2003); in the vascular system (Gonzalez-Freire et al., 2014); in intramuscular adiposity (Alchin, 2014); and in protein intake (Signorelli et al., 2006) are related to the increase in fat-free mass induced by resistance training in older adults.

Contrary to the attention that resistance training has received in recent decades for improving muscle mass in older people, resistance training has not been assigned a major role in obesity prevention or treatment because it is generally believed to be ineffective for weight loss or maintenance. Professional organizations have historically focused exercise guidelines on aerobic training. The most recent guidelines of three key weight management organizations (i.e., the American College of Cardiology, AHA and the Obesity Society) state that there is a need for further research to understand the most appropriate strategies and prescriptions for weight loss in the elderly population, as "*the overall safety of weight loss interventions for patients aged 65 and older remains controversial" (*Jensen et al., 2014). Despite the high prevalence rates of obesity, few studies analyze the effects of resistance training on body composition (i.e., fat mass, fat-free mass); most of them analyzed changes in body weight exclusively.

Our initial study is one of the first studies that analyzes the effects of resistance training on body composition measured by DXA in older adults and the first one that compares the effects of different training intensities. Our results showed that both moderate-to-high intensity and high-intensity resistance training performed with variable resistance are effective training strategies to improve the body composition of older women by significantly

reducing the total percentage of body fat and significantly improving the total fat-free mass, as was previously discussed. In addition, the M group also significantly reduced total body mass. However, no changes in body weight were found for any group.

The findings from our first study align with previous evidence that found positive alterations in fat mass after applied resistance training alone (Banz et al., 2003; Donnelly et al., 2009; Fielding, 1995; Hersey et al., 1994; Hunter et al., 2002; Ibanez et al., 2005; Lemmer et al., 2001; Marx et al., 2001; Nichols et al., 1993; Pollock et al., 2000; Schmitz et al., 2003; Treuth et al., 1994; Williams et al., 2007; Winett & Carpinelli, 2001), as well as with studies that found minimal and non-significant changes in weight loss (Bateman et al., 2011; Church et al., 2010; Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Schmitz et al., 2003; Schmitz et al., 2007; Sigal et al., 2007). As was the case in our study, previous studies highlighted the increase in fat-free mass as the main reason for not finding changes in body weight.

Strength training has a negative reputation as an unhelpful weight-loss strategy. However, this is a paradigm error that has been imposed by the lack of analysis of body composition, due to most previous studies only assessing changes in body weight. Nevertheless, more relevant than changes in total weight are those obtained in body composition by reducing the fat mass and increasing the fat-free mass, as we found in our first study.

The magnitudes of the changes obtained in our study regarding the body fat and body fat percentage were small and trivial. The M group achieved an absolute body fat loss of 2,440 kg (i.e., 0.305 kg per month) which represents a decrease of 8.04% (i.e., ~1% per month) from the initial values while the HI group lost 0.960 kg (i.e., 0.120 kg per month) of

fat mass, 3.33% of initial body fat (i.e., ~0.4% per month). Although there were no significant differences between training groups, the loss of fat mass was 1,480 kg greater in the M group than in the HI group. At the same time, only the M group showed significant differences compared to the C group in this parameter. Regarding the total body fat percentage, the absolute body fat percentage loss by the M group in 32 weeks was 1.29%, which represents the 2.90% from the baseline values. In the case of HI, the percentage of total body fat lost was 0.95% in absolute terms and 2.21% compared to the baseline levels. In this parameter, both training groups showed significant differences compared to the C group.

The differences found between groups may be related to the higher energy expenditure produced by the M group due to the higher volume in terms of number of repetitions performed. In fact, the total number of repetitions per session carried out by the M group during the first eight weeks was 360 (i.e., 24 sets × 15 repetitions), 480 (i.e., 32 sets × 15 repetitions) in the next 16 weeks and 420 in the last eight weeks (i.e., 28 sets × 15 repetitions). However, the HI group performed 144 repetitions in the first eight weeks (i.e., 24 sets × 6 repetitions), 192 in the following 16 weeks (i.e., 32 × 6 repetitions) and 168 in the last eight weeks (i.e., 28 sets × 6 repetitions). In fact, previous studies reported that the energy cost of one set of eight to 15 repetitions of eight resistance training exercises is 70–80 kcal in both young and elderly women (Haddock & Wilkin 2006; Phillips & Ziuraitis 2004). Taking this data into account, the M group sessions could have generated a caloric expenditure between 210–240 kcal in the first eight weeks, between 280–320 kcal in the following 16 weeks and between 240–280 kcal in the last eight weeks of the training program, while the high intensity group would have produced values lower than those of the M group. To this energy expenditure should be added that produced by the activities of an aerobic and coordinative nature carried out during active breaks.

The improvements in the reduction of total body fat and body fat percentage found in both groups adds to the growing body of evidence supporting the fact that resistance training applied at moderate-to-high intensities decreases total adipose tissue, usually in studies of more than 12 weeks in duration, with losses ranging from 1.6–3.4% of fat mass (Bond et al., 2002; Campbell et al., 1994; Cavalcante et al., 2018; Donnelly et al., 2000; Ferley et al., 2013; Hunter et al., 2002; Ibañez et al. 2005; Irwin et al., 2003; Lemmer et al. 2001; Marcos-Pardo, Orquin-Castrillón et al., 2019; Neter et al., 2003; Nickols et al., 1993; Norman et al., 2003; Norris et al., 1990; Olson et al., 2007; Pi-Sunyer et al., 2007; Treuth et al., 1994; Treuth et al., 1995). The loss of body fat achieved by the M group was significantly higher than these percentages, probably due to the high volume, the type of exercises and the longer training duration than previous studies, while the changes accomplished by the HI are situated within the range mentioned above. In addition, a minimum reduction of 3% of body weight or percentage of fat mass has been established as the clinically relevant minimum (Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017). On average, both training groups were close to reaching this goal, especially the M group (+2.90%). Collectively, it was not achieved, but there were subjects who decreased their total body fat percentage below this clinically relevant threshold. At the same time, as we expected, the C group showed an increase of the total body fat (+ 0.310 kg; Δ%: 1.04%) and total percentage of body fat (+ 0.17%; Δ%: 0.37%) in eight months. This evidence is important to understand how accelerated the increase of fat mass is in older people.

Although it seems that moderate intensity could be the most effective strategy to improve the body composition by decreasing the body fat mass, in the elderly population, and specifically in postmenopausal and older women, only a limited number of studies have examined the effects of different training intensities when a resistance training program is conducted (Avila et al., 2010; Campbell et al., 2002; Delecluse et al., 2004; Olson et al.,

2007; Pereira et al., 2007; Shioutsu et al., 2018; Wallerstein et al., 2012). In fact, to date, no studies have directly compared different training intensities (i.e., low, moderate and high) on adipose tissue (whole body and regional) applying resistance training programs alone in older adults, nor with continuous or variable resistance. For that reason, the findings of our first study are highly relevant as they provide new knowledge in the field of older adults, exercise and health.

Furthermore, the results obtained in our first study are consistent with the literature that indicates that a medium-long training period and/or a high-volume of training is necessary to achieve significant changes in fat mass (Donnelly et al., 2009). For example, the results obtained by Hunter et al. (2000) achieved a mean reduction of 2.7 kg of fat mass in older adults aged between 61 and 77 years after applying a strength program for 26 weeks, performed three days a week. In this case, the loss of fat mass was greater than that obtained in our study, possibly due to the increased training frequency and highest volume since they included upper limb, lower limb and core exercises, performing three sets of 10 repetitions with an intensity between 60–85% of 1RM (i.e., moderate-to-high).

On the other hand, Ibañez et al. (2005), after performing a 16-week resistance training program using machines in older adults with Type II diabetes, found a decrease of 8.25% in total body fat and 11.3% in intra-abdominal fat. In this case, the decrease was similar to that obtained by the M group and greater than that shown by the HI group. The greater loss could be explained by a worse baseline state of the sample at the beginning of the study, as well as a smaller sample size. Authors such as Fatouros et al. (2005) and Caserotti et al. (2007) also showed that 24 and 12 weeks of high-intensity resistance training programs (75–80% 1RM) in people over 65 years offer positive effects on body composition, reducing weight by 3.9% in the first study and fat mass by 4% in the second, despite the fact that they did not obtain significant changes in fat-free mass, an effect that was produced in our first study. In

addition, the training programs conducted by these authors were accompanied by the control of nutritional intake, which was not recorded in our first study.

Our results, however, contrast with those studies that found no changes in body fat after conducting a resistance training program in elderly population (Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al.,2007; Schmithz et al., 2007; Polak et al., 2005), even at moderate-to-high intensities (Ferrara et al., 2006; Hintze et al., 2018; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Willis et al., 2012). At the same time, in contrast to the outcomes observed in the first study, the review by Stehr and Lengerke (2012) concluded that exercise is effective to prevent weight gain in the elderly, either in terms of weight loss or weight maintenance. The authors found that for older adults and postmenopausal overweight women, exercise or physical activity was associated with weight loss in all interventions (i.e., 1.1–6 kg), independent of the intensity and the indicators of obesity applied (Stehr & Lengerke, 2012). In addition, the ACSM position stand for physical activity to maintain health and promote weight loss, showed strong evidence that physical activity can attenuate weight gain in those at risk for obesity, showing that many exercise programs are capable of producing at least modest weight loss (i.e., ~2 kg; Donnelly et al., 2009; Haskell et al., 2007).

However, despite consistent evidence from studies indicating that physical activity and exercise training can prevent weight gain and produce modest weight loss in older adults, physical exercise can be performed in numerous ways. In fact, most of the recommendations and evidence to date do not discriminate among exercise modalities, making it difficult to draw firm conclusions. Instead, most refer to improvements produced by aerobic or combined exercise, not resistance training alone. Moreover, the changes in weight and fat mass in response to exercise training without caloric restriction are highly heterogeneous (Barwell et al., 2009; Boutcher & Dunn, 2009; Church et al., 2009; King et al., 2008). The variability

among individuals following an exercise training intervention regarding adipose tissue can be explained by 1) high variability and low adherence to training program (Fedewa et al., 2017); 2) increased dietary intake (Donnelly & Smith, 2005); 3) decreased resting energy expenditure (Byrne et al., 2012; Pontzer, 2015); 4) decreased non-exercise physical activity (reflected as changes in ambulatory physical activity; Herrmann et al., 2015; Melanson et al., 2013); 5) decreased non-exercise activity thermogenesis (reflected as changes in activity-related energy expenditure such as postural changes; Herrmann et al., 2015; Melanson et al., 2013); or 6) different training protocols applied. As a result, weight or fat mass reductions can be substantially less than predicted (i.e., the weight loss achieved is usually 30% of the initial predicted value; Drenowatz, 2015; Manthou et al., 2010; Ross & Janssen, 2001).

In our first study, the high attendance rate and compliance of the subjects may have been an important factor in achieving changes in body composition. In addition, the high sample size and the anthropometric characteristics of the sample could also be determinant factors due to our sample being predominantly overweight and obese. For instance, regarding BMI, 81.8% (i.e., 76 of 93 subjects) of the sample were classified as overweight or obese, with the C group having the highest percentage (i.e., 87% or 20 of 23 subjects) followed by the M (i.e., 83.9% or 26 of 31 subjects) and HI (i.e., 77% or 30 of 39 subjects) groups.

If we take into account a more appropriate measure to define and categorize the level of obesity, such as the total body fat percentage, these percentage increase to 91.4% for the sample (i.e., 84 of 93 subjects), 91.4% for the C group, 87.1 % for the M group and 92.4% for the HI group. The prevalence of overweight and obese individuals in our study was similar to the rate reported by Gomez-Cabello et al. (2001) in a Spanish population 65 years of age, according to their BMI values (i.e., 84% vs 81.8%). However, the prevalence of these two metabolic disorders when the percentage of body fat was used was higher in our study than in the data reported by Gomez-Cabello et al. (2001; i.e., 62.5% vs 91.5%). Thus, our

sample is representative in terms of the prevalence of obese and overweight individuals with respect to the target population of the study, especially if we take the BMI into account. Although subjects were instructed to maintain their normal daily routines and dietary intake during the study period, two important factors (i.e., nutrition intake and physical activity) not being recorded in the first study is a limitation that must be taken into account when interpreting the results.

Most resistance training protocols designed to improve body composition in the elderly have been executed with machines and free-weight resistance exercises, independent of whether they were performed in combination with aerobics or not. However, certain studies have examined the effects of resistance training programs using variable resistance such as elastic bands. Our results from the first study align with those studies that reported significant improvements in the percentage of body fat in postmenopausal women (Colado & Triplett, 2008; Colado et al., 2009; Colado, Garcia-Masso, Rogers et al., 2012; Neves et al., 2017; Sillanpää et al., 2009) and older adults (Frit et al., 2018; Lee & Kim, 2012; Lee, Kim et al., 2014; Park et al., 2016; Sillanpää et al., 2009; So et al., 2013). However, few studies specifically analyzed the effects of resistance training in older women (Coelho-Júnior et al., 2019; Fritz et al., 2015, 2018; Lee et al., 2012, Lee, Kim et al., 2014; Oh et al., 2016; Sillanpää et al., 2009; Souza et al., 2019). In addition, the studies by Fritz et al. (2015, 2018), Oh et al. (2016) and Souza et al. (2019) did not combine resistance training with other training modalities, as in our first study.

Fritz and colleagues (Fritz et al., 2015) found, after an eight-week elastic resistance training program comparing moderate (15RM), moderate-to-high (10RM) and high intensity (6RM) with a similar training protocol to our first study, significant decreases of 2.74% and 2.34% for the moderate and moderate-to-high groups and a non-significant decrease of 0.72% in the high-intensity group. Our results, after applying a longer training program (i.e., eight vs

32 weeks), support the higher effects of moderate intensity over high intensity. The longer the program lasts, the greater the effects are achieved, regardless of the intensity used. Likewise, a study performed by the same group years later found similar changes. The authors investigated the effects of an eight-week resistance training program in older overweight women (twice weekly), using two different types of elastic devices: elastic tubes with handles and traditional elastic bands (Fritz et al., 2018). The training program was also similar to ours, with six overall body exercises, and three to four sets of 10 repetitions at a RPE of 7–9 on the OMNI-RES scale. At the end of the training program, the authors found a significant improvement in total body mass in both training groups (i.e., -3.47% for the elastic tubing group and -2.60% for the traditional elastic band group).

In contrast to our findings, Oh et al. (2016) and Souza et al. (2019) did not find significant changes in BMI and fat mass after 18 and 14 weeks, respectively, of resistance training performed with elastic bands. In both studies, the intensity and the training volume were lower than in our first study, which may be the main causes of the lack of significant changes. In addition, other studies that applied combined training (i.e., resistance and aerobic training) in older adults also reported no changes in body fat mass (Coelho-Júnior et al., 2019, de Alencar Silva et al., 2020; Lubans et al., 2013; Skelton et al., 1995). The mixed findings may be related to the different training methodologies and parameters employed (e.g., intensities, duration, exercise, repetitions, number of sets, rest interval between sets and exercises, time under tension, intervention length), as well as the differences in the subjects' characteristics, dietary intake control or body composition evaluation methods.

The mechanisms behind the improvements achieved in body fat mass in both groups are related to the increase in fat-free mass, which may, in turn, increase resting energy expenditure (or resting metabolic rate) in the subsequent 24 hours, physical activity energy expenditure, insulin sensibility and fat oxidation (Dionne et al., 2004; Giles et al., 2016;

Hunter et al., 2000, 2015; Kirk et al., 2009; Lemmer et al., 2001). The increase in fat-free mass is also an important driver of appetite and energy intake after weight loss (Dulloo et al., 1997).

The recent systematic review and meta-analysis by MacKenzie-Shalders et al. (2020) pointed out that resistance exercise generates increases in resting metabolic rate, while aerobic and combined resistance and aerobic exercise fail to induce a robust effect on changes in resting metabolic rate. Moreover, resistance training induces oxygen consumption after an intense or prolonged training to remain high for several hours. This phenomenon is known as *"excess post-exercise oxygen consumption".* This mechanism increases exponentially according to the training intensity and linearly according to the training duration. Previous studies have shown that high-intensity training produces greater exercise post-oxygen consumption than lower intensity training (Haltom et al., 1999; Thornton & Potteiger, 2002). This high oxygen consumption produces a high energy demand on the whole body, which translates into a reduction in body weight through the decrease in body mass (Paoli et al., 2012).

In summary, although the magnitude of the changes reported in fat-free mass and fat mass were trivial or small, the findings from our first study are highly relevant due to the two training interventions applied allowing the preservation or decrease in the age-related decline of muscle mass in this population while reducing the total body fat mass. The milestone achieved is more important when considering that maintaining skeletal muscle mass in older people may be critical for their physical function. Furthermore, the reduction of the adipose tissue reduces the chronic state of low-grade inflammation that that adversely affects nearly all physiological functions of the human body (Wellen & Hotamisligil, 2003), reducing the risk of developing multiple obesity-associated disease conditions, such as Type 2 diabetes mellitus (Mokdad et al., 2003); dyslipidemia (Poirier et al., 2006); metabolic syndrome

(Kopelman, 2000); insulin resistance (Kopelman, 2000); chronic liver disease such as nonalcoholic fatty liver or cirrhosis (Moore, 2010); cardiovascular diseases (Czernichow et al., 2011; Singh et al., 2013); several types of cancer (Calle & Kaaks, 2004; Lauby-Secretan et al., 2016; Picon-Ruiz et al., 2017); an array of musculoskeletal disorders; and cognitive decline (Anstey et al., 2011; Nguyen et al., 2014), all of which have negative effects on the quality of life and work productivity in older adults. In addition, considering that 23.6% of the sample was classified as sarcopenic, between 25 to 50% had sarcopenic obesity (according to the criteria selected), 79.5% presented osteopenic obesity and 21.5% showed osteosarcopenic obesity, the findings from our study are even more relevant.

V.IX.II. Specific discussion of the second project

In regard to the results obtained in the second study, we observe that the three proposed training modalities improved the body composition of older women in 20 weeks by improving the fat-free mass and reducing the amount of body fat mass and the anthropometric parameters evaluated, although the magnitude of these changes is not equal in all groups. Regarding the changes in fat-free mass, as expected, the T group showed the most significant improvements with an absolute gain of 0.570 kg (+1.58%), closely followed by the MT group, which also achieved a significant improvement of 0.570 kg, although the percentage of improvement between the baseline and post training values was slightly smaller (+1.52). Finally, the P group also improved in total fat-free mass but not significantly, with an absolute increase of 0.230 kg (+0.66%). Despite the differences between groups, especially between the T and MT groups compared to the P group, no significant differences were found between training groups. In addition, the magnitude of these changes was trivial in all training strategies. Nevertheless, all modalities showed significant differences compared to the C group at the end of the intervention.

No studies have previously compared these training modalities. Only some studies compare the multi-component training with other training modalities such as whole body vibration (Marín-Cascales et al., 2015, 2017) or traditional resistance training (de Resende-Neto et al., 2019). For this reason, the results obtained in our study are discussed by analyzing the findings obtained by each modality separately.

In the case of the T group, our results corroborated those reported in the first study and confirmed that this training strategy is a valid and effective training modality to produce fat-free mass gains in older women, even in a shorter period of time. Our results align with previous studies and meta-analyses which showed that high-intensity resistance training is an effective training method to achieve positive changes in muscle size and volume in older adults (Binder et al., 2005; Chalé et al., 2012; Csapo & Alegre, 2016; Fiatarone et al., 1990; Kalapotharakos et al., 2004). The total amount of fat-free mass reached by the T group was lower than that reported by the meta-analysis of Peterson et al. (2011), which concluded that aging men and women experienced a significant main effect equal to a 1.1 kg increase in lean body mass after a training program with these characteristics: 20.5 weeks, three training sessions per week, an intensity of 75% of the 1RM, two to three sets and 10 repetitions with a 110-s rest between sets. The lower training frequency (three vs two days a week) and training volume in terms of the number of repetitions (10 vs six repetitions) in our study could be the reasons for obtaining a lower gain in fat-free mass.

Nevertheless, despite the lower training frequency, the high training volume in terms of the number of sets could have favored the results obtained by this training group, since Petersen et al. (2011) pointed out that a higher volume is related to higher increase in muscle mass in older adults. In fact, the subjects of the T group performed a total of 24 sets per session during the first eight weeks and 32 sets per session in the last 12 weeks. This volume is within the range reported by the studies involved in the meta-analysis by Petersen et al.

(2011), which ranged from seven to 39 total sets per session. Furthermore, our findings in this training modality are in accordance with the increases of 15–16% in muscle size reported by previous meta-analyses in healthy as well as disabled, frail, middle-aged and/or older adults (Raymond et al., 2013; Steib et al., 2010). Additionally, the average increase of the T group was close to the clinically significant cutoff point where the increase in lean mass in older adults is located (Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017; i.e., +1.6% vs +1.58 %), which means that a high percentage of the older women in this group achieved a clinically significant gain in fat-free mass in 20 weeks of training.

Regarding the results of the MT group, our findings are comparable to previous studies that reported improvements in fat-free mass (de Resende-Neto et al., 2019; Grassi et al., 2014; Kemmler, von Stengel, Engelke, Häberle & Kalender, 2010; Marín-Cascales et al., 2015; Rossi et al., 2016), although not all of the changes were statistically significant. In addition, our results are also partially in agreement with Marín-Cascales et al. (2017), who concluded that multi-component training programs that combine resistance training using high-intensity loads and impact-aerobic activities may be the most optimal strategy to enhance muscle in this population. In our study, the intensity applied in the strength block was moderate (i.e., 65–70% 1RM) but with a moderate-to-high perceived exertion (i.e., 6–7 to 8–9), and subjects in the aerobic and coordination blocks did exercises with low-to-moderate impact. In addition, our results support the findings of the recent systematic umbrella review of Beckwée and colleagues (2019), which recommends the multimodal exercise strategy to improve muscle mass in older adults with a moderate quality of evidence due to various systematic reviews reporting significant effects of multimodal exercise programs on sarcopenia in healthy older adults (Bibas et al., 2014; Dublicate et al., 2017; Liberman et al., 2017).

Whereas, in our second study, we compare multi-component training to traditional resistance training and power strength training modalities, previous studies have compared multi-component training to other training modalities (de Resende-Neto et al., 2019; Marín-Cascales et al., 2015, 2017). Similar to our results, de Resende-Neto et al. (2019) found that traditional resistance training is more effective than the multi-component training for improving fat-free mass in older adults after 24 weeks of intervention. In our study, the MT group showed an increase of 1.95%, while the improvement of the T group was 2.92%. However, only the changes achieved by the T group were statistically significant, in contrast to the findings of our study where both groups reached significant improvement in this parameter. Likewise, Marín-Cascales et al. (2015) found similar positive effects (i.e., +1.1%, $p \leq 0.005$) for a 12-week multi-component training program, performed three days a week, on fat-free mass in older women when compared with whole-body vibration training. In addition, two previous studies found a significant increase in fat-free mass in older women. On the one hand, a high-intensity multipurpose exercise program over 18 months improved muscle mass in the study by Kemmler, von Stengel, Engelke, Häberle & Kalender (2010) where 246 women were analyzed. On the other hand, a 24-week multi-component training with low-impact aerobic exercises, resistance and balance training improved muscle mass in older women in a study by Kwon et al. (2008).

Despite the lower number of strength exercises performed by the MT compared to the T group, and therefore the lower volume performed, our results for the M group support the recommendations of the position statement from the NCSA (Fragala et al., 2019); ACSM (Chodzko-Zajko et al., 2009); and AHA (Peterson & Gordon, 2011), which states that moderate intensities of 51–69% of 1RM or to 60–80% of 1RM yield larger effects than either lower or higher intensities on muscle morphology, when older adults engage at least twice a week progressively in muscle strengthening activities. In addition, the total sets per

session performed by the MT group in the strength block reached the range reported by Peterson et al. (2011) of seven to 39 sets per session, which is necessary to produce changes in fat-free mass in older adults. In fact, during the first eight weeks, the subjects of this group performed nine series per session, and the amount increased to 12 in the following 12 weeks. Another important factor along with the intensity and the volume that could explain the positive findings reported by the MT group in fat-free mass are the types of exercises performed. Both exercises selected (i.e., squat plus upright rowing and lunge) involve a large number of muscle groups, most of them large muscle groups in the lower limbs. These three factors, along with the possible increases in protein synthesis produced by aerobic training that which have been confirmed in previous studies (Short et al., 2004), could promote the muscle fiber hypertrophy in this training modality.

However, contrary to our results, other authors reported no significant changes in fat-free mass after a multi-component resistance training in older adults (Bernabei et al., 2014; Calvani et al., 2013; Chien et al., 2000; Landi et al., 2015; Marín-Cascales et al., 2017; Park et al., 2015). For instance, Marín-Cascales et al. (2017) compared the effects of multi-component and whole-body vibration training for 24 weeks with three sessions per week. The authors found no changes in the multi-component group (-0.1%) after the training period. Englund et al. (2005) arrived at the same conclusion when evaluating the effects of a multi-component training program composed by walking, jogging, resistance, balance, coordination, stretching and relaxation exercises after one year. In fact, the authors found a significant decrease in lean mass after the year.

Similar to Marín-Cascales (2017), no changes were observed in fat-free mass after a multi-component training program (two days a week) composed of stretching, weight-bearing activities, muscular endurance exercise, balance and agility training after 32 weeks in the study by Marques, Mota, Machado, et al. (2011). Our results are also in contrast to those

reported by Park et al. (2008), which showed no adaptations in lean mass in the multi-component group (stretching, resistance training, weight-bearing exercise, balance, and posture correction training) after 48 weeks with a training frequency of three days a week. This conflicting evidence is likely due to the heterogeneity in the training parameters, the length of the training period, the characteristics of the participants (e.g., age, basal conditions and comorbidities) and the regions assessed between studies. The small number of studies available makes these differences more noticeable. In addition, one of the main problems is that many of the studies cataloged in the literature as multi-component are concurrent training, due to the training programs being composed only of aerobic and resistance training components and not including balance, coordination or flexibility blocks.

With regard to the results of the P group, our findings demonstrated that high-velocity resistance training is also a valid and effective method to increase the fat-free mass for older women in a short period of time, although the changes were smaller and not significant compared to the other two training modalities analyzed. Our results are in accordance with the conclusion reached by the recent meta-analysis of da Rosa Orssatto and colleagues (da Rosa Orssatto et al., 2020), which revealed that power training is effective to induce muscle hypertrophy in older adults to a similar extent as moderate-velocity resistance training (da Rosa Orssatto et al., 2020). However, to date, results regarding the effectiveness of this kind of training modality remain inconsistent because few studies have analyzed their effects on fat-free mass (Binns et al., 2017; Coelho-Júnior et al., 2019; de Resende-Neto et al., 2019; Gray et al., 2018; Henwood et al., 2008; Reid et al., 2008; Stec et al., 2017), and there is a lack of data that directly compares both training modalities in the same study. In this sense, our study is the first that compares power strength training not only with traditional resistance training but also with the multi-component training strategy using elastic bands, thus

contributing to increasing knowledge of the effects of these training modalities on body composition in older women.

Several studies that conducted power strength training programs alone or in comparison to traditional resistance training in older adults arrived at the same conclusion as us, achieving positive effects on fat-free mass but without significant changes. Gray et al. (2018) found no significant improvements after 24 weeks of high-intensity resistance training (80% 1RM) plus 24 weeks of power strength training (50% 1RM) performed twice weekly, with a training program composed by eight exercises (i.e., seated chest press, seated bent-over row, bicep curl, overhead tricep extension, lateral raise, standing knee curl, heel raises, and chair stand or half lunge), with three sets of 10 repetitions each. The authors did not report the percentage of change achieved. Similar results were found by Coelho-Júnior et al. (2019) after 22 weeks of periodized power training performed twice a week. The first session was based on power training (three sets of eight to 10 repetitions at a "moderate" intensity and three performed as quickly as possible) while the second session of the week was based on traditional resistance training (three sets of eight to 10 repetitions at a "difficult" intensity (i.e., 5–6) prescribed based on the RPE scale. The authors found an increase of 4% at the end of the intervention. Although we obtained a higher increase in our study, it was not significant. Discrepancies across findings may be at least partly related to methodological issues between studies, such as training protocols that used different volumes and/or intensities, differences in characteristics of the participants and differences in baseline values. Further research in this field is necessary to clarify the effects of power training on body composition, and more specifically, on fat-free mass.

In absolute terms, in our study, the P group increased fat-free mass in 0.230 kg (0.46 kg per month). This amount is 340 kg less than the gains obtained by the MT and T groups, which represent the 40% of the profit obtained by these groups. Although the exercises and

the volume in terms of sets per sessions was the same in the P group as in the T group, and the number of repetitions performed by the P group was in the optimal range for muscle gains, the lower intensity and the short time under tension could be determining factors that explain the lower improvements obtained. On the other hand, despite the lack of evidence, it from a physiological point of view, power training can improve muscle mass by reducing the high threshold activation of large motor units in response to the high velocity of concentric contraction, regardless of exercise intensity (Kraemer et al., 1996) while high-intensity resistance training would induce the recruitment of large motor units and, consequently, Type II muscle fibers, based on the size principle (Mendell, 2005) where the size of the recruited motor unit increases according to the muscle tension generated during contraction.

In terms of the magnitude of the ES, the results obtained in our second study on fat-free mass, as in the first study, are especially relevant because the gains obtained in the three training groups can counteract the nearly 0.2 kg annual decline that may occur through sedentary lifestyles beyond 50 years of age (Delmonico et al., 2009), allowing a greater preservation of muscle function and independence in older women. In addition, we can imagine that the gains in muscle mass will have been produced in all the groups mainly in the lower limbs, with the consequent improvements for the functionality of this population. Moreover, muscle atrophy occurs to a greater extent in fast fibers (Type II) than in slow fibers (Type I; Clarkson et al., 1981; Klitgaard et al., 1990; Lexell et al., 1988).

Furthermore, regarding the characteristics of the sample studied, it is important to highlight that 30.2% of the sample (41 of 136 subjects) was identified as sarcopenic in terms of muscle mass based on the classification of sarcopenia by Cruz-Jentoft et al. (2019) and Baumgartner et al. (1999). This prevalence was higher in the MT group (i.e., 44.2% or 15 of 34 subjects), followed by the C (i.e., 32.4% or 11 of 34 subjects), T (i.e., 22.6% or 8 of 34 subjects) and P (i.e., 20.5% or 7 of 34 subjects) groups. Despite there being no differences

between groups at baseline in this parameter, the higher or lower prevalence of the sarcopenic condition across the training groups could have influenced the gains obtained by the groups. The prevalence of sarcopenic subjects found in our second study are slightly higher compared with the studies that reported a prevalence of 13% and 24% in those aged 65 to 70 years when a cutoff point of two SD for the ASM index was used (Baumgartner et al., 1998), as was the case in our study.

In contrast to our first study, in the second project the confounding variables of nutrition intake and level of physical activity were recorded. Regarding the protein intake, all groups showed baseline values over the RDA for protein in older adults that has been established as 0.8 g/kg/day. In fact, in all groups, the values were above 1.0 g/kg/day, an amount that is considered suitable for increasing muscle mass. In addition, all training groups maintained their initial ingestion of protein at the end of the training period except the P group, which showed a significant decrease after adjusting for age and baseline values. This decrease likely affected the final results for this group, although the finals values remained above 1.0 g/kg/day.

With regard to the rest of the body mass parameters, all training modalities significantly decreased the total fat mass and the percentage of total body fat after the training period, with the MT group obtaining the greatest improvements, followed by the P and T groups. Moreover, contrary to our results in the first study, we found significant differences in total body mass in the MT and P groups, with a decrease in body weight of 0.200 kg and 0.190 kg, respectively. Thus, it is feasible to argue that, in these two training groups, the loss of fat mass has been higher than the gain of muscle mass, resulting in the loss of body weight. In addition, it is necessary to note that, as happened with the total fat-free mass, the C group experienced a significant increase in fat mass and in total body fat percentage. No significant

differences between training groups were found in the fat mass parameters, but all training modalities showed significant differences from the C group after the study period.

The magnitudes of the changes obtained in our study regarding body fat and body fat percentage in all groups were trivial. The MT group achieved an absolute body fat loss of 1.290 kg (0.258 kg per month) which represents a decrease of 4.24% (0.84% per month) compared to the initial values. On the other hand, the P group lost 0.780 kg (0.156 kg per month) of fat mass and 2.75% of initial body fat (~0.55% per month), while the T group lost 0.740 kg (0.148 kg per month) of fat mass and 2.44% of the initial body fat (0.48% per month). Although there were no significant differences between training groups, the loss of fat mass was 0.550 kg greater in the MT group than in the T group. Regarding the total body fat percentage, the absolute body fat percentage loss by the MT group in 20 weeks was 1.92%, which represents the 4.53% from the baseline values. In the case of the P group, the percentage of total body fat lost was 1.57% in absolute terms and 3.93% compared with the baseline levels, while the T group lost 1.07% in absolute values, which represents the 2.44% of the total body fat percentage from the initial values.

The differences found between groups may be related to the higher energy expenditure produced by the MT group due to the aerobic block and the volume of the strength block in terms of number of sets and repetitions performed. The lower volume of repetitions in the T group compared to the P (six vs 12 and 10) and MT groups (six vs 15), along with the lower intensity of the P group compared with the T group (10–12 repetitions at a RPE of six as a maximum vs six repetitions at 6–7 to 8–9 RPE) and the MT group in the strength block (10–12 repetitions at a RPE of six as a maximum vs 15 repetitions at 6–7 to 8–9 RPE), could explain the lower changes achieved by power strength and traditional high-intensity resistance training modalities compared to the multi-component strategy.

Our results for the T group support the findings of our first study and previous evidence that found positive alterations in fat mass after applied resistance training alone (Banz et al., 2003; Donnelly et al., 2009; Fielding, 1995; Hersey et al., 1994; Hunter et al., 2002; Ibanez et al., 2005; Lemmer et al., 2001; Marx et al., 2001; Nichols et al., 1993; Pollock et al., 2000; Schmitz et al., 2003; Treuth eta l., 1994; Williams et al., 2007; Winett & Carpinelli, 2001), but with the advantage that the significant changes in our study were achieved with a shorter training program (less than six months) than our first study. In addition, as was the case in our first study, no significant changes were found in the T group in the total body mass parameter, due to loss of fat mass and gains of fat-free mass being similar. This behavior aligns with most previous studies that also found minimally significant changes in weight loss (Bateman et al., 2011; Church et al., 2010; Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Schmitz et al., 2003; Schmitz et al., 2007; Sigal et al., 2007) after applying different resistance training programs in older adults.

In addition, the improvements in the reduction of total body fat and body fat percentage found in the T group support the growing body of evidence that indicates that resistance training applied at moderate-to-high intensities usually decreases total adipose tissue in studies of more than 12 weeks in duration, with losses ranging from 1.6% to 3.4% of fat mass (Bond et al., 2002; Campbell et al., 1994; Cavalcante et al., 2018; Donnelly et al., 2000; Ferley et al., 2013; Hunter et al., 2002; Ibañez et al. 2005; Irwin et al., 2003; Lemmer et al. 2001; Marcos-Pardo, Osquin-Castrillón et al., 2019; Neter et al., 2003; Nickols et al., 1993; Norman et al., 2003; Norris et al., 1990; Olson et al., 2007; Pi-Sunyer et al., 2007; Treuth et al., 1994; Treuth et al., 1995). The loss of body fat and the total body fat percentage at the end of the training period was in the range mentioned above (i.e., total fat mass: -2.44%; total body fat percentage: -2.44%). These percentages are close to reaching the goal

of the minimum clinically relevant reduction for body weight or fat mass percentage stabilized at 3% (Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017). Collectively, it was not achieved, but there were subjects who decreased their total body fat percentage below this clinically relevant threshold.

Comparing the results achieved by the T group with the studies that also used elastic bands as a training device, our findings align with the studies that reported significant improvements in percent body fat in postmenopausal women (Colado & Triplett, 2008; Colado et al., 2009; Colado, Garcia-Masso, Rogers et al., 2012; Neves et al., 2017; Sillanpää et al., 2009) and older adults (Fritz et al., 2015, 2018; Lee et al., 2012, Lee, Kim et al., 2014; Park et al., 2016; Sillanpää et al., 2009; So et al., 2013). Fritz and colleagues (Fritz et al., 2015) found, after eight-weeks of elastic resistance training, a significant decrease of 0.72% in body fat for the training group that trained at high intensities, using a similar protocol to our second study. However, the extra 12 weeks that our subjects trained are reflected in greater losses of fat mass. Likewise, Fritz et al. (2018) found significant improvements in total body mass in both training groups (i.e., elastic tubing and elastic band) after eight weeks of training performed twice weekly. The decrease achieved by both groups (i.e., -3.47% for the elastic tubing group and -2.60% for the traditional elastic band group) in this study was greater than that obtained by the T group in our study. The main reason for these differences could be the different intensities applied and thus the different training volume. The training program of the study by Fritz et al. (2018) was similar to ours, with six overall body exercises, but the subjects performed three to four sets of 10 repetitions at a RPE of 7–9 on the OMNI-RES instead of six repetitions as in our study.

In contrast to our findings, Oh et al. (2016) and Souza et al. (2019) did not find significant changes in BMI and fat mass after 18 and 14 weeks, respectively, of resistance training performed with elastic bands. In both studies, the intensity and the training volume

were lower than in our first study, which could be the main cause of the lack of significant changes. In addition, there were studies performed with machines or free weights that arrived at the same conclusion (Fenkci et al., 2006; Hunter et al., 2002; Ibanez et al., 2005; Klimcakova et al., 2006; Lemmer et al., 2001; Olson et al.,2007; Schmithz et al., 2007; Polak et al., 2005), even using moderate-to-high intensities (Ferrara et al., 2006; Hintze et al., 2018; Lemmer et al., 2001; Olson et al., 2007; Polak et al., 2005; Willis et al., 2012) or combining strength and aerobic training (i.e., concurrent training; Coelho-Júnior et al., 2019, de Alencar Silva et al., 2020; Lubans et al., 2013; Skelton et al., 1995).

At the same time, our results for the T group in our second study are not consistent with the conclusion reported by Stehr and Lengerke (2012) in their review, who indicate that exercise is effective to prevent weight gain in the elderly, either in terms of weight loss or weight maintenance due to exercise or physical activity being associated with a weight loss of 1.1–6 kg in all interventions. In addition, they contradict the ACSM position stand on physical activity being necessary to maintain health and promote weight loss because they indicated that many exercise programs are capable of producing at least modest weight loss (i.e., ~2 kg; Donnelly et al., 2009; Haskell et al., 2007). However, in our second study, the T group achieved a decrease of 0.020 kg (+0.02%). As mentioned previously, the conclusions and recommendations of Stehr and Lengerke (2012) and the ACSM did not discriminate among exercise modalities, but most refer to improvements produced by aerobic or combined exercise, not resistance training alone.

With regard to the results for the MT group, our findings align with those studies that reported beneficial effects of multi-component training on the different body fat mass assessments (BMI, total and regional body fat in absolute [kg] or relative terms [%]) when it was applied alone (Blasco-Lafarga et al., 2020; Carvahlho et al., 2010; Godoy-Izquierdo et al., 2010; Grant et al., 2004; Neves et al., 2017) or in combination with an energy restriction

diet (Arciero et al., 2014; Villareal et al., 2006; Villareal, Erman & Agyar, 2011). For instance, Carvahlho et al. (2010) found significant changes in BMI after eight months of multi-component training three days per week in women aged 60–80 years. The sessions were composed of a warm-up, aerobic exercise (i.e., walking, jogging, dance, aerobics and step choreographies for 20–25 min at 2–14 in the Borg RPE), strength (i.e., muscular endurance using elastic and free weights with one to three sets, eight to 15 repetitions at 12–16 RPE), balance blocks and a cool-down period. Similar results were found by Godoy-Izquierdo et al. (2017) in a study of postmenopausal women that lasted 20 weeks. Likewise, Neves et al. (2017) verified the effect of multi-component circuit training with eight stations related to the development of strength (using elastic bands and free weight) plus four stations focused on balance, coordination, and agility, as well as an 18- to 30-min walk and observed that 16 weeks of this training modality applied in postmenopausal women improved body composition by significantly reducing fat mass (-3.4%).

However, contrary to our findings, other authors found no changes in body weight, body fat mass or BMI after applying multi-component training programs (Cancela et al., 2019; Carvarlho et al., 2010; Grant et al., 2004; Grossman et al., 2016; Kang et al., 2015; Leite et al., 2015; Marques, Mota, Machado et al., 2011; Sousa et al., 2013). Cancela et al. (2019) and Carvarlho et al. (2010) found no changes in fat mass after a training period of eight months while the response of the community-dwelling elderly women analyzed by Kang et al. (2015) was the same after four months. These controversial outcomes in the adipose tissue variables following different multi-component protocols may be explained by differences in the training programs (i.e., length of the training program, sessions per week, number and types of exercises, number of repetitions and series, rest between exercises and sets) and in the participants (i.e., age, gender and health conditions).

In addition, some studies have analyzed the effect of multi-component training in comparison to other training modalities such as resistance training (de Resende-Neto et al., 2019; Grossman et al., 2016; Marques et al., 2009; Leite et al., 2015; Sousa et al., 2013), combined aerobic plus resistance training (Rossi et al., 2017) and whole body vibration (Marín-Cascales et al., 2015, 2017). The positive effects obtained in fat mass in our study by the MT and T groups, with no differences between them, were also reflected in the study by de Resende-Neto et al. (2019) after 24 weeks. The authors compared multi-component and traditional resistance training groups for 24 weeks and found a decrease of 2.97% and 2.45% in fat mass in the MT and T groups, respectively. In addition, they found a decrease of 3–51% in the MT group and 2–50% the T group in body fat percentage. However, the loss of body fat percentage of the MT group was significant. The changes were similar to those obtained in our study, although we found significant differences in both training groups probably because the strength exercises were performed at maximal concentric velocity in the study by de Resende-Neto et al. (2019) and therefore, with less time under tension. The results by Marín-Cascales et al. (2015, 2017) also showed significant positive effects of the multi-component training programs on the body fat mass after 12 (-0.4%) and 24 weeks (-1.7%) although, unlike in our study, they did not obtain significant losses in the body fat percentage (i.e., -0.7% and -1%, respectively). It is necessary to mention that despite the multi-component programs being performed three days a week in both studies, they were composed mainly of aerobic and impact activities and not by strength exercises, which may be one of the reasons why our study obtained better results. Likewise, Marques, Mota, Machado et al. (2011) found a significant decrease in the body fat mass percentage after eight months applying a similar training protocol to ours. Nevertheless, contrary to our results, a number of previous studies that compared multi-component and traditional resistance training in older adults found no changes in body composition parameters in any of the modalities

analyzed (Leite et al., 2015; Sousa et al., 2013). The main characteristic of these studies was their short duration of 12 weeks.

In the case of the MT group, a significant loss of 0.410 kg (-0.58%) was accomplished. This amount is far from reaching the 1.1–6 kg of weight loss proposed by Stehr and Lengerke (2012) or the 2 kg mentioned by the ACSM (Donnelly et al., 2009; Haskell et al., 2007). Nonetheless, it is the only group, along with the P group, that on average achieved the minimum clinically relevant reduction of 3% of body weight or percentage of fat mass (total body fat percentage: -4.53%; Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017), which means that most of the subjects reached that percentage of loss. Along with the strength exercises, the aerobic block may have played a vital role in bringing about increasing energy expenditure and, as a result, a greater loss of fat mass and body weight. In the literature, aerobic training as been associated with greater body and visceral fat mass and weight loss compared to strength training (Schwingshackl et al., 2013).

Evidence suggests that aerobic training at moderate (60–70% MHR or 45–55% of VO_2max or 3.0 to 5.9 METs; Donnelly et al., 2009; Visser et al., 2013) or high-intensity (> 70% MHR or > 55% of VO_2max or > 6 METs; Donnelly et al., 2009; Visser et al., 2013) lead to a reduction in total and visceral adipose tissue in overweight males and females (Donnelly et al., 2009; Visser et al., 2013) and seems to have a greater effect than low intensity aerobic exercise or strength training (60% MHR or 45% VO_2max; Visser et al., 2013). In our study, the intensity of the aerobic component progressed from 65% to 85% of the MHR, therefore working in an optimal range to achieve adaptations in the fat tissue. Interestingly, the results obtained by the MT group were supported by the studies that found superior effects from combining resistance training and aerobic exercise, also known as concurrent training, compared to aerobic or strength training alone on fat mass in overweight and obese adults

and older adults (Arciero et al., 2006; Davidson et al., 2009; Ismail et al., 2011; Laird et al., 2014; Park et al., 2003; Schwingshackl et al., 2013; Vissers et al., 2013; Willis et al., 2012). In fact, current evidence suggests that overweight and obese older adults should participate in both aerobic endurance training and resistance training whether or not they are undertaking caloric restriction (Beavers, Beavers et al., 2017; Daly et al., 2005; Silverman et al., 2009; Villareal et al., 2017).

On the other hand, among older adults, progressive resistance training performed at low velocities has been recommended in recent decades to at least maintain the body weight (Joseph et al., 1999; Latham et al., 2004). However, little is known about the effects of the high-velocity resistance training or power strength training modality on the body fat tissue. Our results for the P group showed that this training modality is an effective strategy to reduce the body fat tissue in older women due to the significant reductions achieved in total fat mass (-0.780 kg, Δ%: -2.75) and total body fat percentage (-1.57%, Δ%: -3.69%). After the MT group, the P group strategy was the most effective modality to modify body composition in older women in terms of body fat. In addition, this group showed the greatest significant reduction of total body mass in absolute terms (0.620 kg), and equal in relative terms to that which the MT group obtained (Δ%: -0.58%). The imbalance between the greater loss of fat mass than gains in fat-free mass produced a greater loss of body weight in this training group. However, the magnitude of the changes, as in the rest of the training groups, was also trivial and small. Nevertheless, the P group, as was the case with the MT group, achieved, on average, the minimum clinically relevant reduction of 3% of body weight or percentage of fat mass (total body fat percentage: -3.69%; Donnelly et al., 2009; Romero-Arenas et al., 2011; Santos et al., 2017), which means that most of the subjects reached that percentage of loss.

In contrast to the results of our second study, most of the previous investigations showed no significant changes in body fat mass or total body fat percentage after a power strength training intervention in older adults. Gray and colleagues (Gray et al., 2018), in the only previous study that compared the effects of low- and high-velocity resistance training on body composition in older adults, found no significant changes between and within groups in total body fat mass and body fat percentage after a training period of 48 weeks (Gray et al., 2018). The training program was performed twice weekly using free weight resistance. The traditional resistance training performed each concentric and eccentric movement at a rate of 2 s per phase at 80% of their 1RM during the 48 weeks, while the power strength group trained at a low velocity at 80% 1RM for 24 weeks before transitioning to high-velocity training at 50% of 1RM for the remaining 24 weeks. Thus, the P group did not implement the power component during the whole training period, but rather only half of the time. This may have contributed to the differences between studies. In addition, the types of exercises selected by Gray et al. (2018) may also have been an important factor; although they performed two additional exercises (i.e., eight vs six), most of them involved only small muscle groups, were monoarticular exercises or were performed in a sitting position (i.e., seated chest press, seated bent-over row, bicep curl, overhead triceps extension, lateral raise, standing knee curl, heel raises and chair stand or half lunge). Thus, lower energy expenditure was generated.

Likewise, de Resende-Neto et al. (2019) and Coelho-Júnior et al. (2019) arrived at the same conclusion after training periods of 12 and 22 weeks. However, neither of the two investigations performed a power strength training alone. In the case of de Resende-Neto et al. (2019), the authors compared a multi-component training program which included certain muscle power exercises with traditional resistance training, but the strength exercises were performed at maximal concentric velocity. After 12 weeks, only the multi-component group

showed a significant decrease in fat percentage (3.51%) while the traditional group saw a significant increase in lean mass (+2.92%). In the case of the study by Coelho-Júnior et al. (2019), the authors compare periodized and non-periodized traditional and power strength training programs. In the traditional strength group, the two sessions were based on three sets of eight to 10 repetitions at a "difficult" intensity (i.e., 5–6) prescribed based on the RPE scale, while in the power strength group, the first session of the week was based on three sets of eight to 10 repetitions at a "moderate" intensity (i.e., 3) performed as quickly as possible, and the second session was similar to the traditional strength group. The power group did not conduct a specific training program alone, but rather one that was combined with a traditional strength training strategy. Conversely, Mero et al. (2013) reported significant improvements in body fat percentage (although not in absolute values of fat mass) in older men after 21 weeks of resistance training with approximately 20% of the exercises performed at high velocity. The shorter duration of the training programs, along with the lack of studies that have analyzed the effects of the high-velocity resistance training strategy alone on body composition in older adults, may contribute to the differences between the previous studies and ours. In addition, the heterogeneity of the power strength programs performed to date could also be an important factor in these conflicting results. For instance, the ideal exercise intensity to improve body composition in older adults performing high-velocity resistance training remains unknown.

Regarding the changes observed in the C group, as we expected, the subjects increased their body weight by 260 kg (+ 0.36%) mainly due to the increase of total fat mass (+390 kg; Δ%: 1.97%) and total percentage of body fat (+0.83%; Δ%: 1.90%), which evidences how accelerated the increase of fat mass is in older adults when the individuals lead a sedentary lifestyle.

Along with the body composition parameters analyzed by DXA, in our second study, anthropometric indicators of central obesity were assessed due to evidence indicating that central obesity involves more health risks compared to total obesity assessed by BMI, total fat mass or total body fat percentage. In fact, more important that the amount of fat mass is how the adipose tissue is redistributed. Waist circumference, WH, WHR have been used as proxies for central obesity, while WHtR is a proxy for central (visceral) adipose tissue, which has recently received attention as a marker of "early cardiovascular risk" (Ashwell et al., 1996; Sahakyan et al., 2015; Roriz et al., 2014).

The findings obtained in our study showed that all training strategies were effective in reducing visceral and ganoid adipose tissue in older women by significantly reducing the WC, HC and WHtR and, therefore, cardiovascular risk. In addition, all training modalities achieved significant differences compared to the C group in these parameters. Supporting the responses obtained in the total body fat tissue, the MT group showed the greatest reductions in all anthropometric parameters, followed by the P and T groups. The only significant differences between training groups were found between the MT and T groups in the HC. Regarding the absolute and percentages of changes from the baseline values obtained by groups, the MT group achieved a reduction of 2.68 cm (-2.75%) in the WC, followed by the P group (-2.20 cm, Δ%: -2.25%) and the T group (-1.28 cm, Δ%: -1.32%). In the HC, the MT group achieved a reduction of 2.50 cm (-2.37%), followed by the P (-2.06 cm, Δ%: -1.97%) and T (-0.97 cm, Δ%: -0.91%) groups. In the WHtR, the MT group achieved a reduction of 0.017 (-2.73%), followed by the P (-0.015, Δ%: -2.26%) and T (-0.008, Δ%: -1.32%) groups. The post training values of WHR were similar to the baseline values for all groups due to the loss of the adipose tissue being similar in both body areas. The ES achieved ranged between trivial and small for the MT and P groups and trivial for the T group.

Our results align with the studies that found a greater effect in reducing visceral adiposity than in reducing total body fat or body weight after applying different types of training protocols (Chin et al., 2016; Jakicic et al., 2019; Ohkawara et al., 2007; Shaw et al., 2006; Verheggen et al., 2016). The greatest results obtained in the MT group are also supported by previous studies that found greater positive effects on visceral fat in overweight and obese older adults after performing aerobic or concurrent training programs compared to strength or aerobic training alone (Arciero et al., 2006; Davidson et al., 2009; Ismail et al., 2011; Laird et al., 2014; Park et al., 2003; Schwingshackl et al., 2013; Vissers et al., 2013; Willis et al., 2012). In support of our results, Straight et al. (2012) found significant improvements of 5.2 cm and 5.3 cm in WC and HC, respectively, after eight weeks of resistance training in the only study to date that reported results for these parameters when the training program was performed with an elastic band. The exercise program was performed twice weekly and composed of three upper-body (i.e., chest press, shoulder press, and back row) and three lower-body (i.e., leg press, knee extension, and leg curl) exercises, and three sets of eight to 12 repetitions conducted for each exercise. The greater improvements shown in this study could be related to the poor baseline status of the subjects (i.e., higher baseline values in both WC and HC parameters) and because exercise was combined with dietary intervention.

Regarding the results for the MT and P groups, few previous studies have analyzed the effects of these training modalities on the anthropometric and cardiovascular risk in older adults. In support of our findings, Marques, Mota, Machado et al. (2011) found significant reductions of 4.7 cm in WC in older women after a 32-week program of progressive multi-component training performed twice weekly. The longer duration of the study could be behind the differences between the study by Marques, Mota, Machado et al. (2011) and ours. However, contrary to our results, Godoy-Izquierdo et al. (2017) failed to note an effect of a

20-week multi-component training performed three days a week on WC and WHR in postmenopausal women. The characteristics of the multi-component program were poorly described by the authors due to only revealed that included *"training for aerobic cardio-respiratory fitness, muscle resistance, and other fitness functions*" (Godoy-Izquierdo et al., 2017). It is difficult to determine why they did not find significant differences performing a multi-component program during the same period as ours and with an additional training session per week, but it seems that the characteristics of the subjects (i.e., postmenopausal vs older women) and the lower baseline values in WC (i.e., ~85 cm vs ~ 98cm) could be important factors. On the other hand, the results achieved by the P group align with the only previous study that analyzed the effects of this training modality, although in combination with traditional resistance training on the HC, WC and WHR. Coelho-Júnior et al. (2019) found significant reductions in WC (-3.3%), HC (-1.53%) and WHR (-2.2%) after 22 weeks, corroborating the findings from in our study.

The findings revealed by the three training modalities on the anthropometric measures are highly relevant because in older adults, and more markedly in older women (Perissinotto et al., 2002), visceral and ganoid fat tissues tend to increase. This increase of the adipose tissue in these regions is strongly related with several risk factors and diseases such as cardiovascular diseases (Prineas et al., 1993); insulin resistance (O'Leary et al., 2006); dyslipidemia (Hunter et al. 2010); Type 2 diabetes (Tiikkainen et al., 2002); metabolic syndrome (Lau et al. 2005); long-term morbidity (Ilich et al., 2014); and mortality (Tiikkainen et al., 2002). In addition, visceral fat has been linked with a negative impact on muscle tissue, favoring the catabolism process, reducing muscle strength and contributing to the development and progression of sarcopenia (Cesari, Kritchevsky, Baumgartner et al., 2005; Zhang et al., 2015).

Accordingly to the WHO (WHO, 2000), central obesity is characterized as a waist circumference greater than 88cm (Lean et al., 1995; Pi-Sunyer, 2000) or a waist to hip ratio >0.80 in women (Center for Disease Control and Prevention, 2011). In our second study, 85.2% of the sample was classified as obese and 95.6% as with obesity or overweight (130 of 136 subjects) taking the WC criteria into account . In all groups, the mean value of WC was higher than 88 cm, with the C group showing the greater values, followed by the P, MT and T groups. At the same time, the average values of WHR in all groups were above 0.80, which corroborates that the sample had high visceral fat values, characteristic of an obese population. On the other hand, the boundary health value of 0.5 for WHtR was suggested 20 years ago, conveying the simple message "keep your waist to less than half your height" to the population (Ashwell et al., 1996; Ashwell & Gibson, 2014). In addition, Ashwell and Gibson (2016) determined a WHtR <0.5 as "no increased risk," WHtR ≥0.5 and <0.6 as 'increased risk' and WHtR ≥0.6 as "very high risk" related to the cardiovascular risk. At baseline, all training groups presented a very high cardiovascular risk. At the end of the training program, all groups significantly decreased their values of WHtR, with the MT group went from having a very high cardiovascular risk to increased cardiovascular risk. The findings obtained in body composition and anthropometric parameters in our second study by the three training modalities in a short period of time are even more important taking into account the characteristics of the sample studied.

As was the case in our first study, several factors may have played a vital role in obtaining positive results regarding fat mass in all three training groups. The high attendance rate and compliance of the subjects in all the groups could be an important factor in achieving changes in body composition. In addition, the high sample size and the anthropometric characteristics of the sample could also be determinant factors due to our sample in the second study being predominantly overweight and obese. For instance, regarding the BMI,

75.8% (i.e., 103 of 136 subjects) of the sample were classified as overweight and obese, with the P, T and C groups having the highest percentage (i.e., 79.5% or 27 of 34 subjects) followed by the MT group (i.e., 64.8% or 22 of 34 subjects). Taking into account the total body fat percentage, this percentage increases to 83.9% for the sample (i.e., 114 of 136 subjects), 85.3% for the P and MT groups (i.e., 29 of 34 subjects) and 82.4% for the T and C groups (i.e., 28 of 34 subjects).

As in our first study, the prevalence of overweight and obese individuals in our second study was similar to the rate reported by Gomez-Cabello et al. (2001) in a Spanish population 65 years of age, according to their BMI values (84% vs 75.8%), but was higher in our study if we compare using the percentage of body fat (62.5% vs 91.5%). Our sample in the second study is again representative in terms of prevalence of obese and overweight individuals with respect to the target population of the study, especially if we take the BMI into account. If we take into account that 30.2% of the total sample was classified as sarcopenic, between 30–55% had sarcopenic obesity (according to the criteria selected), 82.3% presented osteopenic obesity and 23.6% showed osteosarcopenic obesity, the findings accomplished in our study of older women are highly relevant. In addition, in contrast to our first study, potential confounding variables such as nutrition intake and level of physical activity were recorded. We can confirm that the changes in body fat mass were mainly produced by the training programs since no changes were found between the initial and final values in the total energy intake, CHO or lipid macronutrients in any group. Moreover, no significant differences were found between groups in these parameters or in the levels of physical activity at the beginning of the study period.

In summary, the results obtained in our first and second studies revealed that resistance training performed at high and moderate intensities with an elastic band in a short or moderate training period is an effective strategy to improve the body composition of older

women by increasing fat-free mass, decreasing body fat tissue and improving anthropometric parameters and cardiovascular risk, obtaining greater improvements with moderate intensity, although without significant differences between intensities. In addition, multi-component and high-velocity resistance training are effective training modalities in reducing the total and visceral fat and therefore the cardiovascular risk in a short period of time. At the same time, both training strategies generated positive changes in the fat-free mass. It seems that the multi-component modality was the most efficient in terms of producing greater changes on total and regional (i.e., visceral and ganoid fat mass by the anthropometric index) body composition in older women compared to traditional resistance training and power strength training, although no significant changes between modalities were found except in the HC between multi-component and resistance training strategies, in favor of the former.

V.X. RESULTS ON MUSCLE STRENGTH

V.X.I. Project one

A. Hip

The changes in the isokinetic strength of the hip abductor and adductor muscles from the ITT analysis are displayed in Table 45. The repeated-measures ANOVA showed a main effect of time in hip abduction at 180°/s [$F(1, 90) = 8.16$, $p < 0.005$, $\eta^2p = 0.083$, $1\text{-}\beta = 0.807$], hip abduction 60°/s [$F(1, 90) = 28.10$, $p < 0.000$, $\eta^2p = 0.238$, $1\text{-}\beta = 0.999$], and hip adduction 60°/s [$F(1, 90) = 13.37$, $p < 0.000$, $\eta^2p = 0.129$, $1\text{-}\beta = 0.951$]. Pairwise comparisons revealed significant increases in all the hip parameters for the HI group with large ES in hip abduction 180°/s and 60°/s, moderate ES in hip adduction 60°/s, and small ES in hip adduction 180°/s. Additionally, the M group also significantly increased the parameters of hip abduction and adduction at 60°/s (trivial ES in both parameters). No significant changes by time were found in the C group. Furthermore, significant main effects of time × group interaction were found in hip abduction at 180°/s [$F(2, 90) = 6.08$, $p < 0.003$, $\eta^2p = 0.119$, $1\text{-}\beta = 0.877$], hip abduction 60°/s [$F(2, 90) = 13.65$, $p < 0.000$, $\eta^2p = 0.233$, $1\text{-}\beta = 0.998$], and hip adduction 60°/s [$F(2, 90) = 10.19$, $p < 0.000$, $\eta^2p = 0.185$, $1\text{-}\beta = 0.984$]. Differences were found in hip abduction at 180°/s between the M and C groups (moderate ES), hip adduction at 180°/s between both training groups and the C group (moderate ES), hip abduction at 60°/s between the M and C groups (moderate ES), and hip adduction at 60°/s between the HI and C groups (large ES). No significant differences were found between the training groups.

After controlling for baseline values and age, the ANCOVA showed a main effect of time in the same parameters with a similar magnitude of change, but it also indicated a significant difference by time in hip adduction at 180°/s in the M group (small ES). Additionally, after the adjustment, the ANCOVA revealed the same main significant group ×

time interactions but with new significant comparisons between groups. The differences were found in hip abduction at 180°/s between the HI and C groups (large ES), hip abduction at 60°/s between the HI and C groups (large ES), and hip adduction at 60°/s between the M and C groups (moderate ES).

The results of the PPA for the isokinetic strength of hip abductor and adductor parameters found changes similar to the ITT analysis but with some differences. After the applied ANOVA, the same significant changes by time were found as well as a significant difference in the M group in hip abduction at 180°/s (small ES). More differences between both analyses were found in the analysis between groups. The ANOVA revealed the same significant differences between groups as the ITT analysis but also significant differences between the M and H groups in hip abduction at 180°/s and 60°/s. After the ANCOVA analysis, no differences between the ITT and PPA were found, showing the same changes by time and the same time × group interactions. Additionally, the ES revealed after the ANOVA and ANCOVA tests with the PPA were also similar to those obtained with the ITT analysis. The results from the PPA are presented in Supplementary Material G (Table G.1).

Table 45. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Hip abd. 180°/s (N·m)	M	37.89	41.00 ± 28.91 (34.18–47.82)	46.30 ± 15.49 (41.48–51.11)	12.91	0.087 (0.23)	**0.042** (0.27)	M vs HI: 0.059 (0.53)	M vs HI: 1.000 (0.09)
	HI		25.76 ± 10.62 (19.68–31.84)	38.58 ± 13.83 (34.29–42.88)	49.78	**0.000** (1.04)	**0.000** (0.87)	M vs C: **0.029** (0.74)	M vs C: **0.000** (0.88)
	C		39.12 ± 12.62 (31.20–47.03)	36.48 ± 9.30 (30.89–42.07)	-6.73	0.460 (0.24)	0.924 (0.03)	HI vs C: 1.000 (0.17)	HI vs C: **0.001** (0.83)
Hip add. 180°/s (N·m)	M	47.28	49.42 ± 23.64 (42.29–56.54)	52.42 ± 20.40 (45.25–59.59)	6.08	0.255 (0.14)	0.226 (0.14)	M vs HI: 1.000 (0.03)	M vs HI: 1.000 (0.04)
	HI		44.81 ± 13.57 (38.45–51.16)	51.76 ± 19.66 (45.37–58.16)	15.52	**0.004** (0.41)	**0.001**(0.45)	M vs C: **0.021** (0.75)	M vs C: **0.028** (0.46)
	C		38.63 ± 23.48 (30.36–46.90)	37.17 ± 20.40 (28.84–45.49)	-3.78	0.633 (0.07)	0.373 (0.12)	HI vs C: **0.021** (0.73)	HI vs C: **0.011** (0.51)
Hip abd. 60°/s (N·m)	M	45.81	54.90 ± 32.83 (46.07–63.73)	67.92 ± 27.64 (59.73–76.11)	23.71	**0.000** (0.43)	**0.000** (0.5)	M vs HI: 0.096 (0.49)	M vs HI: 1.000 (0.12)
	HI		36.46 ± 18.92 (28.58–44.33)	55.88 ± 21.87 (48.58–63.19)	53.28	**0.000** (0.95)	**0.000** (0.82)	M vs C: **0.011** (0.79)	M vs C: **0.000** (0.67)
	C		52.86 ± 20.43 (42.60–63.11)	49.09 ± 16.93 (39.58–58.60)	-7.12	0.291 (0.2)	0.539 (0.1)	HI vs C: 0.790 (0.34)	HI vs C: **0.000** (0.93)
Hip add. 60°/s (N·m)	M	40.41	39.45 ± 12.98 (34.09–44.81)	45.72 ± 13.33 (39.99–51.46)	15.89	**0.002** (0.48)	**0.004** (0.42)	M vs HI: 0.548 (0.36)	M vs HI: 0.218 (0.32)
	HI		41.37 ± 11.62 (36.58–46.15)	50.91 ± 15.24 (45.80–56.03)	23.07	**0.000** (0.7)	**0.000** (0.75)	M vs C: 0.146 (0.53)	M vs C: **0.007** (0.54)
	C		40.08 ± 21.47 (33.85–46.31)	36.88 ± 20.32 (30.22–43.54)	-7.98	0.160 (0.15)	0.125 (0.16)	HI vs C: **0.004** (0.81)	HI vs C: **0.000** (0.78)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; abd: abduction; add: adduction; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

B. Knee

The changes in the isokinetic strength of knee flexor and extensor muscles from the ITT analysis are presented in Table 46. The repeated-measures ANOVA showed a main effect of time in knee extension at 180°/s [$F(1, 90) = 77.79$, $p < 0.000$, $\eta^2p = 0.464$, $1\text{-}\beta = 1$], knee flexion 180°/s [$F(1, 90) = 25.86$, $p < 0.000$, $\eta^2p = 0.223$, $1\text{-}\beta = 0.999$], knee extension 60°/s [$F(1, 90) = 47.39$, $p < 0.000$, $\eta^2p = 0.345$, $1\text{-}\beta = 1$], and knee flexion 60°/s [$F(1, 90) = 15.12$, $p < 0.000$, $\eta^2p = 0.144$, $1\text{-}\beta = 0.970$]. Pairwise comparisons revealed significant increases in all the isokinetic strength parameters of knee muscles for both training groups. The magnitudes of the changes for the HI group were large in all the variables except for knee flexion at 60°/s (moderate ES). For the M group, the ES achieved were moderate in all the parameters analyzed. No significant changes by time were found in the C group. Furthermore, significant main effects of time × group interaction were found in knee flexion at 180°/s [$F(2, 90) = 4.98$, $p < 0.009$, $\eta^2p = 0.100$, $1\text{-}\beta = 0.800$] and knee flexion at 60°/s [$F(2, 90) = 4.99$, $p < 0.009$, $\eta^2p = 0.100$, $1\text{-}\beta = 0.801$]. Differences were found in knee flexion at 180°/s and 60°/s between both training groups and the C group, achieving a large ES in all cases. No significant differences were found between the training groups. The ANCOVA showed the same significant effects by time and similar ES. The ANCOVA also revealed the following between groups interactions: knee extension at 180°/s [$F(2, 88) = 16.02$, $p < 0.000$, $\eta^2p = 0.267$, $1\text{-}\beta = 0.999$] and knee extension at 60°/s [$F(2, 88) = 18.008$, $p < 0.000$, $\eta^2p = 0.290$, $1\text{-}\beta = 1$]. New significant differences were found between the M and C groups in knee extension at 180°/s and 60°/s (moderate ES in both parameters) and between the HI and C groups in knee extension at 180°/s and 60°/s (large ES in both parameters). The results of the PPA found the same differences by time and a lack of differences between the M and C groups in knee flexion at 60°/s after the applied ANOVA and ANCOVA tests. The results from the PPA are presented in Supplementary Material G (Table G.2).

Table 46. *Intervention effects on isokinetic strength of knee flexor and extensor muscles form ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Knee ext. 180°/s (N·m)	M	40.98	44.24 ± 13.43 (39.59 –48.89)	55.48 ± 15.00 (50.19 –60.78)	25.41	**0.000** (0.79)	**0.000** (0.82)	M vs HI: 1.000 (0.17) M vs C: 0.124 (0.55) HI vs C: 0.391 (0.4)	M vs HI: 0.091 (0.39) M vs C: **0.001** (0.69) HI vs C: **0.000** (1.1)
	HI		34.59 ± 11.39 (30.45 –38.73)	52.98 ± 14.03 (48.27–57.70)	53.17	**0.000** (1.44)	**0.000** (1.35)		
	C		47.44 ± 14.95 (42.04–52.83)	47.03 ± 15.89 (40.89–53.18)	-0.86	0.851 (0.03)	0.635 (0.07)		
Knee flex. 180°/s (N·m)	M	35.12	34.13 ± 9.60 (30.83–37.44)	40.68 ± 12.21 (36.92–44.44)	19.17	**0.000** (0.6)	**0.000** (0.54)	M vs HI: 0.156 (0.47) M vs C: **0.008** (0.79) HI vs C: **0.000** (1.46)	M vs HI: 0.514 (0.28) M vs C: **0.011** (0.62) HI vs C: **0.000** (1.04)
	HI		38.16 ± 9.15 (35.22–41.10)	45.67 ± 9.31 (42.32–49.02)	19.68	**0.000** (0.81)	**0.000** (0.96)		
	C		31.30 ± 8.92 (27.46–35.13)	31.68 ± 9.99 (27.32–36.04)	1.24	0.836 (0.04)	0.301 (0.11)		
Knee ext. 60°/s (N·m)	M	71.15	74.76 ± 19.38 (67.07–82.45)	86.20 ± 20.74 (78.15–94.25)	15.30	**0.000** (0.57)	**0.000** (0.58)	M vs HI: 1.000 (0.1) M vs C: 0.076 (0.62) HI vs C: 0.136 (0.51)	M vs HI: 0.192 (0.26) M vs C: **0.000** (0.59) HI vs C: **0.000** (0.82)
	HI		66.38 ± 21.33 (59.52–73.24)	84.11 ± 22.10 (76.93–91.29)	26.71	**0.000** (0.82)	**0.000** (0.79)		
	C		74.38 ± 24.57 (65.44 –83.31)	72.06 ± 25.51 (62.72–81.41)	-3.11	0.368 (0.09)	0.455 (0.08)		
Knee flex. 60°/s (N·m)	M	40.52	39.89 ± 9.77 (36.20–43.59)	46.57 ± 12.53 (41.82–51.32)	16.73	**0.001** (0.59)	**0.002** (0.57)	M vs HI: 0.518 (0.31) M vs C: **0.023** (0.85) HI vs C: **0.000** (1.05)	M vs HI: 1.000 (0.18) M vs C: **0.026** (0.7) HI vs C: **0.002** (0.78)
	HI		42.81 ± 10.77 (39.51–46.10)	50.97 ± 15.23 (46.73–55.20)	19.06	**0.000** (0.62)	**0.000** (0.67)		
	C		37.49 ± 10.37 (33.20–41.78)	36.58 ± 10.48 (31.07–42.10)	-2.42	0.699 (0.09)	0.449 (0.17)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs).Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ext: extension; flex: flexion; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.

C. Elbow

The changes in the isokinetic strength of elbow flexor and extensor muscles from the ITT analysis are displayed in Table 47. The repeated-measures ANOVA showed a main effect of time in elbow extension at 180°/s [$F(1, 90) = 57.76$, $p < 0.000$, $\eta^2p = 0.391$, 1-β = 1], elbow flexion 180°/s [$F(1, 90) = 21.13$, $p < 0.000$, $\eta^2p = 0.190$, 1-β = 0.995], elbow extension 60°/s [$F(1, 90) = 69.58$, $p < 0.000$, $\eta^2p = 0.436$, 1-β = 1], and elbow flexion 60°/s [$F(1, 90) = 20.55$, $p < 0.000$, $\eta^2p = 0.186$, 1-β = 0.994]. Pairwise comparisons revealed significant increases in all the isokinetic strength variables of elbow muscles for both training groups. The magnitudes of the changes of the HI group were large in all the variables except for elbow flexion at 60°/s (moderate ES). For the M group, the ES achieved were moderate in elbow extension at 180°/s and 60°/s and large in elbow flexion at 180°/s and 60°/s. Furthermore, the significant main effects of time × group interaction were found in elbow flexion at 180°/s [$F(2, 90) = 8.12$, $p < 0.001$, $\eta^2p = 0.153$, 1-β = 0.953], elbow extension 60°/s [$F(2, 90) = 15.97$, $p < 0.000$, $\eta^2p = 0.262$, 1-β = 0.999], and elbow flexion 60°/s [$F(2, 90) = 6.09$, $p < 0.003$, $\eta^2p = 0.119$, 1-β = 0.877]. The significant differences between groups were found between both training groups and the C group in these parameters, with large ES except between M and C groups in elbow flexion at 60°/s (moderate ES). No significant differences between the training groups were found. The ANCOVA showed the same significant effects by time and similar ES. The ANCOVA also revealed, along with the same between effects interactions, a main significant group × time interaction in elbow extension at 180°/s [$F(2, 88) = 10.46$, $p < 0.000$, $\eta^2p = 0.192$, 1-β = 0.986]. This difference was found between both training groups and the C group (moderate and large ES). The results of the PPA were similar to the ITT analysis, with the same changes except for a significant difference between the HI and C groups in elbow extension at 180°/s after the ANOVA. The results from the PPA are presented in Supplementary Material G (Table G.3).

Table 47. *Intervention effects on isokinetic strength of elbow flexor and extensor muscles from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Elbow ext. 180°/s (N·m)	M	27.69	29.76 ± 9.94 (27.10–32.42)	35.21 ± 8.11 (32.54–37.89)	18.33	**0.000** (0.6)	**0.000** (0.68)	M vs HI: 1.000 (0.05) M vs C: 0.217 (0.51) HI vs C: 0.274 (0.47)	M vs HI: 0.110 (0.42) M vs C: **0.022** (0.62) HI vs C: **0.000** (1.1)
	HI		23.79 ± 5.40 (21.42–26.16)	34.82 ±7.61 (32.44–37.21)	46.37	**0.000** (1.67)	**0.000** (1.44)		
	C		31.52 ± 6.51 (28.43–34.61)	31.46 ± 6.36 (28.35–34.57)	-0.21	0.963 (0.01)	0.237 (0.24)		
Elbow flex. 180°/s (N·m)	M	15.36	14.31 ± 4.65 (12.46–16.16)	20.10 ± 8.09 (17.66–22.54)	40.42	**0.000** (0.88)	**0.000** (0.75)	M vs HI: 1.000 (0.16) M vs C: **0.004** (0.89) HI vs C: **0.000** (1.22)	M vs HI: 1.000 (0.09) M vs C: **0.001** (0.9) HI vs C: **0.000** (1.13)
	HI		16.50 ± 4.86 (14.85–18.15)	21.29 ± 6.58 (19.11–23.47)	29.04	**0.000** (0.83)	**0.000** (0.97)		
	C		14.84 ± 6.29 (12.69–16.99)	13.82 ± 5.20 (10.99–16.65)	-6.85	0.457 (0.18)	0.301 (0.23)		
Elbow ext. 60°/s (N·m)	M	30.85	33.33 ± 11.18 (30.26–36.40)	41.50 ± 9.91 (38.42–44.59)	24.51	**0.000** (0.77)	**0.000** (0.86)	M vs HI: 1.000 (0.14) M vs C: **0.003** (0.95) HI vs C: **0.011** (0.86)	M vs HI: 0.691 (0.23) M vs C: **0.001** (0.89) HI vs C: **0.000** (1.24)
	HI		27.73 ± 7.43 (25.00–30.47)	40.17 ± 8.72 (37.42–42.92)	44.83	**0.000** (1.53)	**0.000** (1.38)		
	C		32.78 ± 6.07 (29.22–36.35)	33.36 ± 6.30 (29.79–36.94)	1.78	0.727 (0.09)	0.338 (0.23)		
Elbow flex. 60°/s (N·m)	M	16.23	14.56 ± 4.46 (12.63–16.49)	20.40 ± 7.82 (18.19–22.61)	40.09	**0.000** (0.92)	**0.000** (0.73)	M vs HI: 1.000 (0.17) M vs C: **0.008** (0.76) HI vs C: **0.001** (1.22)	M vs HI: 1.000 (0) M vs C: **0.002** (0.78) HI vs C: **0.002** (1.04)
	HI		18.10 ± 5.77 (16.38–19.83)	21.47 ± 4.97 (19.50–23.44)	18.59	**0.001** (0.62)	**0.000** (0.86)		
	C		15.31 ± 5.93 (13.07–17.56)	15.14 ± 5.49 (12.58–17.70)	-1.14	0.894 (0.03)	0.529 (0.13)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ext: extension; flex: flexion; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70

V.X.II. Project two

A. Hip

The changes in the isokinetic strength of hip abductor and adductor muscles from the ITT analysis are displayed in Table 48. The repeated-measures ANOVA showed a main effect of time in hip abduction at 180°/s [$F(1, 132) = 37.15$, $p < 0.000$, $\eta^2p = 0.220$, $1\text{-}\beta = 1$], hip adduction 180°/s [$F(1, 132) = 36.79$, $p < 0.000$, $\eta^2p = 0.218$, $1\text{-}\beta = 1$], hip abduction 60°/s [$F(1, 132) = 11.08$, $p < 0.001$, $\eta^2p = 0.077$, $1\text{-}\beta = 0.911$], and hip adduction 60°/s [$F(1, 132) = 21.37$, $p < 0.000$, $\eta^2p = 0.139$, $1\text{-}\beta = 0.996$]. Pairwise comparisons revealed significant increases in hip abduction at 180°/s and hip adduction at 180°/s and 60°/s for all training groups with an ES ranging from small to large. Additionally, the T group indicated a significant change in hip abduction at 60°/s (moderate ES). Furthermore, significant main effects of time × group interaction were found in hip abduction at 180°/s [$F(3, 132) = 8.27$, $p < 0.000$, $\eta^2p = 0.158$, $1\text{-}\beta = 0.991$], hip abduction 180°/s [$F(3, 132) = 10.43$, $p < 0.000$, $\eta^2p = 0.192$, $1\text{-}\beta = 0.999$], hip abduction 60°/s [$F(3, 132) = 3.82$, $p < 0.012$, $\eta^2p = 0.080$, $1\text{-}\beta = 0.809$], and hip adduction 60°/s [$F(3, 132) = 4.66$, $p < 0.004$, $\eta^2p = 0.096$, $1\text{-}\beta = 0.886$]. Differences were found in hip abduction and adduction at 180°/s between the P group and the rest of the groups (moderate and large ES), hip abduction at 60°/s between the three training groups and the C group (moderate and large ES), and hip adduction at 60°/s between the P and T groups compared to the C group (trivial and moderate ES). The ANCOVA demonstrated the same significant differences by time, and also a significant difference in the P and MT groups on hip abduction at 60°/s with the same main significant group × time interactions. However, the ANCOVA also indicated a significant difference between the T and C groups in hip adduction at 180°/s. The lack of significant difference between the P and C groups in hip adduction at 60°/s was the only difference between the PPA and ITT analysis. The results from the PPA are presented in Supplementary Material H (Table H.1)

Table 48. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Hip abd. 180°/s (N·m)	MT	12.8	12.07 ± 5.92 (9.65–14.50)	15.07 ± 6.19 (12.20–17.95)	24.84	**0.013** (0.49)	**0.012** (0.49)	MT vs P: **0.005** (0.76)	MT vs P: **0.006** (0.6)
	P		13.84 ± 8.09 (11.42–16.27)	22.05 ± 11.42 (19.18–24.93)	59.28	**0.000** (0.83)	**0.000** (0.86)	MT vs T: 1.000 (0.2)	MT vs T: 1.000 (0.05)
	T		13.05 ± 8.17 (10.62–15.47)	16.50 ± 7.86 (13.63–19.37)	26.46	**0.004** (0.43)	**0.005** (0.41)	MT vs C: 0.935 (0.43)	MT vs C: 0.336 (0.46)
	C		12.25 ± 6.06 (9.83–14.68)	12.14 ± 7.48 (9.27–15.02)	-0.89	0.928 (0.02)	0.867 (0.03)	P vs T: **0.046** (0.57)	P vs T: **0.012** (0.52)
								P vs C: **0.000** (1.03)	P vs C**: 0.000** (0.9)
								T vs C: 0.215 (0.57)	T vs C: 0.207 (0.46)
Hip add. 180°/s (N·m)	MT	4.29	4.43 ± 3.29 (3.58–5.27)	6.07 ± 4.47 (4.73–7.42)	37.16	**0.008** (0.42)	**0.007** (0.42)	MT vs P: **0.043** (0.6)	MT vs P: **0.014** (0.61)
	P		4.41 ± 2.20 (3.57–5.26)	8.70 ± 4.2 (7.35–10.04)	97.07	**0.000** (1.27)	**0.000** (1.28)	MT vs T: 1.000 (0.08)	MT vs T: 1.000 (0.05)
	T		3.77 ± 2.47 (2.92–4.61)	5.73 ± 4.58 (4.39–7.08)	52.18	**0.002** (0.53)	**0.003** (0.51)	MT vs C: 0.224 (0.59)	MT vs C: 0.088 (0.61)
	C		4.57 ± 1.73 (3.73–5.42)	4.06 ± 1.91 (2.72–5.40)	-11.30	0.396 (0.28)	0.450 (0.25)	P vs T: **0.015** (0.67)	P vs T: **0.031** (0.56)
								P vs C: **0.000** (0.67)	P vs C**: 0.000** (1.46)
								T vs C: 0.497 (1.42)	T vs C: **0.050** (0.66)
Hip abd. 60°/s (N·m)	MT	58.53	62.96 ± 21.42 (54.03–71.90)	68.76 ± 25.02 (59.65–77.88)	9.21	0.190 (0.25)	**0.043** (0.35)	MT vs P: 1.000 (0.02)	MT vs P: 1.000 (0)
	P		61.29 ± 28.64 (52.35–70.22)	68.21 ± 28.29 (59.10–77.33)	11.30	0.118 (0.24)	**0.040** (0.29)	MT vs T: 1.000 (0.26)	MT vs T: 0.768 (0.31)
	T		59.12 ± 26.17 (50.19–68.06)	76.01 ± 30.64 (66.89–85.13)	28.55	**0.000** (0.59)	**0.000** (0.59)	MT vs C: **0.034** (0.76)	MT vs C: 0.221 (0.5)
	C		50.76 ± 28.46 (41.83–59.70)	50.44 ± 22.87 (41.32–59.56)	-0.64	0.941 (0.01)	0.343 (0.15)	P vs T: 1.000 (0.26)	P vs T: 0.740 (0.29)
								P vs C: **0.044** (0.69)	P vs C: 0.211 (0.46)
								T vs C: **0.001** (0.95)	T vs C: **0.002** (0.76)
Hip add. 60°/s (N·m)	MT	40.99	39.72 ± 13.56 (34.11–45.33)	46.17 ± 14.75 (40.52–51.82)	16.23	**0.001** (0.45)	**0.001** (0.45)	MT vs P: 1.000 (0.12)	MT vs P: 1.000 (0.03)
	P		42.82 ± 19.40 (37.22–48.43)	48.23 ± 18.49 (42.58–53.88)	12.63	**0.006** (0.29)	**0.002** (0.31)	MT vs T: 1.000 (0.35)	MT vs T: 1.000 (0.11)
	T		43.90 ± 16.49 (38.29–49.50)	51.62 ± 16.50 (45.97–57.27)	17.60	**0.000** (0.47)	**0.000** (0.49)	MT vs C: 0.071 (0.66)	MT vs C: **0.006** (0.56)
	C		37.50 ± 16.13 (31.89–43.11)	35.86 ± 16.64 (30.21–41.51)	-4.37	0.400 (0.1)	0.204 (0.14)	P vs T: 1.000 (0.19)	P vs T: 1.000 (0.13)
								P vs C**: 0.016** (0.19)	P vs C: **0.013** (0.46)
								T vs C: **0.001** (0.7)	T vs C: **0.001** (0.63)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: *n* = 34. MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; abd: abduction; add: adduction; ES: effect size; Δ%: percentage of change;a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

B. Knee

The changes in the isokinetic strength of knee flexor and extensor muscles from the ITT analysis are presented in Table 49. The repeated-measures ANOVA showed a main effect of time in knee extension at 180°/s [$F(1, 132) = 38.24$, $p < 0.000$, $\eta 2p = 0.225$, $1\text{-}\beta = 1$], knee flexion 180°/s [$F(1, 132) = 38.24$, $p < 0.000$, $\eta^2p = 0.225$, $1\text{-}\beta = 1$], knee extension 60°/s [$F(1, 132) = 29.45$, $p < 0.000$, $\eta^2p = 0.182$, $1\text{-}\beta = 1$], and knee flexion 60°/s [$F(1, 132) = 14.65$, $p < 0.000$, $\eta^2p = 1.000$, $1\text{-}\beta = 0.967$]. Pairwise comparisons revealed significant increases in all the isokinetic strength parameters of the knee muscles for all training groups. The magnitude of the changes ranged from trivial to moderate. No significant changes by time were found in the C group. Furthermore, significant main effects of time × group interaction were found in knee extension at 180°/s [$F(1, 132) = 38.24$, $p < 0.000$, $\eta^2p = 0.225$, $1\text{-}\beta = 1$], knee flexion 180°/s [$F(3, 132) = 4.88$, $p < 0.003$, $\eta^2p = 0.100$, $1\text{-}\beta = 0.901$], knee extension 60°/s [$F(1, 132) = 29.45$, $p < 0.000$, $\eta^2p = 0.182$, $1\text{-}\beta = 1$], and knee flexion 60°/s [$F(1, 132) = 14.65$, $p < 0.000$, $\eta^2p = 1.000$, $1\text{-}\beta = 0.967$]. Significant differences between groups were found in knee extension at 180°/s between the P and C groups (small ES), knee flexion at 180°/s between all the training groups and the C group (large ES), knee extension at 60°/s between the T and C groups (small ES), and finally in knee flexion at 60°/s when comparing the MT and T groups to the C group (large ES). No significant differences between the training groups were found. The ANCOVA showed the same significant effects by time and time × group interactions as the ANOVA, also demonstrating similar ES. The results of the PPA found the same differences by time after the ANOVA and ANCOVA tests. The lack of significant differences between the MT and C groups in knee extension at 180°/s and the significant difference between the P and C groups in knee flexion at 60°/s after ANCOVA were the only differences from the ITT analysis. The results from the PPA are presented in Supplementary Material H (Table H.2).

Table 49. *Intervention effects on isokinetic strength of knee flexor and extensor muscles from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Knee ext. 180°/s (N·m)	MT	50.43	52.39 ± 13.49 (25.11–30.56)	56.39 ± 13.31 (27.62–33.11)	7.62	**0.009** (0.3)	**0.004** (0.32)	MT vs P: 1.000 (0.16)	MT vs P: 0.107 (0.38)
	P		49.10 ± 13.48 (23.56–29.01)	58.50 ± 12.60 (29.16–34.65)	19.12	**0.000** (0.72)	**0.000** (0.7)	MT vs T: 1.000 (0.05)	MT vs T: 1.000 (0.02)
	T		51.65 ± 10.78 (26.27–31.72)	55.76 ± 10.94 (29.03–34.52)	7.95	**0.007** (0.38)	**0.002** (0.42)	MT vs C: 0.238 (0.46)	MT vs C: 0.433 (0.25)
	C		48.57 ± 16.14 (21.64–27.08)	49.63 ± 16.21 (21.04–26.52)	2.19	0.480 (0.07)	0.669 (0.04)	P vs T: 1.000 (0.23)	P vs T: 0.146 (0.39)
								P vs C: **0.044** (0.23)	P vs C: **0.000** (0.59)
								T vs C: 0.371 (0.61)	T vs C: 0.328 (0.28)
Knee flex. 180°/s (N·m)	MT	26.87	27.83 ± 7.38 (47.78–57.01)	30.37 ± 7.00 (51.84–60.94)	9.11	**0.029** (0.35)	**0.006** (0.41)	MT vs P: 1.000 (0.2)	MT vs P: 0.644 (0.32)
	P		26.29 ± 7.92 (44.49–53.72)	31.90 ± 8.07 (53.95–63.04)	21.36	**0.000** (0.7)	**0.000** (0.68)	MT vs T: 1.000 (0.19)	MT vs T: 1.000 (0.06)
	T		28.99 ± 7.17 (47.03–56.27)	31.77 ± 7.91 (51.21–60.31)	9.60	**0.017** (0.37)	**0.002** (0.45)	MT vs C: **0.006** (0.8)	MT vs C: **0.027** (0.53)
	C		24.36 ± 9.44 (43.95–53.19)	23.78 ± 9.21 (45.08–54.18)	-2.38	0.614 (0.06)	0.191 (0.15)	P vs T: 1.000 (0.02)	P vs T: 1.000 (0.25)
								P vs C: **0.000** (0.94)	P vs C: **0.000** (0.79)
								T vs C: **0.000** (0.93)	T vs C: **0.013** (0.56)
Knee ext. 60°/s (N·m)	MT	87.01	89.88 ± 18.16 (39.48–46.25)	94.07 ± 21.84 (42.21–48.82)	4.66	**0.015** (0.21)	**0.012** (0.22)	MT vs P: 1.000 (0.21)	MT vs P: 1.000 (0.04)
	P		84.14 ± 19.02 (38.01–44.79)	89.67 ± 21.11 (39.35–45.96)	6.57	**0.001** (0.28)	**0.002** (0.27)	MT vs T: 1.000 (0.27)	MT vs T: 0.427 (0.22)
	T		90.90 ± 20.31 (40.44–47.22)	99.46 ± 18.42 (44.44–51.05)	9.43	**0.000** (0.44)	**0.000** (0.46)	MT vs C: 0.247 (0.46)	MT vs C: 0.400 (0.19)
	C		83.12 ± 24.41 (34.95–41.72)	83.28 ± 24.51 (34.13–40.74)	0.19	0.924 (0.01)	0.952 (0)	P vs T: 0.381 (0.49)	P vs T: 0.904 (0.18)
								P vs C: 1.000 (0.49)	P vs C: 0.151 (0.24)
								T vs C: **0.015** (0.28)	T vs C**: 0.002** (0.41)
Knee flex. 60°/s (N·m)	MT	41.61	42.87 ± 8.27 (82.89–96.88)	45.52 ± 8.94 (86.75–101.40)	6.18	**0.004** (0.31)	**0.001** (0.36)	MT vs P: 1.000 (0.3)	MT vs P: 0.728 (0.2)
	P		41.40 ± 10.06 (77.14–91.13)	42.65 ± 10.18 (82.35–96.99)	3.03	0.168 (0.12)	0.168 (0.12)	MT vs T: 1.000 (0.25)	MT vs T: 1.000 (0.11)
	T		43.83 ± 10.19 (83.90–97.89)	47.75 ± 9.19 (92.14–106.79)	8.93	**0.000** (0.4)	**0.000** (0.42)	MT vs C: **0.005** (0.83)	MT vs C**: 0.002** (0.46)
	C		38.33 ± 11.19 (76.13–90.12)	37.43 ± 10.53 (75.96–90.61)	-2.35	0.321 (0.08)	0.109 (0.13)	P vs T: 0.198 (0.52)	P vs T: 0.121 (0.3)
								P vs C: 0.173 (0.5)	P vs C: 0.213 (0.25)
								T vs C**: 0.000** (1.04)	T vs C: **0.000** (0.55)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: *n* = 34.MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; flex: flexion; ext: extension; ES: effect size; Δ%: percentage of change;a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

C. Elbow

The changes in isokinetic strength of elbow flexor and extensor muscles from the ITT analysis are displayed in Table 50. The repeated-measures ANOVA showed a main effect of time in elbow extension at 180°/s [$F(1, 132) = 48.32$, $p < 0.000$, $\eta^2p = 0.268$, $1\text{-}\beta = 1$], elbow flexion 180°/s [$F(1, 132) = 21.93$, $p < 0.000$, $\eta^2p = 0.143$, $1\text{-}\beta = 0.996$], elbow extension 60°/s [$F(1, 132) = 21.08$, $p < 0.000$, $\eta^2p = 0.138$, $1\text{-}\beta = 0.995$], and elbow flexion 60°/s [$F(1, 132) = 83.20$, $p < 0.000$, $\eta^2p = 0.387$, $1\text{-}\beta = 1$]. Pairwise comparisons revealed significant increases in all the isokinetic strength parameters of the elbow muscles for all training groups, excepting the MT group in elbow extension at 60°/s. The magnitudes of the changes ranged from small to large. No significant changes by time were found in the C group. Furthermore, significant main effects of time × group interaction were found in elbow extension at 180°/s [$F(3, 132) = 14.13$, $p < 0.000$, $\eta^2p = 0.243$, $1\text{-}\beta = 1$], elbow flexion 180°/s [$F(3, 132) = 12.15$, $p < 0.000$, $\eta^2p = 0.216$, $1\text{-}\beta = 1$], elbow extension 60°/s [$F(1, 132) = 21.08$, $p < 0.000$, $\eta^2p = 0.138$, $1\text{-}\beta = 0.995$], and elbow flexion 60°/s [$F(1, 132) = 83.20$, $p < 0.000$, $\eta^2p = 0.387$, $1\text{-}\beta = 1$]. The significant differences between groups were found between all the training groups and the C group in elbow flexion at 60°/s (moderate and large ES), the P and T groups and the C group in elbow extension at 180°/s (trivial and moderate ES), the T and C groups in elbow extension 60°/s (small ES), and the P and T groups and the C group in elbow flexion at 180°/s (moderate and large ES), as well as the training groups (MT vs P, large ES). After adjusting for baseline values and age, the ANCOVA showed the same significant effects by time and similar ES. The ANCOVA also revealed, along with the same main significant group × time interactions, significant differences between the P group and the MT and T groups in elbow extension at 180°/s (small and moderate ES), the MT and C groups in elbow flexion at 180°/s (moderate ES), and the P and C groups in elbow extension at 60°/s (small ES). The results of the PPA were similar to the ITT analysis but with several

different findings. After the ANOVA, the same changes by time were found. Additionally, the differences between the T and C groups in elbow extension at 180°/s disappeared, but a significant difference between the P and T groups was found in the same parameter. The rest of the time × group interactions were maintained after the applied ANOVA tests. Regarding the ANCOVA results in the PPA, the same differences by time were found, as well as similar ES. The differences between the groups were also strikingly similar, with only a new significant difference between the P and T groups in elbow extension at 180°/s compared with the ITT analysis. The results from the PPA are presented in Supplementary Material H (Table H.3).

Table 50. *Intervention effects on isokinetic strength of elbow flexor and extensor muscles from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Elbow ext. 180°/s (N·m)	MT	25.91	25.17 ± 6.76 (1.53–4.12)	26.81 ± 6.79 (3.04–5.23)	6.53	**0.011** (0.24)	**0.019** (0.22)	MT vs P: 0.337 (0.46)	MT vs P: **0.000** (0.5)
	P		24.96 ± 7.90 (1.64–4.24)	30.36 ± 8.43 (5.16–7.35)	21.66	**0.000** (0.66)	**0.000** (0.65)	MT vs T: 0.261 (0.6)	MT vs T: 1.000 (0.17)
	T		28.35 ± 5.86 (3.23–5.82)	30.57 ± 5.57 (4.48–6.67)	7.83	**0.001** (0.39)	**0.000** (0.45)	MT vs C: 1.000 (0.25)	MT vs C: 0.154 (0.25)
	C		25.16 ± 9.19 (3.08–5.67)	24.77 ± 9.10 (2.31–4.50)	-1.55	0.541 (0.04)	0.423 (0.06)	P vs T: 1.000 (0.03)	P vs T: **0.016** (0.38)
								P vs C**: 0.017** (0.03)	P vs C: **0.000** (0.66)
								T vs C: **0.012** (0.64)	T vs C: **0.005** (0.41)
Elbow flex. 180°/s (N·m)	MT	3.67	2.82 ± 1.56 (1.53–4.12)	4.14 ± 2.29 (3.04–5.23)	46.51	**0.010** (0.67)	**0.031** (0.47)	MT vs P: **0.047** (0.94)	MT vs P: **0.003** (0.92)
	P		2.94 ± 1.82 (1.64–4.24)	6.25 ± 2.22 (5.16–7.35)	112.49	**0.000** (1.63)	**0.000** (1.48)	MT vs T: 0.416 (0.35)	MT vs T: 1.000 (0.13)
	T		4.53 ± 5.32 (3.23–5.82)	5.57 ± 5.34 (4.48–6.67)	23.04	**0.039** (0.2)	**0.001** (0.27)	MT vs C: 1.000 (0.36)	MT vs C**: 0.049** (0.78)
	C		4.37 ± 4.92 (3.08–5.67)	3.40 ± 1.73 (2.31–4.50)	-22.11	0.056 (0.26)	0.106 (0.18)	P vs T: 1.000 (0.17)	P vs T: 0.065 (0.38)
								P vs C: **0.002** (1.43)	P vs C: **0.000** (1.84)
								T vs C: **0.039** (0.55)	T vs C: **0.003** (0.54)
Elbow ext. 60°/s (N·m)	MT	9.55	7.99 ± 2.70 (31.65–38.58)	10.87 ± 4.52 (33.39–40.52)	36.09	**0.000** (0.77)	**0.000** (0.71)	MT vs P: 1.000 (0.11)	MT vs P: 1.000 (0.04)
	P		8.86 ± 5.42 (30.33–37.26)	11.45 ± 5.67 (35.35–42.48)	29.16	**0.000** (0.47)	**0.000** (0.44)	MT vs T: **0.005** (0.86)	MT vs T**: 0.020** (0.47)
	T		10.51 ± 7.16 (33.04–39.97)	15.63 ± 6.33 (39.26–46.39)	48.71	**0.000** (0.76)	**0.000** (0.78)	MT vs C: 1.000 (0.09)	MT vs C: 0.154 (0.36)
	C		10.83 ± 5.49 (33.35–40.28)	11.34 ± 6.14 (31.79–38.92)	4.64	0.410 (0.09)	0.228 (0.12)	P vs T: **0.018** (0.7)	P vs T: **0.008** (0.46)
								P vs C: 1.000 (0.02)	P vs C: 0.253 (0.29)
								T vs C: **0.014** (0.69)	T vs C: **0.000** (0.72)
Elbow flex. 60°/s (N·m)	MT	35.56	35.11 ± 9.61 (6.14–9.84)	36.96 ± 6.39 (8.94–12.81)	5.25	0.154 (0.23)	0.133 (0.23)	MT vs P: 1.000 (0.21)	MT vs P: 0.662 (0.3)
	P		33.79 ± 9.24 (7.01–10.71)	38.92 ± 11.67 (9.51–13.38)	15.16	**0.000** (0.49)	**0.000** (0.44)	MT vs T: 0.138 (0.78)	MT vs T: 0.069 (0.6)
	T		36.51 ± 8.97 (8.66–12.35)	42.82 ± 8.48 (13.69–17.57)	17.29	**0.000** (0.72)	**0.000** (0.73)	MT vs C: 1.000 (0.15)	MT vs C: 0.545 (0.27)
	C		36.82 ± 12.59 (8.99–12.68)	35.35 ± 13.89 (9.40–13.27)	-3.98	0.257 (0.11)	0.376 (0.08)	P vs T: 0.768 (0.38)	P vs T: 1.000 (0.17)
								P vs C: 0.989 (0.38)	P vs C: **0.008** (0.45)
								T vs C: **0.024** (0.28)	T vs C: **0.000** (0.65)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: n = 34. MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; flex: flexion; ext: extension; ES: effect size; Δ%: percentage of change;a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97

V.XI. DISCUSSION ON MUSCLE STRENGTH

To the best of our knowledge, the studies presented in this Ph.D. dissertation are the first to investigate the effects of two key training parameters (i.e., intensity and modality training) using an elastic variable resistance during a medium to long training period (i.e., 20 and 32 weeks) on muscle strength of upper and lower limbs throughout the analysis of the isokinetic strength of hip abductor and adductor muscles, knee flexor and extensor muscles and elbow flexor and extensor muscles at low and high velocities in older women.

Regarding the intensity, the main and novel finding of the first study was that both training intensities effectively increase the muscle strength of the upper and lower limbs at low and high velocities after eight months of resistance training with elastic bands in older women because they achieved significant improvements in most of the analyzed parameters. Although there are no significant differences between training intensities, it seems that high-intensity achieve better results at the hip, knee and elbow joints in most of the concentric movements analyzed (i.e., abduction and adduction of hip, flexion and extension of knee and elbow) at both velocities. However, the progressive elastic resistance training at moderate intensity results in a higher increase of strength at the elbow flexion muscles when the task is performed at high velocities. Both training groups achieved significant differences from the C group in all the parameters analyzed.

Furthermore, regarding the training modality, the main and novel finding of the second study was that all training modalities analyzed (i.e., multi-component, power strength training and traditional high-intensity resistance training) effectively increase the muscle strength of upper and lower limbs at low and high velocities after a training period of five month in older women because they achieved significant improvements in most of the parameters analyzed. Power strength training seems to be the most useful strategy for improving strength at high speeds in all the joints, but especially at the hip and elbow

muscles since significant differences were found from the rest of the training modalities. In addition, traditional high-intensity resistance training achieved the greatest adaptations in muscle strength at lower velocities at the hip, knee and elbow joints in all the concentric movements analyzed (i.e., abduction and adduction of hip, flexion and extension of knee and elbow). All the training regimens achieved significant differences from the C group in most of the parameters analyzed.

We hypothesized in H7 (Chapter III, Section III.I.III.) that both training intensities improve upper and lower limb muscle strength at low and high velocities after a 32-week program of progressive resistance training with elastic bands, with the high intensity producing greater effects than the moderate intensity at both velocities and in all the muscle groups assessed. Our findings largely confirmed this hypothesis, as we found that both training intensities significantly improved the muscle strength of upper limbs at low and high velocities, which is reflected in strength gains in the elbow flexor and extensor muscles and in the lower limbs by improving the strength of the knee flexor and extensor muscles and the hip abductor and adductor muscles. In addition, there were no significant differences between the training intensities although the HI group produced greater effects. Next, we hypothesized in H10 (Chapter III, Section III.I.III.) that at the end (32 weeks) and at the midpoint (16 weeks) of the intervention period, there are differences between the training intensity groups in the parameters analyzed. However, our findings refuted these hypotheses because we did not find significant differences between the training groups.

Regarding the influence of the training modality, we hypothesized in H7 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) improve the upper and lower limb muscle strength at low and high velocities after an intervention period of 20 weeks using elastic resistance, with power training producing greater effects at high velocities than multi-

component and high-intensity resistance training in all the muscle groups assessed and high-intensity resistance training achieving greater results than power and multi-component training at low velocities in all the muscle groups assessed. Our findings largely confirmed this hypothesis, as all training modalities significantly improved the muscle strength of upper and lower limbs at low and high velocities by significantly improving the muscle strength of the elbow and knee flexor and extensor muscles and of the hip abductor and adductor muscles. In addition, power training produced greater effects at high velocities than multi-component and high-intensity resistance training in all the muscle groups assessed, while high-intensity resistance training achieved greater results than power and multi-component training at low velocities in all the muscle groups evaluated. Next, we hypothesized in H10 (Chapter III, Section III.II.III.) that at the end of the 20-week intervention period, there are differences between the training modalities groups in the parameters analyzed. Our findings partially confirmed this hypothesis, as we found significant differences between the power strategy and the rest of training modalities analyzed in the results obtained in muscle strength at high velocities in the hip (i.e., both abductor and adductor) and elbow (i.e., both flexor and extensor) muscles. However, in the rest of the parameters, no significant differences were found between training groups.

V.XI.I. Specific discussion of the first project

The findings reported in the first study by both training groups regarding the improvements in muscle strength align with previous high quality and robust evidence from systematic reviews (Hunter et al., 2004; Latham et al., 2004; Liu, & Latham, 2009; Theodorakopoulos et al., 2017; Theou et al., 2011); meta-analyses (Borde et al., 2015; Boutros et al., 2019; Buch et al., 2017; Csapo & Alegre, 2016; de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Guizeli et al., 2018; Martins et al., 2013; Peterson et al., 2010; Raymond et al., 2013; Silva et al., 2014; Steib et al., 2010; Stewart et al., 2014;

Straight et al., 2016; Yoshimura et al., 2017)**;** and even an umbrella review (Beckwée et al., 2019) that concluded that resistance training interventions are effective for combating age-related declines in muscle strength in older adults by promoting improvements in muscle strength.

The improvements showed by two training groups in our first study also support the findings obtained by Peterson and colleagues (Peterson et al., 2010), who found that resistance training produces positive effects on muscle strength outcomes of both the upper and the lower limbs. The authors reported in their meta-analysis an improvement regarding the percentage of change of 29 ± 2, 24 ± 2, 33 ± 3 and 25 ± 2, respectively for leg press, chest press, knee extension and lateral pull among adults >50 years, and with strength increases ranging from 9.8–31.6 kg (Peterson et al., 2010). Although these results are related to the increase in the total load assessed by 1RM test, the improvements reported in our study, particularly in the HI group, were similar, with percentages of change for the knee extension at 60°/s evaluated with an isokinetic dynamometer of +26.71% for the HI group (+18.73 N·m) and +15.30% for the M group (+15.30 N·m). The values obtained by the M group are more similar to those reported by the meta-analysis of Guizelini and colleagues (Guizelini et al., 2018), where the authors concluded that resistance training produces a significant increase of 18.4% in muscle strength. However, our results in both groups contrast with the conclusion reported by Peterson et al. (2010) that lower increases in muscle strength are usually observed in the upper compared to the lower limbs (i.e., 25% vs 30%). In our first study, the improvements in the elbow flexor and extensor muscles in the HI and M groups are similar or even greater compared to the muscle strength gains in the lower muscles evaluated at both low and high velocities. We speculate that these conflicting results may be related to the different methods and devices used to assess muscle strength, to the different movements and muscles evaluated and to the variability in the training programs applied.

In addition, our findings regarding muscle power in both training groups, which were evaluated through the isokinetic dynamometer at high velocities, are also in accordance with the studies where improvements of maximal strength are accompanied by increasing power strength and which reported beneficial effects of traditional slow-to-moderate velocity resistance training on power outcomes in older adults (Balachandran et al., 2014; Behm & Sale, 1993b; Bottaro et al., 2007; Caserotti et al., 2008; Cormie et al., 2010; de Vos et al., 2005; Fielding et al., 2002; Frontera et al., 1988; Hakkinen et al., 1998; Henwood et al., 2008; Izquierdo et al., 2001; Jozsi et al., 1999; Kaneko et al., 1983; Latham et al., 2004; Macaluso et al., 2003; McBridge et al., 2002; Miszko et al., 2003; Moss et al., 1997;Ramirez-Campillo et al., 2014; Sayers et al., 2003; Skelton et al., 1995; Stone et al., 1979; Stowers et al., 1983; Wilson et al., 1993; Toji et al., 1997; Toji & Kaneko, 2004). In fact, when muscle strength was evaluated in our study at high velocities (180°/s), the positive percentages of change by time were even greater than those obtained for the muscle strength at lower velocities, with an improvement of 52.17% (+18.39 N·m) for the HI group and 25.41% (+11.24 N·m) for the M group for the knee extension muscles, for instance. In this case, the improvement in the M group is similar to the reviews that demonstrated an increase of 24–33% after applying a resistance training program (Borde et al., 2015, Peterson et al., 2010; Stewart et al., 2014), while the results for the HI group are higher than the mean increase reported in previous studies. Nevertheless, some authors have reported no effect of traditional resistance training on muscle power outcomes (Correa at al., 2012; Walker et al., 2015; Walker et al., 2017). The training intensity and volume, along with the characteristics of the sample analyzed and the duration of the training program, could be behind these conflicting results between studies.

Regarding the influence of training intensity, the HI group experienced the greatest improvements in muscle strength and muscle power in almost all muscle groups evaluated,

although no significant differences between training intensities were found. In fact, for the lower limbs, the HI group showed greater positive changes than the M group in all muscle groups analyzed (i.e., hip abduction and adduction muscles, knee flexion and extension muscles) at both velocities. For the upper limbs, the HI group also showed higher gains but only for the elbow extension muscles at low and high velocities, while the M group achieved greater improvements in the elbow flexor muscle groups at both training velocities. Despite the lack of significant differences between training intensities, our results are in accordance with a wide range of evidence that observed greater increases in muscle strength when participants performed a resistance training program at higher intensities (~80 % 1RM) compared to lower intensities (<60 % 1RM; Beneka et al., 2005; Cassilhas et al., 2007; DeBeliso et al., 2005; Fatouros et al., 2005, 2006; Harris et al., 2004; Hortobagyi et al., 2001; Hunter et al., 2001; Kalapotharakos et al., 2004, 2005; Pruitt et al., 1995; Seynnes et al., 2004; Singh et al., 2005; Sullivan et al., 2005; Taaffe et al., 1996; Tsutsumi et al., 1997, 1998; Vincent et al., 2002; Willoughby et al., 1998).

Furthermore, our data is supported by the conclusions found in several meta-analyses which observed a dose-response relationship between resistance training intensity and muscle strength gains. For instance, Peterson et al. (2010) found that the mean percentage of change in maximal strength gains when increasing intensity from one subgroup to another was 5.5%. The authors analyzed four subgroups: low intensity (<60% 1RM), low-to-moderate intensity (60–69% 1RM), moderate-to-high intensity (70–79% 1RM), and high intensity (≥80% 1RM). In our study, the intensities used in the training programs were moderate (65–70% 1RM) and high (85% 1RM). Based on the conclusion by Peterson et al. (2010), the improvements in the HI group for maximal strength, equivalent to the strength evaluated in our study at 60°/s, should be approximately 11% higher than those of the M group. However, we found that, only for hip adduction (+7.18%) and knee extension (12.33%) muscles, the maximal strength

of HI was around this value, while in the rest of the parameters the muscle strength gains in HI were higher (~30% for hip abduction) or lower (~3% for knee flexion, ~5% for elbow extension) than this reference point. Even for elbow flexion, the M group achieved higher maximal muscle strength benefits than the HI group.

Moreover, along with Peterson et al. (2010), other meta-analyses have suggested greater effects not only for high intensity compared with moderate or low but also for moderate intensity compared with low intensity (Borde et al., 2015; Peterson et al., 2010; Silva et al., 2014; Steib et al., 2010). For instance, Steib et al. (2010) observed that intensities higher than 75% of 1RM achieved greater effects (with higher ES) on maximal strength than moderate (55–75% of 1RM) or lower intensities (<55% of 1RM) in older adults aged 60 to 80 (Steib et al., 2010). In addition, the authors found that moderate intensity achieved greater effects on maximal strength than low (Steib et al., 2010). The meta-analysis by Raymond et al. (2013) also supports our results because it revealed that high-intensity progressive resistance training improved lower limb strength more than moderate intensity resistance training. In our first study, the ES reported by the HI group was also higher than those observed in the M group for all muscles analyzed, corroborating the findings of aforementioned meta-analyses.

One of the key problems when attempting to compare our results with previous studies is that most of the studies have evaluated dynamic maximal muscle strength with the 1RM test and not with isokinetic dynamometry. Only a few studies reported the peak torque of different muscle groups after directly comparing the effects of different training intensities on isokinetic muscle strength. Beneka et al. (2005) compared high (90% 1RM) vs moderate (70% 1RM) and low (50% 1RM) intensity resistance training programs to determine whether would be more effective in improving the isokinetic knee extension at different velocities (i.e., 60, 90, 120, 150, 180°/s) in healthy inactive men and women. The authors found after

16 weeks (three times a week) that high and moderate intensities significantly improved isokinetic peak torque with no differences between intensities at any velocity, although high-intensity produced the greatest gains at lower velocities, as also occurred in our study.

Likewise, Kalapotharakos et al. (2004) arrived at the same conclusion when comparing the effects of a 12-week resistance training program (three times a week, six exercises performed with machines: chest press, leg curl, latissimus pull-down, arm curl, and triceps extension) at high (i.e., three sets of eight repetitions at 80% 1RM) and moderate velocities (i.e., three sets of 15 repetitions at 60% 1RM) on muscle strength in older adults. After the training period, both intensities significantly increased the peak torque of knee extensor and flexor, with the high-intensity group achieving the greatest improvements in all parameters (Kalapotharakos et al., 2004). As in our study, the authors evaluated the isokinetic peak torque of knee flexor and extensor muscles at 60°/s and 180°/s. As was the case in our study, the HI group achieved the greatest gains in muscle strength and muscle power in all muscles analyzed at the knee joint. Despite the higher training frequency, the improvements obtained by Kalapotharakos et al. (2004) were lower than the changes obtained in our study by both training groups. The shorter length of the training period along with the higher initial values of the subjects in the investigation by Kalapotharakos et al. (2004) could explain these differences between studies. Contrary to our results, the authors observed greater improvements at lower velocities than at higher velocities in both intensities. Discrepancies between the studies may be attributed to the differences in the training intensity evaluated (i.e., HI: 85% vs 80%; M: 65-70% vs 60%), the training devices used (i.e., elastic resistance vs machines), the types of exercises, volume, frequency and duration, and the characteristics of the sample (i.e., initial values and age differ notably).

Our outcomes also corroborate with other resistance training studies in the elderly that have analyzed a resistance training program alone or in comparison to other training

strategies (Fatouros et al., 2019; Lima et al., 2018; Oliveira et al., 2015; Orsatto et al., 2018; Takarada et al., 2000). For instance, Fatouros et al. (2019) evaluated the same three joints and movements at the same velocities (i.e., 60°/s and 180°/s) after a strength training program of 16 weeks at an intensity of 55–80% of 1RM in older men and also found significant improvements in the peak torque of both intensities. Takarada et al. (2000) found a significant improvement in the peak torque of the elbow flexor muscles after a 16-week resistance training at low intensity (30–50% 1RM) with vascular occlusion and at moderate-to-high intensity (50–80% 1 RM) without occlusion.

Moreover, Oliveira et al. (2015) is one of the few studies that used the OMNI-RES scale for monitoring and adjusting training loads, although, unlike our study, the resistance training program was performed with machines. The training program was composed of eight exercises (i.e., chest press, knee extension, hamstrings curl, leg press, hip abduction, seated row, shoulder abduction, and plantar flexion) and followed a linear progression with training loads at 6 (i.e., somewhat hard) during the first four weeks, 7 (i.e., between somewhat hard and hard) during following four weeks, and 8 (i.e., hard) over the remaining four weeks, with repetitions respectively decreasing from 12 to 10 to eight. Each exercise was performed in three sets with approximately one minute of rest between sets. After 12 weeks (three times a week), the isokinetic muscle strength at the knee extensor muscles increased significantly to ~10 N·m at 60°/s (ES = 0.51) and 180°/s (ES = 0.58). The changes and ES achieved in our study by the two training groups were higher than those obtained in the study by Oliveira et al., (2015) using the same tool and methodology to control training intensity. The differences between the resistance training programs applied and the duration of the study period may explain these discrepancies. Contrary to our results, da Rosa Orssatto, Moura et al. (2018) reported significant increases of ~20% in the knee extensor muscles at 60°/s but nonsignificant increases (~18%) in the knee flexor at the same velocity. We speculate that the

lack of significant differences in the flexor muscles may be related to the characteristics of the training program due to only the leg press exercise being conducted during the study period.

Analyzing the results obtained in the first study in depth, regarding the lower limbs, and more specifically hip muscle adaptations, in absolute values, the HI group improved the maximal peak torque of hip abductor muscles at 60°/s by 19.42 N·m (+53.28%) while the gains in the M group reached 19.42 N·m (+23.71%). For the hip adductor muscles, the improvements were lower in both training groups (i.e., HI: + 9.54 N·m, Δ%: +23.07%; M: + 6.27 N·m, Δ%: +15.89%). When muscle strength was assessed at higher velocities to evaluate muscle power strength, the HI group improved by 12.82 N·m (+ 49.78%) in the maximal peak torque of hip abductor muscles, while the gains in the M group reached 5.30 N·m (+ 12.91%). For the hip adductor muscles, the improvements were again lower in both training groups (i.e., HI: + 6.95 N·m, Δ%: +15.52%; M: + 3.0 N·m, Δ%: +6.08%). The patterns in maximal muscle strength or power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, hip abductor muscle strength increased by 53.57% (i.e., pre: 0.56 N·m/kg; post: 0.86 N·m/kg) and 23.45% (i.e., pre: 0.81 N·m/kg; post: 1 N·m/kg) for the HI and M groups, respectively, while the improvements in the hip adductor muscles were 23.80% (i.e., pre: 0.63 N·m/kg; post: 0.78 N·m/kg) and 15.51% (i.e., pre: 0.58 N·m/kg; post: 0.67 N·m/kg) for the same groups. At 180°/s, the positive adaptations in both groups were slightly lower for both abductor (i.e., HI: +51.28% [pre: 0.39 N·m/kg; post: 0.59 N·m/kg]; M: +13.33% [pre: 0.60 N·m/kg; post: 0.68 N·m/kg] and adductor muscles [HI: +14.49%; pre: 0.69 N·m/kg; post: 0.79 N·m/kg]; M: +5.45% [pre: 0.73 N·m/kg; post: 0.77 N·m/kg]). The C group decreased their muscle strength values in all hip parameters analyzed but not significantly, reflecting the loss of muscle suffered by sedentary older adults at these ages.

In absolute and relative values, in both groups, the increase of muscle strength was higher for the hip abductor muscles than for the hip adductor. The increase in the muscle strength at low and high velocities at a higher rate in the hip abductor muscles can be justified by the higher demand in terms of muscle activation at the concentric phase of this group of muscles when the subjects perform the standing hip abduction exercise. In addition, in the rest of the lower limb exercises (i.e., squat and lunge), these muscles also act as stabilizers of the hips, knees and trunk. However, although the muscle strength at the hip adductor muscles also increased, the mechanical stimulus was lower, as this group of muscles did not work concentrically in the standing hip exercises, while in the isokinetic test, the movement was recorded in a concentric way.

In comparing our results with normative values, we found one previous study that reported normative values of hip abduction and adduction muscles for the elderly population, and particularly for older women. Danneskiold-Samsøe et al. (2009) showed that the peak torque for hip muscles in a female cohort of 21 women between 60–69 years was 78.8 N·m for the hip abduction muscles and 86.5 N·m for the hip adduction muscles. In the female group aged 70–79 years old (n = 24), the peak torque for the hip abduction muscles was 68.3 N·m, while for the hip adduction muscles, it was 75.8 N·m. The values in both cohorts were higher than those reported in our study. However, the main reason for these discrepancies is the velocity of the test, due to muscle strength in the study by Danneskiold-Samsøe et al. (2009) being evaluated at 30°/s. As described in the literature review, at higher velocities the force production decreases based on the F-V relationship. In addition, the evaluation of the hip muscle strength was performed sideways instead of standing and with a higher ROM than in our study (i.e., 40° vs 30°). Contrary to our findings, the muscle force of the adductor muscles was higher than the abductor in the study by Danneskiold-Samsøe et al. (2009). It is

likely that the reason mentioned above, along with the differences in the sample characteristics and the small sample size, may explain the discrepancies between studies.

The positive adaptations in muscle strength in both components, force (60°/s) and velocity (180°/s), in the hip muscles found in our first study are highly relevant since the hip abductor and adductor joint torque are highly associated with balance stability; regulating the medio-lateral postural sway (Winter, 1995); stabilizing the pelvis-trunk segments while walking (Mackinnon & Winter, 1993); controlling lateral weight transfer (Rogers & Pai, 1990); and producing limb-movement trajectories during sidestepping (Mille et al., 2005). In addition, older adults have lower maximum isokinetic hip abduction and adduction torque than younger adults (i.e., in older women, 44% less absolute hip torque in abduction and 56% less in adduction; Johnson et al., 2002), and these age-related decrements in strength are greater for older individuals at higher risk for falls than for those at lower fall risk (Hillard et al., 2008; Jonhson et al., 2004). Moreover, an age-associated reduction in the maximum hip abductor-adductor muscle torque has been linked to impaired protective stepping in the lateral direction and prospective risk for falls (Hillard et al., 2008; Rogers & Mille, 2003), as the gluteus medius and minimus muscles contribute most to lateral balance stability, and these are the muscles measured when an isokinetic hip abduction is performed. Thus, the gains in muscle strength and muscle power obtained in both groups may positively affect overall physical function but may especially impact the ability to stabilize standing balance in static and dynamic movements, reducing the risk of falls in this population.

Despite the relevance of these muscle groups in fall prevention in older adults, in contrast to knee and ankle muscle strength, relatively few studies have documented aging-related changes in hip muscle strength after a resistance training program, with our first study being the first that showed the effects of different training intensities in these muscles and also the first that analyzed the effect of a resistance training performed with elastic resistance

in older adults in this joint. Due to this lack of knowledge, the fact that the effects of muscle strength was recorded at two velocities is also important. In fact, the positive and significant improvements in muscle strength at higher velocities are more related to the benefits in lateral postural balance during stepping and walking, partly due to results from the ability to rapidly stabilize the head, arms and trunk in the frontal plane during single-limb support (Johnson et al., 2002). The improvements in the time to reach maximal muscle force would likely influence performance when fast lower-limb movements are required to maintain and recover balance. Thus, greater attention should be given in the future to this muscle group due to its impairment directly contributing to lateral instability and falls in older adults.

Continuing with the results obtained in lower limbs, the HI group improved the maximal peak torque of knee extensor muscles at 60°/s by 18.73 N·m (+26.71%), while the gains in the M group reached 11.44 N·m (+15.30%). For the knee flexor muscles, the improvements were lower in both training groups (HI: +8.16 N·m, Δ%: +19.06%; M: +6.68 N·m, Δ%: +16.73%). When muscle strength was assessed at higher velocities, the HI group improved the maximal peak torque of knee extensor muscles by 18.39 N·m (+52.17%) while the gains in the M group reached the 11.24 N·m (+25.41%). For the knee flexor muscles, the improvements were again lower in both training groups (HI: +7.51 N·m, Δ%: +19.68%; M: +6.55 N·m, Δ%: +19.17%). As was the case at the hip site, the patterns in maximal muscle strength and power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, knee extensor muscle strength increased by 26.47% (pre: 0.53 N·m/kg; post: 0.81 N·m/kg) and by 14.41% (pre: 1.11 N·m/kg; post: 1.27 N·m/kg) for the HI and M groups, respectively, while the improvement in the knee flexor muscles increased by 20% (pre: 0.65 N·m/kg; post: 0.78 N·m/kg) and by 16.94% (pre: 0.59 N·m/kg; post: 0.69 N·m/kg) for the same groups. No significant changes were found in the C group, although they experienced a decrease in the knee flexor and extensor muscles at low

velocities and in the knee extensor muscles at higher velocities. When the strength is normalized to body weight at 180°/s, the positive adaptations in both groups are greater for both extensor (i.e., HI: +52.83% [pre: 0.53 N·m/kg; post: 0.81 N·m/kg]; M: +26.15% [pre: 0.65 N·m/kg; post: 0.82 N·m/kg]) and flexor muscles (i.e., HI: +20.68% [pre: 0.58 N·m/kg; post: 0.70 N·m/kg]; M: +20% [pre: 0.50 N·m/kg; post: 0.60 N·m/kg]).

Contrary to the results obtained by Oh et al. (2017) that reported greater increases in maximum voluntary dynamic isokinetic strength of knee flexor muscles than knee extensor muscles at 60°/s and 120°/s after an 18-week elastic band resistance training program (twice weekly) in older adults, we found that in absolute and relative values, in both groups, the increase of muscle strength was higher at the knee extensor muscles than at the knee flexor. As previously mentioned, increases in force generation capacity are closely related to the muscle activation that occurs during exercise. In our study, the lower limbs exercises selected, especially the lunge, generated greater activation in muscle extensor than flexor muscles (Jacobsen et al., 2013). However, the exercises selected by Oh et al. (2017; i.e., ankle raises, squats, leg presses and leg abductions) have a lower predominance of knee extensor muscles.

In addition, the ratio between concentric hamstring and concentric quadriceps peak torques (H/Q ratio; also known as the conventional ratio) was calculated for both velocities since it provides information about knee joint stability and integrity (da Rosa Orssatto, Moura et al., 2018). Conventional ratios lower than 0.5 indicate a reduced capacity of the knee flexor muscles to brake knee extensor muscles during a concentric movement, thereby increasing strain on the knee anterior cruciate ligament and finally affecting the joint integrity (Aagaard et al., 1998; Holcomb et al., 2007). In our sample, the H/Q ratio at 60°/s (HI= pre: 0.64, post: 0.60; M= pre: 0.53, post: 0.54) was lower than at 180°/s (HI= pre: 1.10, post: 0.86; M= pre: 0.77, post: 0.73) in both groups, although it remained above the reference value of 0.5. Since

the force generated is greater at lower velocities, the differences between the knee extensor and the knee flexor muscles also increase, mainly due to the increase in quadriceps strength, resulting in H/Q ratios closer to the negative limit value of 0.5. In our study, at the end of the training period, almost all ratios decreased due to the increase in muscle strength in the knee extensor muscles being greater than in the hamstrings.

Comparing our results in the first study to normative values, as the isokinetic knee extension peak torque is the gold standard measure to assess muscle strength in older adults, we found three previous studies that have reported reference values of knee flexor and extensor muscles for older women (Danneskiold-Samsøe et al., 2009; Leyva et al., 2016; Pereira et al., 2018). Compared to the values reported by Danneskiold-Samsøe et al. (2009) and Leyva et al. (2016) at 60°/s, the values presented by the HI, M and C groups in knee extensor and flexor muscles are slightly lower, if we take as reference the female cohort between 60 to 69 years of age (peak torque knee extension: 92.4 N·m and 84.6 N·m; peak torque knee flexion: 52.7 N·m and 46.3 N·m from Danneskiold-Samsøe et al. [2009] and Leyva et al. [2016], respectively). However, our values are more similar to those reported for the female group over 70 years (peak torque knee extension: 77.5 N·m and 73.3 N·m; peak torque knee flexion: 46.4 N·m and 40.1 N·m from Danneskiold-Samsøe et al. [2009] and Leyva et al. [2016], respectively) in both studies, which means the initial values of muscle strength of our sample were low compared to their age.

This situation is corroborated by the data reported by Pereira et al. (2018) from 453 older women aged 60 to 84 years because, comparing the values of our sample in the knee extension torque in absolute terms to the values reported for the age group of 65 to 69 years, the training and C groups are situated in the 20^{th} percentile (<75 N·m). If we compare to the age group of 70 to 74 years, only the M group would be located in the 20^{th} to 40^{th} percentile (68.80-79.80 N·m), and the rest would be in the 20^{th} percentile (<68.80 N·m). In relative

terms (i.e., normalized to body weight), the M group is located in the 20th to 40th percentile regardless of age group (65 to 69 years: 1.11-1.34 N·m/kg; 70 to 74 years: 1.08-1.29 N·m/kg), while the HI group is in the 20th percentile (65 to 69 years: <1.11 N·m/kg; 70 to 74 years: <1.08 N·m/kg) at the beginning of the training period and at the 20th to 40th percentile at the end of the training program, also regardless of the age group selected.

Finally, only the study by Leyva et al. (2016) provides reference values at the velocity of 180°/s. The results obtained by the three groups were lower than the reference values from the group of 60 to 69 years and even for the female group older than 70 for the knee extension peak torque (i.e., 60 to 69 years: 57.9 N·m; >70 years: 49.8 N·m). However, for the knee flexion power strength, the values presented by our three groups are similar and greater than those values reported for the group of 60 to 69 years (60 to 69 years: 35.2 N·m; >70 years: 21.1 N·m). In summary, the sample analyzed in our first investigation presented lower strength values at knee extensor muscles compared to their peers at low and high velocities, while for the knee flexor, the values were also lower at low velocities but higher than the reference values at high velocities.

Although knee extension has been commonly measured in resistance training interventions as a marker of lower-limb strength, the strength gains reported at low and high velocities by both training groups in the knee extensor and flexor muscles are also important since the muscle strength of the extensor muscles is a predictor variable for gait performance (Ferrucci et al., 1997); lateral sway stability (Lord et al, 1999); and falls in older persons (Lord et al., 1999). Specifically, maintenance of leg extensor power could be particularly important due to its implications for ambulation in older adults. In fact, this parameter has been identified as a predictor of mobility disability (i.e., inability to ascend a flight of stairs or to walk one kilometer) in older men and women (Brady & Straight 2014).

Finally, regarding the changes reported in the upper limbs, the HI group improved the maximal peak torque of elbow extensor muscles at 60°/s by 12.44 N·m (+44.83%), while the gains in the M group reached 7.17 N·m (+24.51%). For the elbow flexor muscles, the improvement was lower in the HI groups (+3.37 N·m, Δ%: +18.59%) and higher in the M group (+5.84 N·m, Δ%: +40.09%). When muscle strength was assessed at higher velocities, the HI group improved the maximal peak torque of elbow extensor muscles by 11.03 N·m (+46.37%), while the gains in the M group reached 5.45 N·m (+18.33%). For the elbow flexor muscles, the improvements were again lower in the HI group (+4.79 N·m, Δ%: +29.64%) and higher in the M group (M: +5.79 N·m, Δ%: +40.42%). As was the case at the hip and knee joints, the patterns in maximal muscle strength and power were similar when peak muscle strength was normalized to body mass. For the assessment at 60°/s, elbow extensor muscle strength increased by 45.23% (pre: 0.42 N·m/kg; post: 0.61 N·m/kg) and 24.48% (pre: 0.49 N·m/kg; post: 0.61 N·m/kg) for the HI and M groups, respectively, while the improvements in the knee flexor muscles were 22.22% (pre: 0.27 N·m/kg; post: 0.33 N·m/kg) and 42.85% (pre: 0.21 N·m/kg; post: 0.30 N·m/kg) for the same groups. No significant changes were found in the C group, although they experienced a decrease in the elbow flexor and extensor muscles at high velocities and in the elbow flexor muscles at low velocities.

When the strength is normalized to body weight at 180°/s, the positive adaptations in the HI group are greater for both extensor (+47.22% [pre: 0.36 N·m/kg; post: 0.53 N·m/kg]) and flexor muscles (+28% [pre: 0.25 N·m/kg; post: 0.32 N·m/kg]), while in the M group, the beneficial changes were lower for both extensor (+18.18% [pre: 0.44 N·m/kg; post: 0.52 N·m/kg]) and flexor (+38.09% [pre: 0.21 N·m/kg; post: 0.29 N·m/kg]) muscles compared to muscle gains at low velocities. It would be logical to hypothesize that a greater increase in isokinetic muscle strength in elbow flexor muscles would occur in both training groups at low

and high velocities since, in the exercises selected for the upper limbs, the concentric actions of these muscles predominated on the concentric action of the elbow extension muscles. However, our results only confirm this hypothesis for the M group. The greater increases observed in the HI group may be a result of neural adaptations that occur with training at higher intensities, such as increased motor recruitment and increased co-activation of antagonist muscles (Gabriel et al. 2006).

When we compare these results with the only previous study that has reported isokinetic normative values for this joint, we find that the isokinetic peak torques for the elbow extensor muscles are higher in all the groups compared to those reported by Danneskiold-Samsøe et al. (2009) in female groups ranging from 60–69 (18.4 N·m) and 70–79 (16.8 N·m) years old. However, for the elbow flexor muscles, the strength showed in the HI, M and C groups was similar to the values for the female group aged 70–79 (17 N·m). Contrary to Danneskiold-Samsøe et al. (2009), we found higher values of muscle strength and muscle power in elbow extensor muscles than in the elbow flexor muscles. The small sample size (i.e., 21 and 24 women in each age group), along with the different method to assess the isokinetic peak torque in the elbow joint in terms of position, ROM and protocol performed, could explain the differences between the studies. No studies examined the normative values in this joint at higher velocities, such as 180°/s or 240°/s, making it impossible to compare our results with reference values at high velocities.

Despite improvements in muscle strength in lower extremities being more relevant due to the loss of strength in the lower body being faster than in the upper body (Grimby et al., 1982) and lower body strength decreases being associated with impaired physical function and higher risk of falls (Murray et al., 1985), improvements in upper limb strength are also important due to most of the basic and instrumental activities of daily living upper

limbs being used—not only in precision activities but also in activities with high load demands, such as carrying shopping bags or holding grandchildren.

Most of the resistance training protocols applied to improve muscle strength in older adults have been conducted with machines and free weights but not with variable resistance such as elastic bands. Few studies have employed elastic resistance as equipment for older adults to improve muscle strength (Damush & Damush, 1999; Fahlman et al., 2011; Fritz et al., 2018; Gargallo et al., 2018; Krebs et al., 2007; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017; Ribeiro et al., 2009; Rogers et al., 2002; Thiebaud et al., 2013; Topp et al., 1996). Our findings align with the conclusions of previous meta-analyses which stated that resistance training performed with elastic bands is an effective training method to improve muscle strength of upper and lower limbs in adults and elderly population (de Oliveira et al., 2017; Thiebaud et al., 2014; Martins et al., 2013), particularly in healthy subjects (Martins et al., 2013), which promotes similar strength gains to conventional resistance training in different population profiles using diverse protocols (Lopes et al., 2019). As we observed in our first study, most of the studies have demonstrated the effectiveness of the elastic resistance training method to increase isometric, isotonic and isokinetic muscle strength in older adults (Damush & Damush, 1999; Dancewicz et al., 2003; Fritz et al., 2018; Gargallo et al., 2018; Krebs et al., 2007; Martins et al., 2013; Oh et al., 2016; Ribeiro et al., 2009; Thiebaud et al., 2013; Webber & Porter, 2010a; Webber & Porter, 2010b; Woo et al., 2007).

The studies that have also previously evaluated the muscle strength through isokinetic dynamometer after an elastic resistance training program in older adults assessed short- (i.e., 12 weeks) and medium-term (i.e., 12–24 weeks) interventions (Fahlman et al., 2011; Kim et al., 2015; Krebs et al., 2007; Lee, Kim et al., 2014; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017; Rogers et al., 2002). In addition, only the muscle strength of the knee

extensor and flexor muscles were assessed in those previous studies, mostly at 60°/s (Kim et al., 2015; Lee, Kim et al., 2014; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017) but also at 120°/s (Martins , Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017) and 180°/s (Kim et al., 2015). Thus, our first study is the longest intervention to date and the first that analyzes the muscle strength at the hip, elbow and knee joints. Similar to our results obtained in knee peak torque at 60°/s, Lee, Kim et al. (2014) found significant improvements by time in both knee extensor and flexor muscles after eight weeks of elastic resistance training in older women. Moreover, significant differences compared to the control group were also achieved. The training program was comprised of ankle exercises (ankle dorsiflexion, ankle plantar flexion, ankle eversion, ankle inversion); knee exercises (leg press, knee extension, knee flexion); hip exercises (hip extension, hip flexion, hip abduction, hip adduction); abdominal exercises (crunches); and dorsal exercises (hyperextension). As in our study, resistance exercises were performed with elastic bands using Thera-Bands but the intensity and the volume in terms of repetitions and sets was lower than in our study: two sets of 15–20 repetitions.

Likewise, Oh et al., (2017) observed significant improvements in knee flexor and extensor strength after 18 weeks (eight weeks of supervised training and 10 weeks of self-directed training). However, contrary to the findings of Lee, Kim et al. (2014), when muscle strength was assessed after eight weeks, no significant changes were found. However, Oesen et al. (2015) found significant differences in muscle strength in knee extensor muscles after 12 weeks; at the end of the training program (24 weeks), the training group also significantly improved the muscle strength of the knee flexor. The findings by Kim et al. (2015) drew the same pattern after 12 weeks, with significant positive adaptations in knee extensor muscles. Contrary to those studies, Martins, Safons et al. (2015) found neither significant changes in knee flexor and extensor muscles after eight weeks (twice a week) nor significant interactions

between training and control groups. The training program was composed of four exercises for the lower limbs (standing hip flexion and hip extension, sitting knee flexion and knee extension) and three exercises for the upper limbs (standing bench press, rowing and high pulley), performing two to three sets of 15 repetitions with an RPE of 5–7 during the first four weeks and 8–10 for last four weeks. The lack of significant gains may be explained by the low volume, duration and intensity of the training program performed. On the other hand, contrary to our results, Kim et al. (2015), in the only previous study that analyzed the effects of elastic resistance training on muscle strength at high velocities, did not note a significant effect on muscle power strength in the knee extensor and flexor muscles after 12 weeks. The short duration of the training period could be the main factor for the lack of significant improvements in these parameters.

Despite the favorable results obtained by most of the studies, an important aspect to highlight is the low quality of the studies and the wide variety of training protocols and subject populations studied. For instance, most of the studies do not use an appropriate method to control intensity with elastic bands or the intensity was too low for the stated objective. In addition, it is important to note that, to date, no studies have been conducted comparing different training intensities when the resistance training program is performed with elastic bands. In addition, there is a lack of knowledge regarding the effects of this kind of load (i.e., variable resistance) on power outcomes in the older population, and particularly in older women, when it is used in traditional resistance training programs. In general, although most of the resistance training programs performed with machines, free weights or elastic bands achieved positive adaptations in muscle strength, mainly in knee extensor muscles, there is a large variability in the magnitude of the changes between studies and meta-analysis mainly due to the high variety of training protocols applied, as well as the

different methods used to analyze the strength outcomes in elderly population with diverse characteristics.

Factors such as training duration, training frequency, training intensity, time under tension, rest between sets and type of training devices used have a high impact on the results achieved in muscle strength after applying an exercise protocol in older subjects. In fact, Borde and colleagues (Borde et al., 2015) found in their meta-regression that the variables of training period, intensity and total time under tension had significant effects on muscle strength, with the greatest effects for the longest training periods (i.e., 50–53 weeks), intensities of 70–79% of 1RM and the total time under tension in each repetition of 6 s (Borde et al., 2015). They also found a tendency toward significance for the "rest between sets" parameter, with 60 s showing the largest effect on muscle strength (Borde et al., 2015). In addition, two training sessions per week, a training volume of two to three sets per exercise, seven to nine repetitions per set and a 4-s rest between repetitions were more effective than other amounts (Borde et al., 2015). Conversely, Guizelini et al (2018) found that training duration has no influence on the strength gains after short-to-medium periods (i.e., four to 16 weeks) of resistance training.

The influence of volume is especially relevant because some trials have reported similar strength gains with low repetitions at high intensity and with high repetitions at low intensity (Alegre et al., 2015; Léger et al., 2006; Taaffe et al., 1996; Vincent et al., 2002) when both training groups are matched for mechanical work (Raymond et al., 2013). Nonetheless, even though the differences between intensities are minimized, the effects are more pronounced when using heavier loads (increases in strength of 43% for high intensity in front of 35% for low-to-moderate intensity), even when resistance training programs are matched for mechanical work (Csapo & Alegre, 2016). As can be corroborated by the findings from our first study, a "strength-endurance continuum" could exist that implicates

that, to achieve gains in muscle strength, moderate-to-high intensities or high volumes have to be prescribed (Campos et al., 2002).

With regard to our first study, it is reasonable to speculate that the long duration of the training program, the high volume performed in both training groups (three to four sets per exercise), the intensities applied (moderate and high), the type of exercises prescribed (focused on stimulating the main muscles of upper and lower limbs) and the type of load used (variable resistance) helped to promote significant increases in muscle strength at low and high velocities in the upper and lower limbs. In addition, rather than having to be exposed to high loads or high volumes, achieving maximal effort is also an important factor for gains in muscle strength in older adults (Goto et al., 2005; Carpinelli, 2008). In our study, the RPE was moderate but mostly high during most of the training program. This close to maximal effort could maximize the neuromuscular adaptations to enhance the muscle strength response (Goto et al., 2005; Carpinelli, 2008). In fact, some authors have reported that training with heavier loads has been related to a higher rate of perceived exertion than lower loads, even when total mechanical work is matched (Alegre et al., 2015), probably due to a greater sensation of effort. Thus, high intensity could be better because it allows for greater effort, which is closer to maximal effort. Despite the higher perceived exertion and the characteristics of the high-intensity resistance training, it should be noted that neither differences in adherence rates and dropout nor adverse events and injuries were reported between high-and-moderate intensity resistance training in our study, which aligns with previous studies (Raymond et al., 2013).

As happens with muscle strength, it is important to note that previous works have detected factors that act as moderators in the response obtained by muscle power after a resistance training program in older adults. Research has demonstrated that the training volume is a key determinant that has larger effects on muscle output after resistance training

interventions with a moderate volume (product of sets x repetitions = 24) rather than low (< 24) or high volumes (> 24; Straight et al., 2016). In our study, both training groups performed high volumes (> 24) during all training periods. Lower volumes would probably have resulted in greater improvements of muscle strength at high velocities. However, in addition to training volume, the ability to increase the muscle power has also been related to the individual's previous level of strength (Cornie et al., 2011). Thus, increases in maximal muscle power following resistance training are expected to be higher in untrained or moderately trained subjects than in stronger individuals. The lower initial levels of muscle strength in the subjects of our first study compared with the reference values for the same target population could have led to greater changes in muscle strength and muscle power in the elderly women studied, especially because the strength at high velocities due to muscular power is considerably influenced by the individual's level of strength.

The underlying mechanisms for resistance-training-induced improvements in muscle strength have not been elucidated, and there are likely multiple factors at play; however, the mechanism behind the improvements achieved in muscle strength at low velocities in both training groups can be related by structural, neural, and musculotendinous or connective tissue factors. Resistance training can diminish the age-related decline in muscle strength, producing neural adaptations in the first weeks of training by increasing the motor unit recruitment and firing rates (Arnold & Bautmans, 2014; Prevost et al., 1999), motor neuron excitability (Häkkinen et al., 2001), muscle innervation (Messi et al., 2016), and neuromuscular junction function (Deschenes et al., 2015). These neural adaptations occur more markedly at higher training intensities.

Additionally, the muscle strength gains in our study were mediated by learning patterns regarding technique (Kraemer et al., 1995), as well as by increasing activation of the agonist muscles and reducing coactivation of the antagonist muscles (Häkkinen et al., 1998)

in an early or middle phase. Finally, as our study had a long duration, morphological and structural changes of the musculotendinous system, such as hypertrophy (Housh et al., 1992), increased tendon stiffness and hysteresis (Narici et al., 2008; Reeves et al., 2003), and reduction of intramuscular fat (Radaelli et al., 2013) could also be mechanisms that would have favored strength gains. Moreover, the physiological mechanisms by which both resistance training programs improved muscle strength at high velocities may be attributed to the neuromuscular changes that it produced, such as increased CSA of Type I and II fibers (Campos et al., 2002; Dons et al., 1979; Häkkinen et al., 1981; Green et al., 1998; Thorstensson et al., 1976), greater pennation angle and fascicle length (Aagaard et al., 2001; Kawakami et al., 1995), and increased neural drive as well as inter- and intra-muscular coordination (Kaneko et al., 1983; Komi et al., 1978; McBridge et al., 2002; Moss et al., 1997; Narici et al., 1989).

Generally, the results obtained in our first study of upper and lower limbs are highly relevant due to previous studies that have demonstrated a rate of muscle strength decline of approximately 2%–4% per year in older adults above 60 years of age. Especially important are the gains obtained in lower limbs, since previous investigations have observed a decline in isokinetic strength of 16% vs 2% in the lower and upper limbs, respectively, in older women between the 5^{th} and 8^{th} decades (Hughes et al., 2001). Moreover, studies have demonstrated that even in lower or upper limbs, the aging effect on muscle strength is different between individual muscles, with for instance, elbow extensor experiencing greater decline than elbow flexor (26% and 17%, respectively; Klein et al., 2001; Vandervoort & McComas, 1986). The greater gains achieved in elbow extensor by the HI group were probably associated with the lower initial values compared to those of the M group for this muscle group.

It is important to highlight the sample in which results were obtained because older women reach significantly lower levels of muscle strength than men at similar ages, and women also have a greater rate of decline in the lower limbs relative to their upper extremities than men (Lynch et al. 1999; Hughes et al. 2001) Consequently, women experience greater loss of functional ability and independence than men. Additionally, if we consider that muscle strength is inversely associated with mortality risk (Ruiz et al., 2008) and is a better indicator and predictor of frailty, hospitalization, and disability (Barbat-Artigas et al., 2011; Legrand et al., 2014; Syddall et al., 2003) than muscle mass, then the results obtained in our first study demonstrate the importance of the elastic resistance training to reverse the impairments of muscle strength in older women, thus delaying the physical deterioration of the population studied. Particularly important are the gains obtained in the lower limbs since leg muscle strength is correlated with physical function measures, such as typical or maximum gait speed and chair stand tests (Barbat-Artigas et al., 2013; Rantanen et al., 1998); it is also linked to critical activities, including stair-climbing, rising from a chair, and walking (Bassey et al., 1992; Bean, Kiely, Herman et al., 2002; Cuoco et al., 2004; Hernman et al., 2005, Puthoff & Nielsen, 2007).

If the improvements of both training groups in the muscle strength at low velocities are relevant, then we must pay special attention to the improvements obtained at high velocities, since muscle power declines at a faster rate and earlier in life compared with muscle strength and muscle mass as both the force and velocity components decrease (De Vito et al., 1998; Pojednic et al., 2012). The reduction in muscle power with age has been reported at a rate of up to 6% per year (Clark et al., 2013; Skelton et al., 1994), diminishing twice as fast as muscle strength (Aagaard et al., 2010; Cruz-Jentoft et al., 2010; Fielding et al., 2002; Skelton et al., 1994), with the leg extensor muscle power being affected more

significantly than the distal muscles of the lower and upper limbs (Candow & Chilibeck, 2005; Izquierdo et al., 1999; Lanza et al., 2003).

As happens with muscle strength, elderly women are more prone to functional disability and institutionalization due to their absolute, relative, and specific muscle power being lower than men's (Alcaraz et al., 2020; Macaluso & De Vito, 2003a). Therefore, it is more difficult for elderly women to reach the threshold required to maintain functional independence. Additionally, muscle power is a better and stronger predictor of functional performance, disability, and physical impairment than muscle strength in older people (Bean et al., 2003; Reid et al., 2012) because it is more related to the ability to perform daily activities, such as rising from a chair or climbing a flight of stairs (Bassey et al., 1992; Izquierdo et al., 1999). It seems that the velocity component of power is related to physical impairment in older adults independently of the strength component of the power (Bean et al., 2003; Pojednic et al., 2012), which may be the reason that power has been demonstrated to be a stronger predictor of physical limitations than strength. Therefore, the improvements obtained by both training groups in the muscle strength at high velocities could be particularly important due to their implications for the basic and instrumental ADLs in older adults. Additionally, the proposed training strategies could delay the appearance of functional consequences related to reductions in power strength, such as the increased risk of falls (Bassey et al., 1992; Suzuki et al., 2001), hip fractures (Dean et al., 2004; Foldvari et al.,2000), decreased walking speed (Cuoco et al., 2004; Himann et al., 1988; Skelton et al., 1994), risk of dependence and institutionalization, (Christensen et al., 2008), cognitive decline (Alfaro-Acha et al., 2006), osteoporosis (McGrath et al., 2017), diabetes (Peterson et al., 2016), and early all-cause mortality (McLean et al., 2014; Metter et al., 2004; Wu et al., 2017).

In summary, both moderate and high elastic resistance training strategies are effective in improving muscle strength at low and high velocities in upper and lower limbs since both training groups achieved significant changes after the training intervention in all parameters, with the magnitude of the changes reported as moderate to large.

V.XI.II. Specific discussion of the second project

Regarding the results obtained in our second study, our investigation is the first to examine the modality response effect of 20 weeks of multi-component, power strength and traditional high-intensity elastic resistance training on neuromuscular strength in upper and lower limbs produced at low and high velocities in older women. In contrast to previous studies, we directly compared the three modalities' effects on the isokinetic peak torque of the hip, knee, and elbow muscles at 60°/s and 180°/s. Our results indicated that high-velocity resistance training is the most effective modality for improving force production at high velocities in the tested hip, knee, and elbow muscles, achieving significant differences from the other training modalities at hip and elbow joints. However, our findings also indicated that the traditional high-intensity elastic resistance training strategy results in greater improvements of force production at low velocities in the three joints evaluated. Unlike the P group, however, this modality did not produce significant differences from the other training groups in any parameter. Finally, the multi-component training strategy produced significant improvements at both high and low velocities in almost all parameters analyzed, although to a lesser extent in the P and T groups.

To our knowledge, this is the first RCT addressing the effects of these three training modalities for muscle strength in older women. Because of the novelty of our analysis, it is difficult to make direct comparisons with the current literature due to the lack of studies that compare these training modalities with each other. Much of the research on resistance

exercise and muscle strength in older adults has been performed utilizing a traditional strength training strategy, which focuses primarily on isokinetic knee extension strength.

However, some studies have investigated the effects of high-velocity resistance training vs traditional resistance training on muscle strength in older adults and particularly in older women (Bottaro et al., 2007; Caserotti et al., 2008; Fielding et al., 2002; Häkkinen et al., 1998; Henwood et al., 2008; Henwood & Taaffe, 2005; Pereira et al., 2012; Tiggemann et al., 2016; Webber & Porter, 2010a). Our results obtained in the second study regarding muscle strength at low velocities align with the findings of those studies that have indicated that power resistance training is an effective exercise modality leading to gains in upper- and lower-extremity muscle strength in a way that is similar to traditional strength training (Bottaro et al., 2007; Henwood et al., 2008; Marsch et al., 2009; Müller et al., 2020; Ramírez-Campillo et al., 2014; Tiggemann et al., 2016; Wallerstein et al., 2012), especially in lower limbs. In fact, in our study, although the T group obtained greater improvements in all of the muscles analyzed at low velocities, the differences between groups were not large enough to be significant. As we observed, the shorter differences between these two training modalities were obtained in the knee, followed by the elbow and hip. For instance, in the knee, the muscle gains obtained by the T group in absolute terms were 8.44 N·m (+ 9.43%) for the extensor muscles and 3.92 N·m (+ 8.93%) for the flexor muscles, while for the P group, the improvements were 5.53 N·m (+ 6.57%) and 1.25 N·m (+ 3.03%), respectively. Thus, based on the findings of our study, in lower limbs, the positive effects of the power strength modality are similar to those obtained by the traditional high-intensity modality in the knee only; differences in the hip were more noticeable between groups.

The similarities of the effects between both training modalities on muscle strength at low velocities that our study reveals were also previously reported in both dynamic (Balachandran et al., 2014; Bottaro et al., 2007; Correa et al., 2012; Fielding et al., 2002;

Henwood et al., 2008; Lopes et al., 2015; Ramírez-Campillo et al., 2014) and isometric strength (Henwood et al., 2008; Lopes et al., 2015); concurrently, the same conclusion has been reached when the studies evaluated only traditional (Walker et al., 2015, 2017; Walker & Häkkinen, 2014) or power modalities (Caseroti et al., 2008; Conlon et al., 2017; Radaelli et al., 2018; Ramírez-Campillo et al., 2017; Reid et al., 2005).

For instance, in elderly women, Pereira et al. (2012) report similar gains in dynamic and isometric leg press and bench press muscle strength after a 12-week training period of power resistance training vs traditional resistance training. Additionally, Marsh et al. (2013) have found that there was no difference between groups (power vs traditional strength training) in isometric quadriceps strength after 16 weeks of resistance training in older women. Finally, Tiggemann et al. (2016) compared the effects of 12 weeks of traditional resistance training and power training utilizing RPE in 30 healthy elderly women and have found that after 12 weeks, both groups had significant increases in 1RM for leg press (56.3 ± 14.5% for the traditional group and 60.3 ± 20% for the power group) and knee extension (16.1 ± 5.9% and 22.9 ± 11.6% for traditional and power group, respectively; Tiggemann et al., 2016). Intensities in the power resistance training groups from these studies usually ranged between low and moderate (40%–60% of 1RM), and the majority of the studies lasted less than 16 weeks.

Our results align with previous studies that have found that training at fast velocities allows for gains at both fast and slow testing velocities (Caiozzo et al., 1981; Coyle et al., 1981; Lesmes et al., 1978; Moffroid & Whipple, 1970; Timm, 1987); however, previous investigations have also demonstrated that training at specific velocities allows for gains only at that specific velocity (Caiozzo et al., 1981; Ewing et al., 1990; Garnica, 1986; Smith & Melton, 1981). The main problem in those previous studies that compare the effects of power strength and traditional resistance training is that all of them have evaluated muscle strength

through isometric or 1RM tests, but there are no studies that have compared the effects of these two training modalities on muscle strength with a dynamic isokinetic test. Furthermore, the majority of the studies conducted training programs that lasted less than 16 weeks, and none of them utilized variable resistance as a training device for the power resistance training program.

The recent meta-analysis by Guizelini et al. (2018) agrees with our findings since the authors have found that the training type did not affect muscle strength gains, indicating similar improvements between high-intensity, low-velocity resistance training and low-intensity, high-velocity resistance training (Guizelini et al., 2018). The data obtained in our study suggest that, in older women, high loads or high intensities are not necessary to induce muscle strength gains because not only the load, but also the velocity of muscle contractions could be important factors in strength gains. In fact, the neural adaptations induced by high-speed contractions are essential for strength gains, especially during the first weeks of training (Behm & Sale, 1993b). Nevertheless, the training intensity at which power training is performed does seem to be a determining factor to achieve muscle strength gains. The results obtained by the P group in all the muscles tested at low velocity corroborated the current scientific knowledge: resistance training programs utilizing a high velocity of movement during the concentric phase at moderate intensity (i.e., 40%–60% of 1RM) seem to induce greater increases in muscle strength (Bean et al., 2009; Bottaro et al., 2007; Cadore et al., 2014; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Steib et al., 2010). Therefore, power resistance training to increase maximum strength in older women may be a suitable alternative training modality compared to traditional resistance training because lower intensities achieve similar results in muscle strength with a lower RPE, which may increase the adherence of participants.

The specific muscle strength gains obtained by the T group at low velocity in the joints assessed allowed us to observe that, as with the first study, the findings reported align with the umbrella review (Beckwée et al., 2019) and meta-analyses (Borde et al., 2015; Boutros et al., 2019; Buch et al., 2017; Csapo & Alegre, 2016; de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Guizeli et al., 2018; Martins et al., 2013; Peterson et al., 2010; Raymond et al., 2013; Silva et al., 2014; Steib et al., 2010; Stewart et al., 2014; Straight et al., 2016; Yoshimura et al., 2017) that have demonstrated the effectiveness of resistance training for improving muscle strength in older adults. Additionally, the results obtained by the T group support the wide range of evidence that significant increases in muscle strength in older adults are achieved after performing high-resistance training programs (Beneka et al., 2005; Cassilhas et al., 2007; DeBeliso et al., 2005; Fatouros et al., 2005; Fatourus et al., 2006; Harris et al., 2004; Hortobagyi et al., 2001; Hunter et al., 2001; Kalapotharakos et al., 2004, 2005; Pruitt et al., 1995; Seynnes et al., 2004; Singh et al., 2005; Sullivan et al., 2005; Taaffe et al., 1996; Tsutsumi et al., 1997; Tsutsumi et al., 1998; Vincent et al., 2002; Willoughby et al., 1998). Although the improvements obtained in the T group were lower than those obtained in the first study by the HI group, obtaining significant improvements in 5 months of intervention in all the muscles groups analyzed is a considerably relevant milestone.

In this second study, the improvements reached by the T group in the knee extensor at 60°/s were lower than the mean positive strength gains after resistance training interventions that have been reported by Peterson et al. (2010) and Guizelini et al. (2018) in their meta-analyses. The shorter duration of the study as well as the different tests utilized to evaluate the muscle strength could explain the differences. Again, as with the first study, our results in the T group were in contrast to the findings reported by Peterson et al. (2010), which state that lower increases in muscle strength are usually observed in upper rather than lower limbs.

In fact, the greatest improvement from this group was obtained in the elbow flexor (+ 48.71%). Indeed, the magnitude of the muscle strength gains obtained in elbow and hip muscles were similar, while those for the knee muscles were lower.

Regarding the lower limbs and specifically the muscle hip adaptations, in absolute values, the T group improved by 16.89 N·m (+ 28.55%) the maximal peak torque of hip abductor at 60°/s, while the gains obtained in the hip adductor were lower (+ 7.72 N·m, Δ%: + 17.60%). When the muscle strength was assessed at higher velocities to evaluate the muscle power strength, the T group improved by 3.45 N·m (+ 26.46%) the maximal peak torque of hip abductor and by 1.96 N·m (+ 52.18%) in the hip strength of the hip adductor. The patterns in maximal muscle strength or power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, hip abductor strength increased by 27.90% (pre: 0.86 N·m/kg; post: 1.10 N·m/kg), while the improvement at the hip adductor was 17.18% (pre: 0.64 N·m/kg; post: 0.75 N·m/kg). At 180°/s, the positive adaptations were lower for the hip abduction muscles [26.31% (pre: 0.19 N·m/kg; post: 0.24 N·m/kg)] and higher for the hip adduction muscles [60% (pre: 0.05 N·m/kg; post: 0.08 N·m/kg)] than those obtained at low velocities. The C group decreased their muscle strength values, but not significantly, in all hip parameters analyzed, which describes the typical pattern of age-related decline in muscle strength in sedentary older adults at these ages.

As we observed, in absolute and relative values, the increase of muscle strength was higher at the hip abductor when the strength was tested at low velocity, while at high velocity, the adductor achieved greater results. It is difficult to explain these differences because the training program was composed of exercises that produce higher demands in muscle activation from the abductor than the adductor (standing hip abduction, squat plus upright rowing, and lunge). It is probable that the lower initial levels presented in the T group's hip adductor compared to the other groups was assessed at high velocity; conversely,

the high initial levels observed in the hip abductor may explain the differences in gains of muscle strength compared to the changes obtained at lower velocities. Comparing the results obtained by the T group in the hip muscles with the typical values provided by Danneskiold-Samsøe et al. (2009), we observed that our values in all muscles analyzed and at both velocities were lower than the values of the cohorts reported by Danneskiold-Samsøe et al. (2009). As discussed previously, in the first study, the main reason for these discrepancies was the velocity of the test because Danneskiold-Samsøe et al.'s (2009) study evaluated muscle strength at 30°/s.

Continuing with the results obtained in lower limbs, the T group improved by 8.44 N·m (+ 9.43%) the maximal peak torque of knee extensor at 60°/s, while the gains in the knee flexor reached 3.92 N·m (+ 8.93%). When the muscle strength was assessed at higher velocities, the T group improved by 4.11 N·m (+ 7.95%) the maximal peak torque of knee extensor, while the gain in knee flexor was 2.78 N·m (+ 9.60%). As with the hip site, the patterns in maximal muscle strength and power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, knee extensor muscle strength increased by 9.84% (pre: 1.32 N·m/kg; post: 1.45 N·m/kg), while the improvement at the knee flexor was 9.52% (pre: 0.63 N·m/kg; post: 0.69 N·m/kg). When the strength was normalized to body weight at 180°/s, the positive adaptations were greater for both extensor [+ 8% (pre: 0.75 N·m/kg; post: 0.81 N·m/kg)] and flexor [+ 9.52% (pre: 0.63 N·m/kg; post: 0.69 N·m/kg)]. No significant changes were found in the C group, although they experienced a decrease in the knee flexor at low and high velocities while maintaining their muscle strength in knee extensor at both velocities. Additionally, regarding the conventional ratio, the T group's H/Q ratio at 60°/s (pre: 0.48; post: 0.48) was lower than at 180°/s (pre: 0.56; post: 0.56). Only when muscle strength was produced at high velocities was the ratio above the reference value of 0.5, which means that when force is produced at low velocities, the

integrity and stability of the knee joint is at risk. The training protocol proposed for the T group was not able to improve the conventional ratios at any velocity; the improvements of muscle strength at knee extensor and flexor were similar.

Comparing the results in the T group with typical values at the knee joint, when muscle strength was assessed at 60°/s, the values presented by the T group in the extensor were similar to those reported by Danneskiold-Samsøe et al. (2009) and Leyva et al. (2016) for a cohort of women between 60 and 69 years of age, while the values of the knee flexor were lower and similar to those values reported for a female group over 70 years of age (Danneskiold-Samsøe et al., 2009; Leyva et al., 2016). If we compare our results with the values provided by Pereira et al. (2018), then in absolute numbers, the subjects of this group are situated in the 40^{th}–60^{th} percentile (87.31–98.10 N·m) for the age group of 65–69 years in knee extension strength. In relative terms (normalized to body weight), the T group was located in the 20^{th}–40^{th} percentile at the beginning of the study, taking as a reference the age group of 65–69 years (1.11–1.34 N·m/kg), and in the 40^{th}–60^{th} (1.35–1.52 N·m/kg) percentile at the end of the training period. Finally, only the study by Leyva et al. (2016) provides reference values at the velocity of 180°/s. The results obtained by the T group were similar to the reference values for the female group older than 70 years for knee extension (49.8 N·m) and knee flexion peak torque (31.1 N·m). In summary, it seems that the T group analyzed in our second investigation presented similar strength values at knee extensor compared to their peers at low and high velocities.

Regarding the changes reported in the upper limbs, the T group improved by 6.31 N·m (+ 17.29%) the maximal peak torque of elbow extensor at 60°/s, while the gain in the elbow flexor was 5.12 N·m (+ 48.71%). When the muscle strength was assessed at higher velocities, the T group improved by 2.22 N·m (+ 7.83%) and 1.04 N·m (+ 23.04%), respectively, the maximal peak torque of elbow extensor and flexor. As with the hip and knee

joints, the patterns in maximal muscle strength and power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, elbow extensor muscle strength increased by 46.66% (pre: 0.15 N·m/kg; post: 0.22 N·m/kg), and elbow flexor improved by 16.98% (pre: 0.53 N·m/kg; post: 0.62 N·m/kg). When the strength was normalized to body weight at 180°/s, the improvements were 7.31% (pre: 0.41 N·m/kg; post: 0.44 N·m/kg) and 33.33% (pre: 0.06 N·m/kg; post: 0.08 N·m/kg) for elbow extensor and flexor, respectively. Contrary to the results obtained in the first study, a greater increase in isokinetic muscle strength in elbow flexor was achieved by the T group at both velocities due to the exercises selected for the upper limbs in which the concentric actions of these muscles predominated over the concentric action of the elbow extension muscles. No significant changes were found in the C group, although they experienced a decrease in the elbow flexor and extensor at high velocities and in the elbow extensor at low velocities.

We compared these results with the only previous study that reports isokinetic typical values for this joint, and we have found that the isokinetic peak torques for the elbow extensor are higher than those reported by Danneskiold-Samsøe et al. (2009) in females aged 60–69 (18.4 N·m) as well as 70–79 (16.8 N·m) years. However, for the elbow flexor, the muscle strength was lower than the values for these female groups. As with the first study, contrary to Danneskiold-Samsøe et al. (2009), we found higher values of muscle strength and muscle power in elbow extensor muscles than in elbow flexor muscles.

We analyzed the results obtained by the P group by zones and compared them with those obtained by the T group, and we observed that the absolute gains in the hip abduction and adduction muscles at high velocity were approximately ~ 5 N·m (35%) and ~ 2.5 N·m (40%) greater than the gains obtained by the T group (P group: + 8.21 N·m and Δ%: 59.28% for hip abduction muscles at 180°/s; P group: + 4 .29 N·m and Δ%: 97.07% for hip adduction muscles at 180°/s). Nevertheless, at low velocity, the force produced by the P group in the hip

abductor (+ 6.92 N·m, Δ%: 11.30%) and adductor (+ 5.41 N·m, Δ%: 12.63%) were lower than the force generated by the T group. The patterns in maximal muscle strength or power in the P group were similar when peak muscle strength was normalized to body mass. For the assessment at 60°/s, hip abductor muscle strength increased by 10.86% (pre: 0.92 N·m/kg; post: 1.02 N·m/kg), while the improvement at the hip adductor muscles was 12.5% (pre: 0.64 N·m/kg; post: 0.72 N·m/kg). At 180°/s, the change obtained for the hip abduction muscle was 65% (pre: 0.20 N·m/kg; post: 0.33 N·m/kg), while the hip adduction muscles achieved 116% (pre: 0.06 N·m/kg; post: 0.13 N·m/kg). As we can appreciate, when values are normalized to body weight, the muscle gains, particularly at high velocities, are even greater than when they are reported in absolute values. In absolute and relative values, the increase of muscle strength was higher at the hip adductor at both high and low velocities. These findings may be attributed to the higher coactivation generated when the muscle contraction is performed at maximal velocity. We compared the results obtained by the P group in the hip muscles with the typical values provided by Danneskiold-Samsøe et al. (2009), and we observed that our values in all muscles analyzed and at both velocities were lower than the values of the cohorts reported by Danneskiold-Samsøe et al. (2009) due to the lower velocity utilized in the test by these authors.

The results obtained by the P group in the knee joint improved by 9.40 N·m (+ 19.12%) the maximal peak torque of knee extensor at 180°/s, while the gains in the knee flexor reached 5.61 N·m (+ 21.36%). Therefore, approximately ~ 5 N·m (12%) and ~ 2.5 N·m (12%) more force was produced at high velocities than in the T group. However, contrary to findings for the hip, no differences between groups were found. When the muscle strength was assessed at lower velocities, the P group improved by 5.53 N·m (+ 6.57%) the maximal peak torque of knee extensor, while the gain in knee flexor was 1.25 N·m (+ 3.03%). As with the hip site, the patterns in maximal muscle strength and power were similar

when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, knee extensor muscle strength increased by 7.14% (pre: 1.26 N·m/kg; post: 1.35 N·m/kg), while the improvement at the knee flexor was 3.22% (pre: 0.62 N·m/kg; post: 0.64 N·m/kg). When the strength was normalized to body weight at 180°/s, the positive adaptations were greater for both extensor [+ 18.91% (pre: 0.74 N·m/kg; post: 0.88 N·m/kg)] and flexor [+ 23.07% (pre: 0.39 N·m/kg; post: 0.48 N·m/kg)]. Additionally, regarding the conventional ratio, the P group's H/Q ratio at 60°/s (pre: 0.49; post: 0.47) was lower than at 180°/s (pre: 0.53; post: 0.54). As was the case with Group T, only when muscle strength was produced at high velocities was the ratio above the reference value of 0.5, which means that when force is produced at low velocities, the integrity and stability of the knee joint is at risk. The training protocol proposed for the P group improved the conventional ratio at high but not at low velocities; the increase of the knee flexor at high velocities was greater than the improvements observed for the knee extensor.

Comparing the results in the P group with the normative values at the knee joint, when muscle strength was assessed at 60°/s, the values presented in the extensor muscles were similar to those reported by Danneskiold-Samsøe et al. (2009) and Leyva et al. (2016) for a cohort of women between 60 and 69 years of age, while the values for the knee flexor were lower and similar to those values reported for a female group over 70 years of age (Danneskiold-Samsøe et al., 2009; Leyva et al., 2016). The P group was located in the same reference group values as the T group. If we compare our results with the values provided by Pereira et al. (2018), then in absolute numbers, the subjects of this group are situated in the 20^{th}–40^{th} percentile (75.31–87.30 N·m) for the age group of 65–69 years in knee extension strength, being located one group lower than the T group. In relative terms (normalized to body weight), the P group was located in the 20^{th}–40^{th} percentile at the beginning of the study, taking as a reference the age group of those 65–69 years of age (1.11–1.34 N·m/kg);

they were in the 40^{th}–60^{th} (1.35–1.52 N·m/kg) percentile at the end of the training period. This classification was the same as the T group. Finally, comparing the values obtained at 180°/s with the reference values provided by Leyva et al. (2016), the results obtained by the P group are similar to the reference values for the female group older than 70 years for the knee extension (49.8 N·m) and knee flexion peak torque (31.1 N·m). In summary, it seems that the P group analyzed in our second investigation presented similar strength values in knee extensor muscles compared to their peers at low and high velocities, although it presented lower values than those reported by the group T.

Regarding the changes reported in the upper limbs, the P group improved by 5.40 N·m (+ 21.66%) the maximal peak torque of elbow extensor at 180°/s, while the gain in the elbow flexor improved by 3.31 N·m (+ 112.44%). The gains achieved by the P group were three times higher than those reached by the T group, demonstrating significant differences between groups. When the muscle strength was assessed at lower velocities, the P group improved by 5.13 N·m (+ 15.16%) and 2.59 N·m (+ 29.16%) the maximal peak torque of elbow extensor and flexor, respectively. As with the hip and knee joints, the patterns in maximal muscle strength and power were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, elbow extensor muscle strength increased by 33.33% (pre: 0.06 N·m/kg; post: 0.08 N·m/kg), and elbow flexor improved by 16% (pre: 0.50 N·m/kg; post: 0.58 N·m/kg). When the strength was normalized to body weight at 180°/s, the improvements were 21.62% (pre: 0.37 N·m/kg; post: 0.45 N·m/kg) and 125% (pre: 0.04 N·m/kg; post: 0.09 N·m/kg) for elbow extensor and flexor, respectively. As in the T group, the P group demonstrated greater increases of muscle strength at both high and low velocities in elbow flexor than in elbow extensor. We compared these results with values reported by Danneskiold-Samsøe et al. (2009), and we have found that the isokinetic peak torques for the elbow extensor are higher than those reported for females 60–69 (18.4

N·m) and 70–79 (16.8 N·m) years of age. However, for the elbow flexor, the muscle strength was lower than the values for these female groups. As with the first study, contrary to Danneskiold-Samsøe et al. (2009), we have found higher values of muscle strength and muscle power in elbow extensor than in elbow flexor.

If we pay attention to the changes obtained in the force production at high velocity, then our findings support the recent reviews and meta-analyses, which corroborate the effectiveness of high-velocity resistance training at improving muscle power when compared with traditional resistance training (Byrne et al., 2016; Steib et al., 2011; Straight et al., 2016), particularly for lower limbs (Straight et al., 2016). Additionally, our results align with previous studies that compare the traditional resistance training strategy with the power strength modality and reveal superior effects of the latter in lower- (Balachandran et al., 2014; Bottaro et al., 2007; Correa et al., 2012; Fielding et al., 2002; Henwood et al., 2008; Sayers et al., 2003, 2012) or upper-limb (Ramírez-Campillo et al., 2014) muscle power in older adults. The power strength program has been designed for and is fulfilled with the main characteristics of high-velocity resistance training to achieve muscle power gains: volume ranges from 1–6 sets of 4–20 repetitions at intensities ranging from 20%–80% of 1RM. Additionally, between 1 and 11 exercises may be performed, training sessions are between 10 and 90 minutes in length, training duration is from 6 to 52 weeks, and training frequency is between 2 and 3 days per week (Byrne et al., 2016).

Especially of note is that the only two previous studies that compare traditional resistance training and power strength training utilize the perceived exertion method to control intensity and employ elastic bands as training devices. The study by Tiggemann and colleagues (Tiggemann et al., 2016)—the only one to date that has utilized the perceived exertion method to control intensity in traditional and power training programs for older women—indicates significant increases in muscle strength and power in lower limbs (as

tested with leg press and knee extension) in both traditional and power training groups after 12 weeks of a twice-weekly training period. Contrary to our results, these authors have not found significant differences between groups. The shorter training period (12 weeks vs 20 weeks); the fact that both training strategies were matched in terms of sets, number of repetitions, and RPE; and the volume and intensities applied could explain the differences between the study by Tiggemann et al. (2016) and our study.

However, our results are partially in accordance with those reported by Yoon et al. (2016) in the only previous study to date that utilized elastic bands as a training device when traditional resistance training and power strength training were compared. Yoon et al. (2016) have found that the two training regimens produce small-to-large improvements in isokinetic knee extension and flexion at 60°/s and 180°/s after a training period of 12 weeks, as we also found in our study. However, in the study by Yoon et al. (2016), the high-velocity resistance training induced significantly higher changes in peak torque of knee extension at 60°/s and 180°/s than the traditional resistance training modality. Nevertheless, we did not find significant differences between groups at any velocity in the knee extensor or flexor. The discrepancies between the studies may be related to the greater changes obtained in the knee extensor by our P group than Yoon et al.'s (2016) group, which are probably due to the lower initial level of the older women analyzed. However, the knee flexor achieved lower force production at high velocity in the P group in the Yoon et al. (2016) study, contrary to our findings. We speculate that these conflicting results are due to methodological issues or characteristics of the studied population. In fact, the level of evidence that compares both training modalities to date was considered in the meta-analyses by Steib et al. (2010) and Tschopp et al. (2011) as "moderate" and "weak" due to the low quality, small sample sizes, and wide CIs. For instance, in the study by Yoon et al. (2016), the exercises performed in the training programs were not described, which makes comparisons between studies difficult.

Additionally, the results reported by the P group in our second study align with previous studies that analyzed high-velocity resistance training in older adults compared with a control group and have constantly and consistently demonstrated evidence regarding the significant benefits of this kind of training modality on different muscle power outcomes in this population (Bean, Kiely, Herman et al., 2002, 2004; Beltran Valls et al., 2014; Cadore et al., 2014; Caserotti et al., 2008; Chen et al., 2012; de Vreede et al., 2005; Earles et al., 2001; Gianoudis et al., 2014; Henwood et al., 2008; Henwood & Taaffe, 2005; Hruda et al., 2003; Jozsi et al., 1999; Lohne-Seiler et al., 2013; Paul et al., 2014; Pereira et al., 2012; Portegijs et al., 2008; Ramsbottom et al., 2004; Skelton et al., 1995; Webber & Porter, 2010a; Wilhelm et al., 2014). Specifically, our results support the studies that reveal significant improvements in muscle power when high-velocity resistance training was applied in older women (Bean et al., 2004; Fielding et al., 2002; Marsh et al., 2013; Pereira et al., 2012; Sayers et al., 2003; Tiggemann et al., 2016).

Nevertheless, the findings obtained by the T group in our second study when force is produced at high velocity also align with those studies in which improvements of maximal strength are accompanied by increasing power strength; moreover, these studies report beneficial effects of traditional slow-to-moderate velocity resistance training on power outcomes in older adults (Balachandran et al., 2014; Behm & Sale, 1993b; Bottaro et al., 2007; Caserotti et al., 2008; Cormie et al., 2010; de Vos et al., 2005; Fielding et al., 2002; Frontera et al., 1988; Häkkinen et al., 1998; Henwood et al., 2008; Izquierdo et al., 2001; Jozsi et al., 1999; Kaneko et al., 1983; Latham et al., 2004; Macaluso et al., 2003b; McBridge et al., 2002; Miszko et al., 2003; Moss et al., 1997; Ramírez-Campillo et al., 2014; Sayers et al., 2003; Skelton et al., 1995; Stone et al., 1979; Stowers et al., 1983; Wilson et al., 1993; Toji et al., 1997; Toji & Kaneko, 2004).

In our second study, when muscle force production was evaluated at high velocity, the positive percentages of change by time were greater than those obtained for muscle strength at low velocities in all muscle groups analyzed for the P and T groups, with the exception of elbow flexor and extensor when evaluated at 60°/s in the T group. Furthermore, the percentage of gains of muscle output varies among studies, mainly due to the different assessment methods applied; however, the percentage of changes obtained by the P group in the lower limbs and specifically in the knee muscles at high velocities were similar to the mean percentage improvement in lower-extremity muscle power (watts), as reported in the meta-analysis by Straight et al. (2016), which finds a mean positive gain of 16.96% derived from the power strength strategies applied in older women. All the studies performed in older women utilized a wide range of resistance equipment, such as machines, weighted vests, or body weight, but none employed variable resistance.

It is important to note that, in contrast to the findings regarding muscle strength, training intensity has not been established as a primary moderating parameter in the response of muscle power to resistance training in older adults, at least in lower limbs (as tested with leg press and knee extension; Straight et al., 2016). Classically, the force-velocity relationship in isotonic concentric contractions indicates that peak muscle power is developed at 30%–40% of maximal velocity and at 60%–70% of maximal force (McComas, 1996); however, it seems that, based on the literature available, gains in muscle power can be achieved utilizing a wide range of loads or intensities (20%–80% of 1RM; da Rosa Orssatto, Cadore et al., 2019). The results obtained by the P group corroborate that intensities equivalent to 40%–60% of 1RM (low-to-moderate intensity) are effective for improving the force produced at high velocities in upper and lower limbs when high-velocity resistance training is performed for 20 weeks in older women. In fact, the high magnitude of the ES (moderate to large) obtained by this training modality when muscle strength was assessed at high velocities could

be related to the fact that moderate intensities (i.e., 40%–60% of 1RM) seem to be the most appropriate to increase peak muscle power in older adults (da Rosa Orssatto, Cadore et al., 2019; Fragala et al., 2019). Nevertheless, it is necessary to note that the optimal intensity to produce the maximal power output may differ between exercises (Potiaumpai et al., 2016; Strand et al., 2019), but little is known about it. It seems that multijoint exercises have a narrow optimal load range (~ 40%–60% of 1RM) compared to single-joint exercises (~ 40%–80% of 1RM; Strand et al., 2019). The intensity applied in our study falls within the range of improvement of both types of exercises, favoring the improvements obtained.

It should be noted that current guidelines stress the importance of multi-component exercise interventions to improve health in older adults (Cress et al., 2006). However, contrary to the conventionally established benefits of traditional resistance training on muscle strength in older adults, data are often contradictory regarding the role of multi-component training on muscle strength improvements. Additionally, studies that have determined how strength changes with multi-component training programs have primarily utilized functional tests, with 1RMs or isokinetic tests being considerably less frequent. The findings obtained by the MT group in our study align with those that describe positive effects on muscle strength in older adults (Ansai et al., 2015; Binder et al., 2002; Carmell et al., 2000; Carvalho et al., 2009; Freiberger et al., 2012; Izquierdo et al., 2016; Justine et al., 2012; Lambert et al., 2008; Levy et al., 2012; Nakamura et al., 2007; Rubenstein et al., 2000; Smith et al., 2012; Shubert et al., 2010; Taguchi et al., 2010; Toraman & Sahin, 2004; Toraman et al., 2004; Toto et al., 2012; Villareal, Erman & Agyar, 2011; Worm et al., 2001).

The improvements demonstrated by the MT group support the findings of the systematic reviews performed by Baker, Atlantins & Fiatore (2007) and Bouaziz et al. (2016), which reveal that the relative ES for strength measures after multi-component interventions ranged from -0.08–1.67 with a mean of 0.41 across all strength measures

(Baker, Atlantins & Fiatore, 2007); additionally, muscle strength gains ranged from 1.4%–95.0% (Bouaziz et al., 2016). For instance, in the hip joint, the magnitude of the changes achieved in the hip abductor (ES = 0.49) and adductor (ES = 0.42) at 180°/s and in the hip adductor at 60°/s (ES = 0.45) was above the reported ES from Baker, Atlantins & Fiatore (2007). Indeed, the gains of muscle strength at low and high velocities in this joint ranged between 9.21% (hip abduction muscles at 60°/s) and 37.16% (hip adduction muscles at 60°/s). In the knee, in all muscles analyzed, the ESs were below the 0.41 reported by Baker, Atlantins & Fiatore (2007; ESs were established at approximately 0.30) despite the significant changes obtained by this group in all parameters. In fact, the muscle strength gains obtained by the MT group in the knee extensor and flexor at both velocities ranged between 4.66% (knee extensor muscles at 60°/s) and 9.11% (knee flexion muscles at 180°/s), which is within the range reported by Bouaziz et al. (2016). In the upper limbs, the ESs varied markedly, obtaining moderate ESs in the elbow flexor at 180°/s (0.67) and elbow extensor at 60°/s (0.77) but small ESs in the rest of the muscles evaluated. However, the greatest gains in muscle strength by the MT group were achieved in this joint, with improvements ranging between 5.25% (elbow extensor at 60°/s) and 46.41% (elbow flexor at 180°/s).

Our results demonstrate that a 20-week multi-component training program seems to provide sufficient stimuli to induce neuromuscular strength gains in lower and upper limbs, increasing the force production at both high and low velocities in older women. Previous studies have indicated the positive effects of multi-component training on muscle strength in older women (Marques, Mota, Machado et al., 2011; Marín-Cascales et al., 2015; de Resende-Neto et al., 2019; Karikanta et al., 2007; Otero et al., 2017). However, the majority of these studies evaluated muscle strength through functional tests (Marques, Mota, Machado et al., 2011; Otero et al., 2017), handgrip strength (Marques, Mota, Machado et al., 2011), or isokinetic dynamometers in isometric mode (de Resende-Neto et al., 2019). Additionally,

when isokinetic dynamometers were utilized to measure dynamic strength, only the knee extensor and flexor were measured (Marín-Cascales et al., 2015; Marques, Mota, Machado et al., 2011).

However, our results contrast with the studies that have found no positive results on muscle strength (Barnett et al., 2003; Jessup et al., 2003; Nakamura et al., 2007; Nelson et al., 2004; Puggaard, 2003) or at least those that are not across all strength measures (Judge et al., 1993; Lazowski et al., 1999; Rubenstein et al., 2000). Discrepancies between the studies may be attributed to the high heterogeneity of the multi-component programs applied (different components and training parameters were utilized) and to the considerable variety of methods utilized to measure strength outcomes (1RM, maximum voluntary isometric contractions, handgrip strength, isokinetic dynamometry, and field tests). Another main reason for the lack of positive results is the short duration of the training programs: the majority lasted 8, 12, or 16 weeks. In fact, only a small number of studies utilizing multi-component prescriptions report significant improvements in muscle strength after a relatively short period (Nakamura et al., 2007; Rubenstein et al., 2000; Toraman & Sahin, 2004; Toraman et al., 2004), although these studies utilized field tests to assess lower body strength.

One of the main problems in analyzing the results obtained by the MT group compared to other training modalities is the lack of evidence on comparison interventions between multi-component training and other training strategies. In fact, only the studies by Carvarlho et al. (2010) and Marín-Cascales et al. (2015, 2017) compared the effects of multi-component training with multi-component plus resistance training and whole-body vibration on isokinetic muscle strength, respectively. Contrary to our findings, the study by Carvarlho et al. (2010) has indicated that a twice-weekly multi-component training program over 24 weeks has a limited effect on isokinetic muscle strength at low and high velocities in older adults. The authors have found no significant changes in muscle strength in knee extensor or

flexor when evaluating them at 60°/s and 180°/s, while the group that combined a multi-component training and resistance training program demonstrated a significant increase in maximum voluntary knee extensor (22.3%) and knee flexor (29.6%) at 180°/s in the non-dominant leg and a significant increase in knee extensor torque at 60º/s in the dominant (6.7%) and non-dominant (17.3%) legs as well as in knee flexor torque at 60º/s in the dominant (16.4%) and non-dominant (24.2%) legs. Despite the training frequency, which was the same as in our study, and the length of the training program, which was also similar, the higher initial values of the sample by Carvarlho et al. (2010) could have affected the final result.

Additionally, the multi-component training programs of both studies were similar in terms of the number of components trained (aerobic, strength, balance, and stretching). However, Carvarlho et al. (2010) do not explain the characteristics of the strength block. They do not provide information about the exercises selected, the volume and training intensity, or the progression of the training load performed in this block. The correct prescription of strength exercises in the strength block of multi-component training programs is essential to obtain improvements in muscle strength; therefore, the differences in the training parameters applied in this component could probably explain the discrepancies between the studies.

Our results support the findings of Marín-Cascales et al. (2015, 2017), indicating significant positive effects in knee extension peak torque at 60º/s and 270º/s in older women after 12 and 24 weeks of multi-component resistance training performed 3 times per week. It is important to note that in both studies, the authors classified the training programs performed as multi-component when they were compared with the effects of a whole-body vibration program; however, the multi-component training programs designed by the authors cannot be classified as such since they were composed of two training components: drop

jumps and aerobic activity. The multi-component training modality must comprise at least three components (strength and resistance training, aerobic and cardiovascular endurance training, balance and stability, flexibility, or coordination) to be defined as multi-component (Cress et al., 2006). The strength gains obtained by the female cohort in both studies by Marín-Cascales et al. (2015, 2017) were higher for the knee extension at low velocity and lower for the force production at high velocity compared to our results. The higher training frequency and duration could probably explain the differences of force production at low velocity, whereas the differences at high velocity may be related to the different isokinetic velocities utilized to assess the force production at high velocities.

As we observed, if little and poor-quality evidence exists in relation to the effects of multi-component training on muscle strength in older adults, then the number of studies that analyze its effects on muscle power is almost non-existent because the majority of the studies only analyze isokinetic strength at low velocities. Our results as well as the studies of Marín-Cascales et al. (2015, 2017) support de Resende-Neto et al. (2019), which reveal that a 12-week multi-component training program, in this case performing strength exercises at high velocity, is effective to improve muscle power in the same manner as traditional resistance training. Muscle power was evaluated through leg press and rowing machines at 50% of 1RM. As can be appreciated, our study is the only one to date that provides information about the changes produced by the multi-component training modality on the force produced at high velocity in upper limbs and in the hip abductor and adductor. Therefore, future research should include robustly designed RCTs that specifically involve multi-component training in older adults, and especially older women, and compare its effects with other training modalities, such as resistance training or high-velocity strength training in these areas and muscle groups.

With respect to strength gains achieved through multi-component training programs that were performed alone, as in our investigation, Kang et al. (2015) have found positive effects on muscle strength after a 4-week protocol that combined balance, strengthening, and stretching exercises in elderly women. Likewise, Cadore et al. (2014) have demonstrated beneficial results on the strength of knee extensor in nonagenarians after a 12-week training period that encompassed resistance training with progressive loads, balance, and walking exercises. Similarly, Carmeli et al. (2000) have observed a statistically significant change in the muscle strength of both knee extensor and flexor in institutionalized elderly adults, while Rubenstein et al. (2000) note a significant increase in knee extensor assessed at 60°/s among frail elderly men. Especially of note are the studies of Lee, Kim et al. (2014) and Marques, Mota, Machado et al. (2011), since the former utilized elastic bands as a training device, and the latter evaluated muscle strength at the same velocities as in our study as well as in a sample of older women. The combined program designed by Lee, Kim et al. (2014) has presented a significant increase at 60°/s in knee extension and flexion muscles after an 8-week training program. Moreover, Marques, Mota, Machado et al. (2011) have found significant improvements on strength in knee flexor at 180°/s, knee extension for the right leg at 180°/s, and knee flexion for both legs at 60°/s after an 8-month multi-component training program. As we observed, the results obtained by the studies mentioned above support the muscle gains produced by the MT group in our research.

We analyzed the results obtained by the MT group by zones and compared them with those obtained by the T and P groups, and we observed that the absolute gains in hip abduction muscles at low velocity were lower than those reported by the T and P groups (+5.80 N·m, Δ%: +9.21%), while the hip adduction muscles were the second group with the highest improvements behind the T group (+6.45 N·m, Δ%: +16.23%). Nevertheless, at high velocity, the force produced by the MT group was lower than changes produced by the T and

P groups in both abductor (+3 N·m, Δ%: +24.84%) and adductor (+1.64 N·m, Δ%: +37.16%). Additionally, significant differences were found between the MT and P groups in these parameters, favoring the P group. As with the other groups, the patterns in maximal muscle strength or power in the MT group were similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, hip abductor muscle strength increased by 8.88% (pre: 0.90 N·m/kg; post: 0.98 N·m/kg), while the improvement in the hip adductor muscles was 15.78% (pre: 0.57 N·m/kg; post: 0.66 N·m/kg). At 180°/s, the change obtained for the hip abduction muscles was 23.52% (pre: 0.17 N·m/kg; post: 0.21 N·m/kg), whereas the hip adduction muscles improved by 33.33% (pre: 0.06 N·m/kg; post: 0.08 N·m/kg). In absolute and relative values, the increase of muscle strength was higher in the hip adductor muscles at both high and low velocities. These findings may be attributed to the lower initial level of this muscle group as well as the greatest stimulus it could be produced the exercises selected for the multi-component training program, not only those performed in the strength block, but also the aerobic, balance, and coordination exercises. Comparing the results obtained by the MT group in the hip muscles with the normative values provided by Danneskiold-Samsøe et al. (2009), we observed that our values in all muscles analyzed and at both velocities were lower than the values of the cohorts reported by Danneskiold-Samsøe et al. (2009) due to the lower velocity utilized in the test by these authors.

The results obtained by the MT group in the knee joint improved by 4.19 N·m (+ 4.66%) the maximal peak torque of the knee extensor at 60°/s, while the gains in the knee flexor reached 2.65 N·m (+ 6.18%). This means that the MT group obtained lower gains compared to the other training modalities in the knee extensor and indicated the second highest improvement in the knee flexor, behind the T group. When muscle strength was assessed at high velocity, the MT group improved by 4 N·m (+ 7.62%) the maximal peak torque of knee extensor, whereas the gain in knee flexor was 2.54 N·m (+ 9.11%). As with

the hip site, these gains were lower than those obtained by the T and P groups. In the knee, the patterns in maximal muscle strength and power were again similar when the peak muscle strength was normalized to body mass. For the assessment at 60°/s, knee extensor muscle strength increased by 4.65% (pre: 1.29 N·m/kg; post: 1.35 N·m/kg), while the improvement at the knee flexor was 6.55% (pre: 0.61 N·m/kg; post: 0.65 N·m/kg). When strength was normalized to body weight at 180°/s, the positive adaptations were greater for both extensor [+ 6.66% (pre: 0.75 N·m/kg; post: 0.80 N·m/kg)] and flexor [+ 10.25% (pre: 0.39 N·m/kg; post: 0.43 N·m/kg)]. Additionally, regarding the conventional ratio, the MT group's H/Q ratio at 60°/s (pre: 0.47; post: 0.48) was lower than at 180°/s (pre: 0.53; post: 0.53). As with the other training groups, only when muscle strength was produced at high velocities did the ratio rise above the reference value of 0.5, which means that when force is produced at low velocities, the integrity and stability of the knee joint is at risk. The training protocol proposed for the MT group improved the conventional ratio at low but not high velocities. Contrary to the other two training groups, the MT group experienced greater positive changes in knee flexor than in knee extensor at both velocities tested. The characteristics of the exercises selected for aerobic and balance blocks as well as the lower number of exercises and volume for lower limbs performed in the strength block compared with the P and T groups could explain the differences in the findings.

Comparing the results in the MT group with normative values at the knee joint, when muscle strength was assessed at 60°/s, the values presented in the extensor were similar to those reported by Danneskiold-Samsøe et al. (2009) and Leyva et al. (2016) for a cohort of women from 60 to 69 years of age, while the values of the knee flexor were lower and similar to those values reported for a female group over 70 years of age (Danneskiold-Samsøe et al., 2009; Leyva et al., 2016). The MT group was located in the same reference group values as the P and T groups. If we compare our results with the values provided by Pereira et al.

(2018), then in absolute numbers, the subjects of this group were situated in the 40^{th}–60^{th} percentile (87.31–98.10 N·m) for the age group of 65–69 years in knee extension strength, which is in the same range as the T group. In relative terms (normalized to body weight), the MT group was located in the 20^{th}–40^{th} percentile at the beginning of the study, taking as a reference the age group of 65–69 years of age (1.11–1.34 N·m/kg); they had advanced to the 40^{th}–60^{th} (1.35–1.52 N·m/kg) percentile by the end of the training period. This classification was the same as the T and P groups. Finally, comparing the values obtained at 180°/s with the reference values provided by Leyva et al. (2016), the results obtained by the MT group were similar to the reference values for the female group older than 70 years of age for knee extension (49.8 N·m) and knee flexion peak torque (31.1 N·m). In summary, it seems that the MT group analyzed in our second investigation presented similar strength values in the knee extensor muscles at low and high velocities compared to their peers.

Regarding the changes reported in upper limbs, the MT group improved by 1.85 N·m (+ 5.25%) the maximal peak torque of elbow extensor at 60°/s, while the gain in the elbow flexor was 2.88 N·m (+ 36.09%). The gains achieved by the MT group at this velocity were the lowest for the elbow extensor compared to the changes reported by the P and T groups, and they were the second highest improvement in the elbow flexor, only behind the T group. When muscle strength was assessed at high velocity, the MT group improved by 1.64 N·m (+ 6.53%) and 1.32 N·m (+ 46.51%) the maximal peak torque of elbow extensor and flexor, respectively. As with the other training groups, elbow flexor achieved greater strength gains compared to elbow extensor. In the elbow joint, the patterns in maximal muscle strength and power were again similar when peak muscle strength was normalized to body mass. For the assessment at 60°/s, elbow extensor muscle strength increased by 36.36% (pre: 0.11 N·m/kg; post: 0.15 N·m/kg), and elbow flexor improved by 6% (pre: 0.50 N·m/kg; post: 0.53 N·m/kg). When strength was normalized to body weight at 180°/s, the improvements were

5.55% (pre: 0.36 N·m/kg; post: 0.38 N·m/kg) and 25% (pre: 0.04 N·m/kg; post: 0.05 N·m/kg) for elbow extensor and flexor, respectively. When we compared these results with values reported by Danneskiold-Samsøe et al. (2009), we found that the isokinetic peak torques for the elbow extensor were higher than those reported from a female group of those aged 60–69 (18.4 N·m) and 70–79 (16.8 N·m) years. However, the elbow flexor' muscle strength was lower than the values for these female groups. As with the first study and contrary to Danneskiold-Samsøe et al. (2009), we found higher values of muscle strength and muscle power in elbow extensor than in elbow flexor.

Overall, the results obtained in our second study are considered important, as for the first time, they demonstrate and compare the effectivity of probably the three most relevant training strategies to reverse or at least reduce the effects of aging in older women, confirming that all strategies tested are effective for improving force production at low and high velocities in lower and upper limbs. In particular, this is also the first time that all training groups performed their training programs with elastic bands as training devices, which can provide advantages such as convenience, portability, and cost savings to older women. Specifically, the strength gains obtained in the hip muscles are considerably relevant because the strength of the hip abductor are related to stability, and falls are a predominant cause of morbidity and mortality in society and especially in older women (Winter, 1995). Therefore, to improve the strength of these muscle groups, any of the three modalities analyzed is effective. However, high-velocity resistance training seems to provide the most significant benefits and must be located in the first line since the force produced at high velocities are more closely related with the ability to rapidly stabilize the head, arms, and trunk in the frontal plane during single-limb support (Johnson et al., 2002) and are therefore required to maintain and recover balance. Despite the relevance of this muscle group in fall

prevention in older adults, to our knowledge, our study is the first to analyze the effect of power strength training on muscle strength in the hip abductor and adductor in older women.

Regarding the results obtained for the knee, knee extension movements have been the most common exercise for testing muscle strength in older adults; however, our study demonstrates that despite the higher volume of strength exercises performed by the T and P groups, the multi-component strategy could also be effective for improving the muscle strength of knee extensor and flexor at low and high velocities if we properly select the type, volume, and training intensity of lower limb exercises. As was mentioned previously, the gains obtained in the knee extensor are important since lower levels of strength in these muscle groups are associated with reduced gait speed and stability in older people (Lord et al., 1999).

Moreover, the three training strategies produced significant strength gains in upper limbs, although in this case, the gains obtained by the multi-component modality in the elbow extensor at 60°/s did not reach significant differences. It seems that contrary to the findings reported in lower limbs, the lower number of upper-limb exercises and the lower volume prescribed could cause participants to achieve a reduced increase in the elbow extensor but not in the elbow flexor. Based on our results, the prescription of any of the training modalities analyzed in our study could be utilized to improve the muscle strength of upper limbs in older adults, and therefore, could improve the basic and instrumental ADLs related to the upper limbs and high load demands.

Several factors may account for the beneficial effect on muscle strength obtained by the three training groups. Common to the three groups is the specificity of the exercises selected compared to the movement assessed by the isokinetic dynamometer, the training volume, and the training intensity prescribed. In the case of the T group, the high intensity

that was employed has been widely validated as one of the most effective means to achieve strength gains. Regarding the P group, the intensities utilized were from 40% to 60% of 1RM, which are also the most convenient to produce improvements in muscle strength. Additionally, the velocity of the concentric phase is sufficient to produce strength gains at low and high velocities due to this intensity, which favors the improvement of the force and velocity components of strength. The MT group's moderate intensity as well as the number of series performed and the exercises selected favored positive results. The time under tension, rest between sets, and type of training device utilized could also have impacted the results achieved in muscle strength by the three training groups. Furthermore, for the T group and the strength block in the MT group, achieving maximal effort was an important factor for gains in muscle strength rather than being exposed to high loads or high volumes. As in our first study, the RPE was moderate but typically high throughout the training program. This close-to-maximal effort could maximize the neuromuscular adaptations to enhance the muscle strength response (Goto et al., 2005; Carpinelli, 2008).

Additionally, some studies have indicated that training at fast velocities allows for gains at both fast and slow testing velocities (Caiozzo et al., 1981; Lesmes et al., 1978; Moffroid & Whipple, 1970), while other studies have presented that training at specific velocities only allows for gains at that specific velocity (Ewing et al., 1990; Smith & Melton, 1981). One of the main reasons for the results obtained by the P group is the proportion of the muscle fiber types that are utilized when the force is produced at high or low velocities. The appendicular muscles tested are commonly composed of approximately 50:50 distribution of Type I (slow) and Type II-twitch (fast) fibers (Johnson et al., 1973). However, during isokinetic assessments, when force production is tested at low velocity, both slow- and fast-twitch muscle fibers contribute to torque production; conversely, when muscle strength is

tested at high velocity, fast-twitch muscle fibers contribute primarily to torque production (Faulkner et al., 1986).

The underlying mechanisms by which these training modalities induce improvements in muscle strength at low and high velocities are related to structural, neural, and musculotendinous or connective tissue factors. Specifically, the neural factors could have played a significant role in the P group since training at high velocity produces increased motor unit recruitment, elevated spinal motor neuronal excitability, changes in agonist coactivation, enhancement of maximal motor unit firing rates, and increased efferent motor drive (Aagaard et al., 2010). Additionally, the fast contractions increase the Type II fibers' CSA, pennation angle, and fascicle length (Aagaard et al., 2001; Kawakami et al., 1995). However, neural factors could also be important in the benefits obtained by the T and MT groups due to the high intensity applied in the traditional resistance training program and the variety of stimuli prescribed through the balance, aerobic, strength, and coordination components in the multi-component training program. However, in these two groups, structural and musculotendinous factors could have had greater weight in the improvements obtained than in the P group.

The main research focus has been on traditional resistance training and muscle strength at low velocities; nevertheless, we believe the results obtained in our second study to be considerably important due to the improvements obtained by the three training modalities but especially by the high-velocity resistance training in force production at high velocity in the upper and lower limbs. If we consider that muscle power declines with aging at an earlier and faster rate than muscle strength (De Vito et al., 1998; Lauretani et al., 2003; Macaluso & De Vito, 2003a; Reid, Pasha et al., 2014; Runge et al., 2004; Siglinsky et al., 2015; Skelton et al., 1994; Zengin et al., 2017) and that it is more strongly related to mobility limitations and mortality than muscle mass and strength in elderly people (Bean et al., 2003; Foldvari et al.,

2000; Martinikorena et al., 2016; Metter et al., 2004) – especially in older women – then the findings are even more relevant. The results obtained in our second study additionally demonstrate the importance of the elastic resistance training applied at slow and fast contractions in reversing the impairments of muscle strength in older women.

In summary, in our second study, the training modality did not have an effect on muscle strength gains at low velocity since all training modalities achieved significant improvements in the parameters analyzed. However, the modality training utilized was decisive in improving force production at high velocity in hip abduction and adduction muscles as well as in elbow flexor and extensor. Therefore, these data suggest that in older women, the velocity of contractions could be an important factor involved in strength gains at high velocities, whereas high loads or intensities are not as decisive in inducing muscle gains at low velocities. Consequently, power resistance training to increase maximum strength in older people may be a suitable alternative training modality because, compared to traditional resistance training, lower intensities achieve similar results in muscle strength with a lower RPE, which may increase the adherence of participants. It is important to note that this kind of training modality can achieve enhancements of maximal strength, muscle size, and power strength at low-to-moderate intensities and at 40%–60% of 1RM (Cadore et al., 2014; Ramírez-Campillo et al., 2014), simplifying access to exercise for older people with comorbidities. An appropriate alternative for older women who cannot or do not want to perform high-speed or high-load contractions is the multi-component training strategy since it is also able to increase muscle strength and muscle power.

V.XII. RESULTS ON PHYSICAL FUNCTION

V.XII.I. Project one

The changes in physical function from the ITT analysis are displayed in Table 51. The repeated-measures ANOVA showed a main effect of time in 30sec-CS [$F(1, 90) = 157.45$, $p < 0.000$, $\eta^2p = 0.636$, $1-\beta = 1$], 30sec-AC [$F(1, 90) = 234.36$, $p < 0.000$, $\eta^2p = 0.723$, $1-\beta = 1$], TUG [$F(1, 90) = 89.35$, $p < 0.000$, $\eta^2p = 0.498$, $1-\beta = 1$], and 6MWT [$F(1, 90) = 27.49$, $p < 0.000$, $\eta^2p = 0.234$, $1-\beta = 0.999$]. Pairwise comparison revealed significant improvements in all the parameters analyzed in both training groups. The magnitudes of the changes obtained by the HI group were large in the four parameters, while M group also obtained large ES in 30sec-CS, 30sec-AC and TUG, along with moderate ES in the 6MWT. No significant changes by time were found in the C group. Furthermore, significant main effects of time × group interaction were found in 30sec-CS [$F(2, 90) = 47.54$, $p < 0.000$, $\eta^2p = 0.514$, $1-\beta = 1$], 30sec-AC [$F(2, 90) = 43.05$, $p < 0.000$, $\eta^2p = 0.489$, $1-\beta = 1$], TUG [$F(2, 90) = 26.24$, $p < 0.000$, $\eta^2p = 0.368$, $1-\beta = 1$], and 6MWT [$F(2, 90) = 15.40$, $p < 0.000$, $\eta^2p = 0.255$, $1-\beta = 0.999$]. Differences were found in all the variables tested between both training groups and the C group, obtaining large ES in all of them. No significant differences between the training groups were found. After controlling for baseline values and age, the ANCOVA revealed the same significant main effects of time and group × time interactions. The magnitude of the changes also remained stable, with one exception in the M group, where the ES after the training period in 6MWT changed from moderate to large. The results of the PPA found the same significant differences as the ITT analysis but with higher ES. The results from the PPA are presented in Supplementary Material I (Table I.).

Table 51. *Intervention effects on physical function from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
30sec-CS (rep)	M	13.02	11.70 ± 2.69 (10.48 –12.93)	21.32 ± 6.06 (19.31–23.32)	82.09	**0.000** (2.05)	**0.000** (2.0)	M vs HI: 1.000 (0.08) M vs C: **0.000** (1.05) HI vs C: **0.000** (1.27)	M vs HI: 1.000 (0.01) M vs C: **0.000** (1.67) HI vs C: **0.000** (1.91)
	HI		12.35 ± 2.59 (11.26–13.45)	21.74 ± 4.88 (19.95–23.53)	75.93	**0.000** (2.4)	**0.000** (2.41)		
	C		15.95 ± 5.15 (14.53–17.37)	14.91 ± 6.16 (12.58–17.24)	-6.54	0.268 (0.18)	0.422 (0.15)		
30sec-AC (rep)	M	16.34	16.16 ± 4.50 (14.59–17.73)	28.00 ± 7.61 (25.83–30.16)	73.25	**0.000** (1.89)	**0.000** (1.88)	M vs HI: 1.000 (0.15) M vs C: **0.000** (1.31) HI vs C: **0.000** (1.47)	M vs HI: 1.000 (0.01) M vs C: **0.000** (1.61) HI vs C: **0.000** (2.04)
	HI		15.07 ± 3.47 (13.67–16.47)	27.00 ± 5.41 (25.06–28.93)	79.08	**0.000** (2.62)	**0.000** (2.57)		
	C		18.73 ± 5.52 (16.91–20.56)	19.43 ± 4.61 (16.91–21.95)	3.71	0.508 (0.14)	0.261 (0.24)		
TUG (s)	M	6.66	6.98 ± 0.95 (6.62–7.33)	5.28 ± 0.71 (4.89–5.68)	-24.28	**0.000** (2.01)	**0.000** (1.75)	M vs HI: 1.000 (0.11) M vs C: **0.001** (0.92) HI vs C: **0.001** (0.87)	M vs HI: 1.000 (0.18) M vs C: **0.000** (1.14) HI vs C: **0.000** (1.04)
	HI		6.61 ± 0.87 (6.29–6.92)	5.37 ± 0.83 (5.01–5.72)	-18.80	**0.000** (1.45)	**0.000** (1.56)		
	C		6.33 ± 1.19 (5.92–6.74)	6.45 ± 1.76 (5.99–6.91)	1.93	0.533 (0.08)	0.875 (0.02)		
6MWT (m)	M	495.79	522.16 ± 61.82 (499.53–544.78)	563.58 ± 62.53 (539.10–588.06)	7.93	**0.000** (0.67)	**0.000** (1.47)	M vs HI: 0.384 (0.43) M vs C: **0.000** (1.34) HI vs C: **0.000** (1.09)	M vs HI: 1.000 (0.06) M vs C: **0.000** (0.87) HI vs C: **0.000** (0.99)
	HI		487.07 ± 46.47 (466.90–507.24)	538.23 ± 54.86 (516.40–560.05)	10.50	**0.000** (1.01)	**0.000** (0.99)		
	C		475.04 ± 86.64 (448.77–501.31)	460.39 ± 93.39 (431.97–488.81)	-3.08	0.136 (0.16)	**0.040** (0.22)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 31), HI (*n* = 39), C (*n* = 23). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; 30sec-CS: 30 second sit-to-stand test; 30sec-AC: 30 second arm-curl test; TUG: timed up and go test; 6MWT: 6 minutes walking test; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70

V.XII.II. Project two

The physical function outcomes from the ITT analysis are presented in Table 52. The repeated-measures ANOVA indicated a main effect of time in 30sec-CS [$F(1, 132) = 84.24$, $p < 0.000$, $\eta^2p = 0.390$, $1\text{-}\beta = 1$], 30sec-AC [$F(1, 132) = 84.32$, $p < 0.000$, $\eta^2p = 0.390$, $1\text{-}\beta = 1$], 5STS [$F(1, 132) = 106.39$, $p < 0.000$, $\eta^2p = 0.446$, $1\text{-}\beta = 1$], timed stair-climbing [$F(1, 132) = 88.86$, $p < 0.000$, $\eta^2p = 0.402$, $1\text{-}\beta = 1$], SCS [$F(1, 132) = 88.86$, $p < 0.000$, $\eta^2p = 0.402$, $1\text{-}\beta = 1$], SCP [$F(1, 132) = 75.25$, $p < 0.000$, $\eta^2p = 0.363$, $1\text{-}\beta = 1$], FRT [$F(1, 132) = 27.63$, $p < 0.000$, $\eta^2p = 0.173$, $1\text{-}\beta = 0.999$], TUG [$F(1, 132) = 64.03$, $p < 0.000$, $\eta^2p = 0.327$, $1\text{-}\beta = 1$], and 6MWT [$F(1, 132) = 22.59$, $p < 0.000$, $\eta^2p = 0.146$, $1\text{-}\beta = 0.997$]. Pairwise comparison revealed significant improvements in all the parameters analyzed for the three training groups studied. The magnitude of the changes at the end of the training period varies between groups. In the case of the 30sec-CS, the ES ranged between moderate (MT) and large (P and T groups). The ES ranged from small (SCP: MT and P; FRT: MT and P; 6MWT: MT and P) to moderate (30sec-CS: MT and P; 5STS: MT; timed stair-climbing: MT, P and T; SCS: MT, P and T; SCP: T; FRT: P; TUG: P; 6MWT: T) and large (30sec-CS: T; 30sec-AC: MT, P and T; 5STS: P and T; TUG: MT and T). No significant changes by time were found in the C group.

Significant main effects of time × group interaction were found in 30sec-CS [$F(3, 132) = 13.94$, $p < 0.000$, $\eta^2p = 0.241$, $1\text{-}\beta = 1$], 30sec-AC [$F(3, 132) = 11.66$, $p < 0.000$, $\eta^2p = 0.209$, $1\text{-}\beta = 0.999$], 5STS [$F(3, 132) = 17.82$, $p < 0.000$, $\eta^2p = 0.288$, $1\text{-}\beta = 1$], TUG [$F(3, 132) = 10.03$, $p < 0.000$, $\eta^2p = 0.186$, $1\text{-}\beta = 0.998$], and 6MWT [$F(3, 132) = 6.08$, $p < 0.001$, $\eta^2p = 0.121$, $1\text{-}\beta = 0.956$]. The differences between the P and T groups and the C group were found in 30sec-CS (trivial and large ES), 30sec-AC (moderate ES), timed stair-climbing (trivial and moderate ES), and SCS (trivial and moderate ES). Additionally, differences between the three training groups and the C group were found in 5STS (moderate and large

ES), TUG (moderate and large ES), and 6MWT (large ES). No differences between the training strategies were found.

After controlling for baseline values and age, the repeated measures ANCOVA showed the same significant effects by time and similar ES. However, along with the differences obtained with the ANOVA analysis, significant main effects of time × group interaction were found in timed stair-climbing [$F(3, 130) = 19.07$, $p < 0.000$, $\eta^2p = 0.306$, $1\text{-}\beta = 1$], SCS [$F(3, 130) = 19.07$, $p < 0.000$, $\eta^2p = 0.306$, $1\text{-}\beta = 1$], SCP [$F(3, 130) = 12.38$, $p < 0.000$, $\eta^2p = 0.222$, $1\text{-}\beta = 1$], and FRT [$F(3, 130) = 3.58$, $p < 0.016$, $\eta^2p = 0.076$, $1\text{-}\beta = 0.781$]. The differences in timed stair-climbing, SCS and SCP were found between all the training groups and the C group (small and moderate ES). In the FRT, a significant effect was found between the MT and C groups (moderate ES). Furthermore, the ANCOVA also revealed new significant differences between groups in other variables, such as between the MT and C groups in 30sec-CS (moderate ES) and 30sec-AC (large ES). Additionally, significant differences were found between the training modalities in the measure of power of 5STS between the P group and the rest of the training strategies (moderate ES).

The results of the PPA for the physical function parameters found changes similar to the ITT analysis but with some differences. After the applied ANOVA test, the same significant changes by time were found, while significant differences appeared between the P and MT groups in 30sec-CS and 5STS. Additionally, new significant differences were found between the MT and C groups and between the P and T groups in 30sec-AC and 5STS, respectively. After the ANCOVA analysis, the significant change by time in 6MWT in the C group disappeared, while a new significant difference appeared between the P and C groups in the FRT. The results from the PPA are presented in Supplementary Material J (Table J.).

Table 52. *Intervention effects on physical function from ITT analysis.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
30sec-CS (rep)	MT	18.94	17.97 ± 4.54 (16.27–19.66)	21.29 ± 6.01 (19.28–23.30)	18.49	**0.000 (**0.62)	**0.000** (0.62)	MT vs P: 0.189 (0.45) MT vs T: 1.000 (0.38)	MT vs P: 0.498 (0.22) MT vs T: 1.000 (0)
	P		19.61 ± 6.12 (17.92–21.31)	24.41 ± 7.71 (22.40–26.41)	24.44	**0.000 (**0.69)	**0.000 (**0.69)	MT vs C: 0.101 (0.62)	MT vs C: **0.000** (0.68)
	T		19.94± 3.99 (18.24–21.63)	23.26 ± 4.27 (21.25–25.27)	16.67	**0.000** (0.80)	**0.000** (0.80)	P vs T: 1.000 (0.18)	P vs T: 0.481 (0.24)
	C		18.26 ± 5.05 (16.57–19.95)	17.82 ± 5.08 (15.81–19.83)	-2.42	0.463 (0.09)	0.452 (0.09)	P vs C: **0.000** (0.18) T vs C: **0.001** (1.01)	P vs C: **0.000** (0.81) T vs C: **0.000** (0.8)
30sec-AC (rep)	MT	20.66	20.47 ± 4.36 (18.92–22.01)	24.11 ± 3.40 (22.56–25.67)	17.82	**0.000** (0.93)	**0.000** (0.93)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.25)	MT vs P: 1.000 (0.14) MT vs T: 1.000 (0.22)
	P		19.97 ± 3.81 (18.42–21.51)	24.50 ± 5.14 (22.94–26.05)	22.68	**0.000** (1)	**0.000** (0.94)	MT vs C: 0.120 (0.61)	MT vs C: **0.001** (0.8)
	T		20.41 ± 4.48 (18.86–21.95)	25.11 ± 4.52 (23.56–26.67)	23.05	**0.000** (1.04)	**0.000** (1)	P vs T: 1.000 (0.13)	P vs T: 1.000 (0.05)
	C		21.79 ± 5.42 (20.24–23.34)	21.50 ± 5.05 (19.94–23.05)	-1.35	0.669 (0.06)	0.766 (0.04)	P vs C: **0.047** (0.59) T vs C: **0.009** (0.75)	P vs C: **0.000** (0.8) T vs C: **0.000** (0.9)
5STS (s)	MT	8.67	8.51 ±1.52 (7.91–9.11)	7.28 ± 1.71 (6.63–7.93)	-14.42	**0.000** (0.76)	**0.000 (**0.8)	MT vs P: 0.735 (0.38) MT vs T: 1.000 (0.09)	MT vs P: **0.022** (0.48) MT vs T: 1.000 (0.08)
	P		8.80 ± 1.99 (8.20–9.39)	6.56 ± 2.10 (5.90–7.21)	-25.47	**0.000** (1.09)	**0.000 (**1.08)	MT vs C: **0.007 (**0.71)	MT vs C: **0.000 (**0.63)
	T		8.62 ±1.17 (8.02–9.22)	7.40 ± 0.96 (6.75–8.05)	-14.14	**0.000** (1.13)	**0.000 (**1.1)	P vs T: 0.434 (0.52)	P vs T: **0.007** (0.63)
	C		8.75 ± 2.16 (8.16–9.35)	8.82 ± 2.54 (8.17–9.47)	0.77	0.765 (0.03)	0.760 (0.03)	P vs C: **0.000** (0.97) T vs C: **0.017** (0.74)	P vs C: **0.000** (0.97) T vs C: **0.001** (0.65)

Table 52. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Timed stair-climbing (s)	MT	13.55	13.84 ± 2.11 (12.91–14.77)	12.37 ± 1.81 (11.49–13.26)	-10.59	**0.000** (0.74)	**0.000** (0.72)	MT vs P: 1.000 (0.13) MT vs T: 1.000 (0.26) MT vs C: 0.086 (0.61) P vs T: 1.000 (0.14) P vs C: **0.026** (0.14) T vs C: **0.004** (0.67)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0.1) MT vs C: **0.000** (0.68) P vs T: 1.000 (0.15) P vs C: **0.000** (0.58) T vs C: **0.000** (0.65)
	P		13.35 ± 2.30 (12.42–14.29)	12.10 ± 2.31 (11.22–12.99)	-9.38	**0.000** (0.54)	**0.000** (0.56)		
	T		13.37 ± 3.29 (12.44–14.31)	11.72 ± 2.95 (10.84–12.61)	-12.34	**0.000** (0.53)	**0.000** (0.53)		
	C		13.65 ± 3.08 (12.71–14.58)	13.94 ± 3.13 (13.06–14.83)	2.17	0.173 (0.1)	0.136 (0.1)		
SCS (steps/s)	MT	1.23	1.25 ± 0.19 (1.17–1.34)	1.12 ± 0.16 (1.04–1.20)	-10.59	**0.000** (0.74)	**0.000** (0.72)	MT vs P: 1.000 (0.13) MT vs T: 1.000 (0.26) MT vs C: 0.086 (0.61) P vs T: 1.000 (0.14) P vs C: **0.026** (0.67) T vs C: **0.004** (0.73)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0.1) MT vs C: **0.000** (0.68) P vs T: 1.000 (0.15) P vs C: **0.000** (0.58) T vs C: **0.000** (0.65)
	P		1.21 ± 0.20 (1.13–1.29)	1.10 ± 0.21 (1.02–1.18)	-9.38	**0.000** (0.54)	**0.000** (0.56)		
	T		1.21 ± 0.29 (1.13–1.30)	1.06 ± 0.26 (0.98–1.14)	-12.34	**0.000** (0.53)	**0.000** (0.53)		
	C		1.24 ± 0.28 (1.15–1.32)	1.26 ± 0.28 (1.18–1.34)	2.17	0.173 (0.1)	0.136 (0.1)		
SCP (W)	MT	202.61	198.20 ± 41.96 (184.31–212.09)	220.52 ± 48.04 (204.88–236.16)	11.26	**0.000** (0.49)	**0.000** (0.49)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.31) MT vs C: 1.000 (0.33) P vs T: 0.580 (0.39) P vs C: 1.000 (0.39) T vs C: 0.056 (0.25)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.15) MT vs C: **0.000** (0.57) P vs T: 0.393 (0.22) P vs C: **0.001** (0.22) T vs C: **0.000** (0.51)
	P		197.35 ± 42.14 (183.46–211.24)	216.74 ± 45.63 (201.10–232.38)	9.83	**0.000** (0.44)	**0.000** (0.44)		
	T		205.76 ± 41.10 (191.87–219.65)	235.45 ± 49.49 (219.81–251.09)	14.43	**0.000** (0.65)	**0.000** (0.65)		
	C		209.12 ± 38.44 (195.23–223.01)	205.95 ± 40.75 (190.31–221.58)	-1.52	0.421 (0.08)	0.452 (0.08)		

Table 52. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
FRT (cm)	MT	25.14	26.56 ± 5.58 (24.69–28.43)	28.94 ± 4.94 (27.13–30.75)	8.96	**0.001** (0.45)	**0.000** (0.58)	MT vs P: 0.200 (0.57) MT vs T: 0.923 (0.36)	MT vs P: 1.000 (0.14) MT vs T: 1.000 (0.18)
	P		22.94 ± 5.53 (21.06–24.81)	26.15 ± 4.87 (24.35–27.97)	14.02	**0.000** (0.62)	**0.001** (0.46)	MT vs C: 0.173 (0.52)	MT vs C: **0.013** (0.53)
	T		24.54 ± 5.22 (22.67–26.42)	27.08 ± 5.46 (25.27–28.89)	10.35	**0.001** (0.48)	**0.002** (0.4)	P vs T: 1.000 (0.18)	P vs T: 1.000 (0.05)
	C		26.51 ± 5.74 (24.64–28.38)	26.08 ± 5.98 (24.27–27.89)	-1.63	0.557 (0.07)	0.828 (0.02)	P vs C: 1.000 (0.18) T vs C: 1.000 (0.01)	P vs C: 0.132 (0.41) T vs C: 0.250 (0.34)
TUG (s)	MT	6.02	5.93 ± 0.73 (5.62–6.24)	5.19 ± 0.69 (4.89–5.50)	-12.40	**0.000** (1.03)	**0.000** (1.12)	MT vs P: 1.000 (0.31) MT vs T: 1.000 (0.21)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.22)
	P		6.15 ± 0.95 (5.84–6.46)	5.44 ± 0.85 (5.13–5.74)	-11.60	**0.000** (0.78)	**0.000** (0.72)	MT vs C: **0.001** (0.83)	MT vs C: **0.000** (0.84)
	T		6.04 ± 0.86 (5.73–6.35)	5.34 ± 0.69 (5.03–5.65)	-11.61	**0.000** (0.89)	**0.000** (0.83)	P vs T: 1.000 (0.13)	P vs T: 1.000 (0.01)
	C		5.94 ± 1.05 (5.63–6.25)	6.04 ± 1.24 (5.73–6.34)	1.62	0.455 (0.08)	0.660 (0.04)	P vs C: **0.043** (0.56) T vs C: **0.011** (0.69)	P vs C: **0.000** (0.66) T vs C: **0.000** (0.69)
6MWT (m)	MT	533.23	544.70 ± 51.23 (521.88–567.53)	562.02 ± 51.91 (539.69–584.36)	3.18	**0.010** (0.34)	**0.001** (0.42)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0.23)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.16)
	P		536.73 ± 68.07 (513.91–559.55)	558.14 ± 60.23 (535.81–580.48)	3.99	**0.001** (0.33)	**0.001** (0.34)	MT vs C: **0.001** (0.9)	MT vs C: **0.001** (0.49)
	T		544.61 ± 55.37 (521.79–567.44)	575.61 ± 63.46 (553.28–597.95)	5.69	**0.000** (0.52)	**0.000** (0.53)	P vs T: 1.000 (0.28)	P vs T: 1.000 (0.15)
	C		506.88 ± 88.21 (484.05–529.70)	499.73 ± 83.57 (477.40–522.06)	-1.41	0.280 (0.08)	**0.050** (0.15)	P vs C: **0.002** (0.8) T vs C: **0.000** (1.02)	P vs C: **0.001** (0.47) T vs C**: 0.000** (0.59)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group at pre and post-test: *n* = 34.MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; 5STS: five times sit-to-stand test; 30sec-CS: 30 second sit-to-stand test; 30sec-AC: 30 second arm-curl test; SCS: stair-climbing speed; SCP: stair-climbing power; TUG: timed up and go test; 6MWT: 6 minutes walking test. ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.97.

V.XIII. DISCUSSION ON PHYSICAL FUNCTION

To the best of our knowledge, the studies presented in this PhD dissertation are the first to investigate the effects of two key training parameters (intensity and modality training) utilizing an elastic resistance during a medium-to-long training period (20 and 32 weeks, respectively) on the muscle strength of lower and upper limbs, muscle power of lower limbs, proactive and dynamic balance, and aerobic capacity through the performance of 30sec-CS, 30sec-AC, 5STS, timed stair-climbing, SCS, SCP, FRT, TUG, and 6MWT field tests in older women.

Regarding the intensity, the main and novel finding of the first study is that both training intensities are effective in improving muscle strength in lower and upper limbs, balance, and aerobic capacity after eight months of resistance training with elastic bands in older women; they achieved significant improvements in all parameters analyzed. Although there were no significant differences between training intensities, it seems that the high-intensity training achieved better results in muscle strength of upper limbs and aerobic capacity. Moreover, progressive elastic resistance training at moderate intensity results in a higher increase in lower-extremity muscle strength and in a greater improvement in dynamic balance. Both training groups achieved significant differences from the C group in all the parameters analyzed.

Furthermore, the main and novel finding of the second study is that all training modalities analyzed – multi-component, power strength training, and traditional high-intensity resistance training – are effective in improving muscle strength in upper and lower limbs, muscle power in lower limbs, proactive and dynamic balance, and aerobic capacity after a training period of 5 months in older women; they achieved significant improvements in all physical function parameters analyzed.

Power strength training seems to be the most useful strategy for improving lower-limb muscle strength and proactive balance; specifically, the muscle power of lower limbs measured with the 5STS test revealed significant differences from the other training modalities studied. Additionally, traditional high-intensity resistance training achieved the greatest adaptations in muscle strength in upper limbs, muscle power in lower limbs (measured by timed stair-climbing), and aerobic capacity, although no significant differences from other training strategies were found. Finally, the multi-component training modality produced the highest adaptations in dynamic balance, without significant differences from the other two training modalities analyzed. All training regimens achieved significant differences from the C group in all parameters analyzed.

We hypothesized in H8 (Chapter III, Section III.I.III.) that both experimental groups increase their physical function values in terms of muscle strength and endurance of upper and lower limbs, dynamic balance, and aerobic capacity by similar amounts after a 32-week program of progressive resistance training with elastic bands. Our findings largely confirm this hypothesis, as we have found that both training intensities significantly improved the muscle strength and endurance of upper and lower limbs through increasing the number of repetitions performed in the 30sec-CS and 30sec-AC tests. Furthermore, both training groups improved dynamic balance and aerobic capacity by reducing the time in the TUG test and increasing the total distance in the 6MWT. Next, we hypothesized in H10 (Chapter III, Section III.I.III.) that at the end (32 weeks) and at the midpoint (16 weeks) of the intervention period, there are differences between the training intensity groups in the parameters analyzed. However, our findings refute this hypothesis because we have found no significant differences between the training groups.

Regarding the influence of training modality, we hypothesized in H8 (Chapter III, Section III.II.III.) that all the training modalities studied (multi-component, power, and

traditional high-intensity resistance training) increase physical function in terms of muscle strength and endurance of the upper and lower limbs, muscle power strength of the lower limbs, proactive and dynamic balance, and aerobic capacity by similar amounts after an intervention period of 20 weeks using elastic resistance, with the power training producing greater effects in power strength than multi-component and high-intensity training programs and the multi-component training achieving greater results in proactive and dynamic balance than the other training modalities. Our findings partially confirm this hypothesis, as we have found that all training modalities significantly improved all physical function parameters analyzed, but the power strength and multi-component exercise modalities did not significantly improve all the muscle power and balance parameters, respectively. In fact, the P group achieved the greatest power outcomes in the 5STS test but not in the stair-climbing test, while the MT group reached higher results in the TUG test (dynamic balance) but not in the FRT (proactive balance).

Next, we hypothesized in H10 (Chapter III, Section III.II.III.) that at the end of the 20-week intervention period, there are differences between the training modalities groups in the parameters analyzed. This hypothesis is partially refuted because we have found that all training modalities significantly improved the physical function parameters, but significant differences were only found in the muscle power of lower limbs, as assessed by 5STS, between the power strength strategy and the other training modalities, in favor of the former. However, in the rest of the parameters, no significant differences were found between training groups.

V.XIII.I. Specific discussion of the first project

The findings reported in the first study by both training groups regarding the improvements in physical function align with previous meta-analyses that have found that progressive resistance training is a successful strategy for improving functional outcomes in older adults, regardless of the training intensity applied (Liu & Latham, 2009; Mcleod et al., 2018; Raymond et al., 2013; Steib et al., 2010). Our results are additionally in accordance with those reported by Mcleod et al. (2018), which have presented that high intensity achieves greater improvements with a small and moderate but not significant effect over moderate and low intensities in the 6MWT. In our study, the HI group reported a significant increase (10.50%) in the aerobic capacity, while the gains observed in the M group were 7.93%.

Some factors could explain the differences between the training groups in this component of physical function. On the one hand, it is well understood that lower baseline levels likely achieve greater improvements in functional performance (Barbalho et al., 2017). In this case, despite the lack of significant differences between groups at the beginning of the study, the baseline levels observed in the HI group were lower than those reported by the M group. Second, due to the higher baseline values illustrated by the M group, a possible ceiling effect of this test could have appeared when a certain distance was reached in well-functioning older adults. Third, there is a threshold above which strength gains do not lead to further functional improvements (Steib et al., 2010). In this sense, the M group demonstrated greater initial and final values in knee extension strength at 60°/s and 180°/s than the HI group; however, the HI group achieved the highest adaptations in these two parameters, especially in force production at high velocities. Considering that changes in knee extensor power explain approximately 20% of the variance in 6MWT (Hruda et al., 2003), the greater

gains obtained by the high-intensity strategy in the aerobic capacity could be related to the higher improvements obtained in knee extension strength at high velocities.

Our results in physical function were additionally consistent with previously published studies, suggesting that high-intensity resistance training is better than training at low intensities for strength outcomes but may not be required for improvement of functional outcomes, where lesser intensities may suffice (Borde et al., 2015; Peterson et al., 2010), especially when the older adults in question are not frail and do not present relevant comorbidities (Raymond et al., 2013). One possible explanation for the lack of difference in functional outcomes is that there may be a threshold above which strength gains do not lead to further functional improvements (Steib et al., 2010). Another frequently utilized argument is that the relatively high training volume of low- or moderate-intensity training (10–15 repetitions) compared with high-intensity training (4–8 repetitions) may considerably impact adaptation when the number of sets and exercises is equal between groups (Steib et al., 2010), as was the case in the first study.

It is necessary to highlight that there is no consensus regarding the optimal training intensity for achieving improvements in functional status in older adults due to the small number of studies that have compared in the same study the effects of different resistance training intensities on physical function outcomes in this population (Fatouros et al., 2005; Kalapotharakos, 2005; Seynnes et al., 2004; Sullivan et al., 2005; Sullivan et al., 2007). Results similar to ours have been reported by Kalapotharakos et al. (2005), who have observed that high (80% of 1RM; 3 sets x 8 repetitions) and moderate (60% of 1RM; 3 sets x 15 repetitions) intensity similarly improved physical function (stair-climbing, chair rise, and walking speed tests) of healthy, sedentary adults after 12 weeks without significant differences between training protocols. Similarly, Seynnes et al. (2004) have reported that both high intensity (80% of 1RM; 3 sets x 8 repetitions) and low intensity (40% of 1RM; 3

sets x 8 repetitions) significantly improved the physical function in a group of frail, institutionalized older adults after 10 weeks (3 times per week). However, contrary to our findings, the authors have reported significant improvements in the 6MWT for the high-intensity intervention but not for the low-intensity protocol. The differences in the training intensity and population studied may explain the differences between results.

Likewise, different from our first study, Fatouros et al. (2005) have demonstrated different improvements in physical functional parameters between high (80%–85% of 1RM; 2–3 sets x 6–8 repetitions) and moderate-to-low intensity (50%–55% of 1RM; 2–3 sets x 14–16 repetitions) after 24 weeks in inactive older women. The authors have indicated that higher intensity training protocols induced greater gains in whole-body physical function (stair-climbing, TUG, and walking speed tests) in older men. Compared to our results, Fatouros et al. (2005) have reported lower improvements in the TUG test with positive changes of 6.5% and 13.4% for low and high intensities, respectively, despite the lower baseline values presented by their subjects. The characteristics of the training program as well as the shorter duration of the training period may explain the difference from our first study.

Regarding the results obtained by both resistance training programs in our first study, without considering the training intensity, our findings align with previous reviews and meta-analyses that have demonstrated with a high quality of evidence the positive and significant effects of resistance training on the overall physical performance in older adults (Beckwée et al., 2019; Borde et al., 2015; Byrne et al., 2016; Csapo and Alegre, 2015; Fiatarone et al., 1990; Jadczak et al., 2018; Liu & Latham, 2009; Mangione, Miller & Naughton, 2010; da Rosa Orssatto, de la Rocha Freitas et al., 2019; Papa et al., 2017; Skelton et al., 1995; Steib et al., 2010; Theodorakopoulos et al., 2017; Tschopp et al., 2011; Yoshimura et al., 2017). However, it is important to note that the ES reported in all parameters analyzed by both training groups were higher than the SMD reported by the Cochrane review by Liu and

Latham (2009), who have indicated a small effect (SMD = 0.14) in favor of progressive resistance training for improving physical function and decreasing physical disability in older adults. Thus, our results suggest that progressive resistance training can be fundamental in improving physical function in older adults by improving all the components studied with a large ES.

Next we focus on the results obtained for each physical function component. For muscle strength and endurance of lower limbs (in absolute values), the HI group improved by 9.39 repetitions (+ 75.93%) the number of sit-to-stand cycles, while the M group achieved similar results, improving by 9.62 repetitions (+ 82.09%) in the same test at the end of the training program. The MDC of 3.49 and 1.64 sit-to-stand cycles that have been previously reported in the literature regarding older people with dementia (Blankevoort et al., 2013) and end-stage hip and knee osteoarthritis (Gill et al., 2008) were widely exceeded by the changes obtained by both training groups.

Additionally, although all experimental groups were above the cutoff point of 10 sit-to-stand cycles (which determines an increased risk for falls in older women), the baseline values of the HI and M groups were below the reference value for maintaining physical independence as proposed by Rikli and Jones (2013b), which is 15 repetitions for women between 65 and 69 years of age. Furthermore, the values portrayed by both training group were below the mean reference values reported by Chen et al. (2009) and McKay et al. (2017), who have presented values of 15.8 and 15.9 repetitions, respectively. Specifically, the baseline values of both groups were within an average range when compared with the normative values reported by Rikli and Jones (2013b; 11–16 repetitions for the age group of 65–69 years); however, it is important to note that, at the beginning of the training period, the HI group indicated a value equivalent to the criterion-reference value for maintaining physical independence for an 80- to 84-year-old age group (12 repetitions), while the M

group demonstrated an initial value equivalent to an 85- to 89-year-old age group (11 repetitions). The CG was the only group that presented results that approached the reference values for their age group. Comparing these values with those reported by Chen et al. (2009), the HI and M subjects placed in the 10^{th}–30^{th} percentiles at the beginning of the study. In contrast, after completion of the resistance training program, the values for the lower-limb dynamic strength tests in both experimental groups were equivalent to those of women aged less than 60 years and were located in the 90^{th} percentile, according to the values provided by Chen et al. (2009). Thus, both progressive elastic resistance training programs produced a highly relevant improvement in physical function of the older women studied through the enhancement of lower-limb muscle strength and endurance.

Regarding muscle strength and endurance of upper limbs, in absolute values, the HI group improved by 11.93 repetitions (+ 79.08%) the number of bicep curls (elbow flexion-extension cycle) performed in 30 s, while the M group achieved similar results, improving by 11.84 repetitions (+ 73.25%) in the same test at the end of the training program. Again, although less pronounced, the baseline values of the HI and M groups were below the reference value for maintaining physical independence as proposed by Rikli and Jones (2013b) in this test, which is 17 repetitions for women between 65 and 69 years of age. However, the C group indicated higher initial values that were above this reference value. As with lower-limb muscle strength, the baseline values of both groups were within a normal range when compared with the normative values reported by Rikli and Jones (2013b) for the 30sec-AC test (12–18 repetitions for the age group of 65–69 years); however, the HI group presented a value equivalent to the criterion-reference value for maintaining physical independence for a 75- to 79-year-old age group (15 repetitions), while the M group demonstrated results equivalent to a 70- to 74-year-old age group (16 repetitions).

As we observed, the upper-limb muscle strength and endurance at the beginning of the study period presented by both training groups was also low, although to a lesser extent than the lower-limb muscle strength and endurance. Positively, after 32 weeks, the values for the upper-limb dynamic strength tests in both experimental groups were equivalent to those of women aged less than 60 years, while the values for the C group remained similar. On this occasion, the muscle force production improvements observed at low and high velocities in lower and upper limbs through the isokinetic assessment in both training groups appeared to be reflected in functional improvements as well, contrary to some previous studies (Boshuizen et al., 2005; Keysor, 2003; Liu, Shiroy et al., 2014; Turpela et al., 2017).

In accordance with the improvements observed in muscle strength and endurance, the HI and M groups also significantly increased dynamic balance. The HI group achieved a significant reduction of 1.24 s (-18.80%) in the time taken to perform the TUG test, while the M group reached even greater improvements (-1.7 s; -24.28%). Additionally, in both groups, the ES was large, with the magnitude of the changes exceeding the 2 points in the M group. The walking speed (m/s) during this agility task also improved in both groups, from 0.71 m/s to 0.94 m/s in the M group and from 0.75 m/s to 0.93 m/s for the HI group. The C group achieved similar values at the end of the study period. The changes and ESs obtained by both training groups are higher than those reported by Liu and Latham (2009), who have found that strength training performed 2–3 times per week has a small positive effect on balance (SMD = 0.12), improving the time to complete the TUG test by 0.69 s compared to a CG. Our findings also align with previous reviews and meta-analyses that have reported positive effects of resistance training on the TUG test in older adults (Lopez et al., 2018; Papa et al., 2017; Vlietstra & Hendrickx, 2018). Despite the significantly positive adaptation achieved in our first study, the time reduction was far from the 4.30 s reported by Howe, Rochester et al. (2011). However, the population of the three studies included in this meta-analysis was

composed of older adults over 80 years of age living in community and institutionalized dwellings.

The MDC of 1.09 s reported by Mangione, Miller & Naughton (2010) for elderly populations or from the 0.8 to 1.4 s determined for individuals with hip osteoarthritis by Wright et al. (2011) were reached in both training groups. All experimental groups achieved times far from the cutoff value of 10 s, which is predictive of near falls in older people with hip osteoarthritis (Arnold & Faulkner, 2007) and further from the cutoff value of 20 s, which is recommended for assessing sarcopenia (Cruz-Jentoft et al., 2019). Nevertheless, it is important to note that at baseline, only the C group presented values within a normal range when compared with the normative values reported by Rikli and Jones (2013b; 6.4–4.8 s for the age group of 65–69 years). The values of the HI and M groups at baseline were equivalent to the women's age group of 70–74 years. If we compare the initial values of all experimental groups with the normative values reported by Gusi et al. (2012) and Pondal and Del Ser (2008) for older adults in Spain, then all groups were far below the reference values for the female group aged 65–69 years.

Specifically, compared with the reference values reported by Gusi et al. (2012), the HI and M groups achieved values equivalent to the reference times for an 80- to 84-year-old age group (6.8 s); the normative value for women between 65 and 69 years of age is established as 5.20 s. Moreover, the HI and M groups were below the reference value for maintaining physical independence as proposed by Rikli and Jones (2013b), which is 5.3 s for women between 65 and 69 years of age; they achieved values equivalent to individuals 80–84 years of age (6.5 s). However, at the end of the training period, both HI and M groups reached the reference value associated with physical independence; each group required approximately 5.3 s to complete the TUG test. Additionally, the 5.28 s and 5.37 s utilized by the M and HI groups in the TUG test at the end of the training period are within the typical

range for the age group of 60–64 years (6–4.4 s), as posited by Rikli and Jones (2001), improving by 10–15 years the age reference values after 32 weeks.

Clinical trials and research have demonstrated that TUG scores have a high correlation with other physical function components, such as reduced muscle strength and muscle power (Coelho-Junior et al., 2018). In fact, variability in TUG scores is primarily explained by lower-limb muscle strength (13%; Coelho-Junior et al., 2018). The higher improvements obtained by the M group in the TUG test were probably associated with the highest knee extension strength values reported at high and low velocities compared with the HI group. Additionally, the poor baseline values in the M group may also explain the differences between groups.

The improvements obtained by both training programs in the TUG test are significantly relevant since previous literature has demonstrated the association between poor TUG scores and increased risk of falls (Alexandre et al., 2012; Rydwik et al., 2011; Shumway-Cook et al., 2000; Viccaro et al., 2011), hospitalizations (Viccaro et al., 2011), nursing home placements (Nikolaus et al., 1996), and ambulatory abilities (Cole & Basmajian, 1994). Furthermore, increased time required to complete this test is related to reduced physical function (Rydwik et al., 2011; Van Iersel et al., 2008; Viccaro et al., 2011), health status (Viccaro et al., 2011), cognitive function (Donogue et al., 2012), and ability to perform ADLs (Rydwik et al., 2011; Viccaro et al., 2011) in older adults. However, the most important consequence of improving dynamic balance is reducing the risk of falls in the population studied and increasing the ability to anticipate and respond to the demands of different tasks or environments.

Finally, regarding the changes in aerobic capacity, the HI group improved by 51.16 m (+ 51.15%) the distance covered in the 6MWT, while the M group achieved an improvement

of 41.42 m (+ 41.42%). These gains in aerobic capacity, especially those achieved by the HI group, were consistent with the significant average increase of 52.37 meters reported by Liu and Latham (2009) after resistance training interventions compared to the CGs (11 studies with 325 participants). However, the HI group reached the substantial MCID for this test, which has been established as 50 m (Perera et al., 2006), while the gain obtained by the M group was also clinically significant because it ranged from 24 to 54 m (Holland et al., 2010; Mangione, Miller & Naughton, 2010). The walking speed (m/s) during this long-walk task also improved in both groups, from 1.45 m/s to 1.56 m/s for the M group and from 1.35 m/s to 1.49 m/s for the HI group. The C group presented similar values at the end of the study period. The initial and final scores of all experimental groups were above the cutoff point of 300 m or less, which is associated with increased risk of morbidity and mortality (Rostagno et al., 2003; Salzman, 2009). Nevertheless, as with the physical function measures described previously, both training groups achieved lower values than the same age reference group. For instance, the baseline value for the HI group was within the normative range for women from 70–74 years of age (480–615 m) as proposed by Rikli and Jones (2001), while the C group revealed initial values similar to those for women from 75–79 years of age (430–585 m). Only the M group demonstrated initial values appropriate for their age group, according to the reference values (500–635 m; Rikli & Jones, 2001).

Furthermore, the initial values of all experimental groups were below the reference value for maintaining physical independence that is proposed by Rikli and Jones (2013b), which is 605 m for women between 65 and 69 years of age. In fact, the M group presented a value equivalent to the criterion-reference value for maintaining physical independence in this test that was appropriate for an 80- to 84-year-old age group (510 m), while the HI group's results were equivalent to an 85- to 89-year-old age group (460 m). In contrast, after 32 weeks of training, the distance covered by both experimental groups was equivalent to the

reference values for women aged 65–69 years (500–635 m) or even less in the case of the M group (545–660 m for women aged 60–64 years; Rikli & Jones, 2001). Neither of the two groups reached the 605 m proposed by Rikli and Jones (2013b) as the reference value for maintaining physical independence in older adults; however, both groups achieved values close to that cutoff point. In fact, the M group was close to reaching the reference value for the age group of 70–74 years (580 m), while the HI group was close to reaching the reference value for the age group of 75–79 years (550 m). Therefore, both training groups decreased the age reference group by 10 years.

An important advantage of the 6MWT is that there are regression formulas to predict the VO_2max values based on the final result (in meters) obtained in the test (Mänttäri et al., 2018). Utilizing the regression formula proposed by Mänttäri et al. (2018), which considers the 6MWT distance, age, and body weight, the M group achieved an improvement of 2.11 mL/min/kg (+ 7.99%; pre: 26.42 mL/min/kg; post: 28.54 mL/min/kg), while the HI group improved by 2.60 mL/min/kg (+ 10.37%; pre: 25.13 mL/min/kg; post: 27.74 mL/min/kg). The C group reached lower values than the training groups (pre: 24.17 mL/min/kg; post: 23.42 mL/min/kg). As we can see, the improvements in the 6MWT were reflected by an increase in aerobic capacity through adaptations in the cardiovascular system that enabled an increase in the VO_2max of the elderly subjects. Comparing the initial and final values obtained by experimental groups, all presented levels of VO_2max were above the reference values proposed by Myers et al. (2017) for women aged 60–69 and 70–79 years, which are 20.7 ± 5.0 mL/min/kg and 18.3 ± 3.6 mL/min/kg, respectively.

One of the main goals of the first study was to make the exercise program more accessible for the elderly population through the usage of elastic bands. As with our findings, previous studies that utilized similar protocols, methods, and training devices (Colado et al., 2010; Colado, Garcia-Masso, Rogers et al., 2012; Colado & Triplett, 2008; Flandez et al.,

2017; Fritz et al., 2018; Uba-Chupel et al., 2017) have also reported improvements in physical functioning in older adults after utilizing elastic materials (Frantke et al., 2015; Hoffman et al., 2016; Kwak et al., 2016; Liao et al., 2018; Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2017; Oliveira et al., 2018; Park et al., 2016; Silva et al., 2020; So et al., 2013; Straight et al., 2012; Yamauchi et al., 2005). Additionally, our results align with previous systematic reviews that have demonstrated that elastic resistance training is effective in improving muscle strength in older adults (Martins et al., 2013; Thiebau et al., 2014) and physical function in healthy adults (De Oliverira et al., 2016).

Nevertheless, the duration of the training program in the majority of the participants was less than 16 weeks and therefore, the improvements were lower compared to the results of our study. Conversely, our first study is the longest study conducted to date with this training device, thus demonstrating the greatest changes obtained to date in all physical function components in an elderly population. For instance, in our study, muscle strength and endurance in lower limbs were improved by both training groups, reaching 9 repetitions (~ 80%), while previous studies have reported improvements between 20% and 60% (de Oliveira et al., 2018; Fritz et al., 2018) or approximately 4 repetitions (Liao et al., 2018; Oesen et al., 2015; Yamauchi et al., 2005). Only the study by Park et al. (2016) has obtained similar results in absolute terms, with improvements of approximately 8–9 repetitions. Likewise, in our study, the improvements in upper-limb muscle strength and endurance reached 11 repetitions (~ 75%). However, the changes registered in previous elastic resistance training programs were lower, reaching approximately 20%–30% (4–6 repetitions; de Oliveira et al., 2018; Fritz et al., 2018; Liao et al., 2018; Oesen et al., 2015; Park et al., 2016; Yamauchi et al., 2005).

In contrast to muscle strength and endurance, despite the shorter duration of the training programs, other authors have also found similar results (Fritz et al., 2018; Liao et al.,

2018; Park et al., 2016), as well as lower (de Oliveira et al., 2018; Yamauchi et al., 2005) and even higher (So et al., 2013) changes than those reported in our first study (~ 20%; -1.5 s). The general lower balance ability and therefore, lower initial values in the TUG test reported in other studies as well as the faster adaptation of the systems involved in balance may explain the positive results achieved in short-period programs. Finally, changes reported in aerobic capacity in our study (~ 9%; 45 m) were also higher than those reported by Fritz et al. (2018) and Oesen et al. (2015).

It is important to note that despite the heterogeneity between studies regarding the population studied (institutionalized elderly, sarcopenic older women, older women with sarcopenic obesity, women with Type II diabetes, community-dwelling older adults), the length of the training interventions (from 8 weeks to 6 months), and the characteristics of the elastic resistance training programs in intensity, volume, and number or type of exercises selected, all of the studies that analyzed the effect of elastic resistance training have found significant positive results in the different components of physical function after the resistance training program, which aligns with the results found in our first study. Moreover, as with our study, the majority of these studies have found significant differences between groups when resistance training was compared to CGs. Thus, it seems that elastic resistance training may allow greater adherence and accessibility with similar results in the different components of physical function in older adults than resistance training performed with machines and free weights.

Additionally, it is important to highlight that our first study is the first to compare the effects of two progressive elastic resistance training protocols performed at different intensities in older adults. Thus, it is the first study that reveals that both moderate and high elastic resistance training are effective exercise strategies to improve general physical

function in older women by increasing the muscle strength and endurance in upper and lower limbs, dynamic balance, and aerobic capacity.

Factors such as training duration, training frequency, training intensity, time under tension, rest between sets, and type of training devices utilized have a considerable impact on the results achieved in physical function after applying an exercise protocol in older subjects. It is reasonable to speculate that, in our first study, the long duration of the training program, the high volume performed in both training groups (3–4 sets per exercise), the intensities applied (moderate and high), the type of exercises prescribed (focused on stimulating the main muscles of the upper and lower limbs), and the type of load utilized (variable resistance) promoted significant increases in the different components of the physical functions evaluated. Additionally, the moderate and high RPE performed during the training period could have maximized neuromuscular adaptations associated with the enhancement of physical function responses. The lower initial levels of physical function in the subjects of our first study compared with the reference values for the same target population could have led to greater changes in the different components of physical function in the elderly women studied.

Although the underlying mechanisms for resistance-training-induced improvements in physical function have not been elucidated and are likely multifaceted, it seems that the improvements in the different components of the physical function obtained in our first study could be related to the improvements observed in the neuromuscular function, specifically with the increase in muscle strength and muscle power. In fact, the relationship between these two physical conditions and physical function in older adults has been previously established (Newman et al., 2003; Visser et al., 2002). Additionally, the positive adaptations in body composition with the increase in muscle mass and reduction of body fat mass may also be

important factors in the physical function improvements since low muscle mass has been associated with poor physical function (Visser et al., 2002).

The results obtained in our first study on the components of physical function are highly relevant because physical function is a strong indicator of an individual's health status (Beaudart et al., 2019). The age-associated impairments in physical function can hinder the ability of older adults to perform the basic tasks required for independent living (Ahlqvist et al., 2016; Hyatt et al., 1990). Thus, our first study favored healthy aging through the development of functional ability, enabling well-being in older age, and optimizing the intrinsic capacity of the elderly population, which are goals that the WHO has noted as essential in its new paradigm of healthy aging in 2015 (WHO, 2015). Considering the high prevalence and incidence rates of disability in older adults and the increased risk for disability that women have compared to men (FIFoA-R, 2010; Newman & Brach, 2001), it is important to highlight the positive adaptations achieved in our first study by both training programs because reduced levels of functional capacity are related to lower quality of life and higher risk of hospitalization and mortality in older adults (Hennessy et al., 2015; Millán-Calenti et al., 2010; Na et al., 2017; Nascimento et al., 2018).

In summary, both moderate and high elastic resistance training strategies are effective in improving physical function in older women, as demonstrated by both training groups' achievement of significant changes after the training intervention in all parameters studied, with the magnitude of the changes reported being primarily large.

V.XIII.II. Specific discussion of the second project

Regarding the results obtained in our second study, our investigation is the first to examine the modality-response effect of 20 weeks of a multi-component, power strength and traditional high-intensity elastic resistance training on physical function in older women. In

contrast to previous studies, we directly compared the three modalities' effects on the muscle strength and endurance of lower and upper limbs, muscle power of lower limbs, proactive and dynamic balance, and aerobic capacity. Our results indicate that high-velocity resistance training is the most effective modality for improving lower-limb muscle power and muscle strength and endurance, as significant improvements were obtained in the 5STS and 30sec-CS tests; additionally, participants achieved significant differences with the other training modalities in the 5STS test. However, our findings also indicate that the traditional high-intensity elastic resistance training strategy produces the greatest improvements in upper-limb muscle strength and endurance, lower-limb muscle power, and aerobic capacity by significantly improving results in the 30sec-AC, stair-climbing, and 6MWT tests. Unlike the P group, however, this modality did not obtain significant differences for the other training groups in any parameter. Finally, the multi-component training strategy produced the highest improvements in dynamic balance by producing significant changes in the TUG tests. Nevertheless, this modality did not obtain significant improvements in its favor compared to the other groups. The C group maintained similar levels of physical function in all parameters analyzed at the end of the study period.

To our knowledge, this is the first RCT addressing the effects of these training modalities on physical function in older women. Because of the novelty of our analysis, it is difficult to make direct comparisons with the current literature due to the lack of studies that compare these training modalities with each other. Much of the research on physical function has been performed by applying these training modalities separately.

However, there have been several studies, mainly in the past decade, that have attempted to elucidate whether power strength or traditional resistance training produces greater functional enhancements in older adults by comparing these training modalities in the same study (Balachandran et al., 2014, 2017; Bean et al., 2004, 2009; Beltran Valls et al.,

2014; Coelho-Júnior et al., 2019; Correa et al., 2012; Bottaro et al., 2007; Drey et al., 2012; Englund et al., 2017; Gray et al., 2018; Henwood & Taaffe, 2006; Henwood et al., 2008; Lopes et al., 2016; Macaluso et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Pamukoff et al., 2014; Ramírez-Campillo et al., 2014; Reid, Martin et al., 2014; Richardson, Duncan, Jimenez, Jones et al., 2018; Sayers et al., 2003; Sayers et al., 2012; Tiggemann et al., 2016; Yoon et al., 2017; Zech et al., 2012). The findings obtained in our second study in relation to this question are in agreement with those studies that have indicated that, generally, both power strength and traditional resistance training are effective strategies for improving physical function in older adults, reporting no significant differences between groups (Bean et al., 2004; Tiggemann et al., 2016; Henwood et al., 2008).

Additionally, our results are only partially in accordance with the studies that have reported greater functional enhancements from power strength training than with traditional resistance training in older individuals (Bean et al., 2009; Miszko et al., 2003; Bottaro et al., 2007; Ramírez-Campillo et al., 2014). In our study, significant differences in favor of the high-velocity resistance training strategy were found only in the lower-limb muscle power, but only in the 5STS test and not in the stair-climbing test. This heterogeneous response between muscle power tests in the P group are related to the fact that functional activities that require a higher percentage of maximal strength, such as stair-climbing, are associated with muscle strength more than with muscle power (Katsoulis et al., 2018). In fact, the activation of knee extensor during stair ascent and chair-rise tests was estimated in 78% and 80% of maximum strength, respectively (Hortobagyi et al., 2003). The requirements of muscle strength during stair-climbing are also higher than in the 5STS test because stair-climbing involves a phase in which all body weight is supported on one leg. This task requires a higher intensity dose than the intensity prescribed for the P group. However, the traditional resistance training group did not train at high velocities, although the higher training

intensities and higher muscle strength gains obtained in the knee muscle extensor and flexor at 60°/s allowed greater improvements in this power test compared to the P group.

Additionally, the lack of significant differences between training modalities in the majority of the physical function parameters could be related to the significant isokinetic muscle strength gains in the lower and upper limbs obtained at low and high velocities by the three groups. It is possible that subjects in all three training groups reached the threshold beyond which additional muscle strength gains may not provide additional benefits to physical function and ADLs' performance, as has been highlighted in previous studies (Boshuizen et al., 2005; Damush & Damush, 1999; Keysor, 2003; Keysor & Jette, 2001; Latham et al., 2003; Liu, Ilich et al., 2014; Liu & Latham, 2011; McMurdo & Johnstone, 1995; Skelton et al., 1995). In fact, isokinetic muscle gains at high velocity were higher in the P group, and the gains obtained at low velocity were greater in the T group, although the final values of force produced at low and high velocities in all training groups were similar in the knee extensor and flexor, which have been proven to be the most relevant for physical function in older adults. The higher muscle strength values obtained by the T group in the knee and in the elbow flexor and extensor at 60°/s may explain the better results obtained by this group in the 30sec-AC, stair-climbing, and 6MWT tests. However, in proactive balance, as measured by the FRT, the P group achieved the best results.

The higher muscle strength levels obtained by this group in the hip abduction and adduction muscles at high velocities could be related to this improvement due to the response of the muscles against an external force. In this case, the action was a consequence of voluntary movement, but it should be as fast as possible to maintain the body's center of mass within manageable limits of the base of support (Howe, Rochester et al., 2011). However, the MT group achieved better results in the TUG test, which is a task that combines the ability to rise from a chair, walk, turn around, and sit as quickly as possible. It cannot be a

coincidence that in this multitask test, the MT group obtained the best improvement, as the multi-component training program was based on the prescription of strength, aerobic, balance, and coordination exercises, among others. Thus, the specificity of the training modality performed could be reflected in the improvements obtained in the different physical function tests.

We compared our results with previous studies that analyzed the effect of both training modalities specifically in older female populations, and our findings are in accordance with the study by Tiggemann et al. (2016), who have not found significant differences between traditional resistance training and power training after 12 weeks (twice weekly) in lower-limb power strength (as proven in 5STS and stair-climbing tests) and dynamic balance (as proven in TUG tests), although they have found significant differences between groups in aerobic capacity (as proven in 6MWTs). Despite the training protocol applied, Tiggemann et al.'s (2016) study was different from ours (participants in both groups exercised at 45%–65% of 1RM, utilizing six exercises: bilateral leg press, bench press, bilateral knee extension, seated row machine, bilateral leg curl, and abdominal crunch). The authors, as in our study, utilized an RPE scale – in this case, the Borg scale – to control training intensity. However, our results are contrary to other studies that have found superior gains with power training in functional performance in older women (Correa et al., 2012; Lopes et al., 2016; Ramírez-Campillo et al., 2014).

From these studies, only a few focused specifically on older women (Correa et al., 2012; Lopes et al., 2016; Ramírez-Campillo et al., 2014; Tiggemann et al., 2016; Yoon et al., 2017). For instance, Lopes et al. (2016) have found that only the power strength training group improved the 30sec-CS and the TUG test after 12 weeks of a training program performed 3 times per week. However, the training intensity (40%–80% for the power strength training group and 60%–80% for the traditional resistance training group), volume

(3–4 sets of 6–8 repetitions for both groups), exercises (horizontal leg press; bilateral knee extension; bilateral knee flexion; and plantar flexion in the step, abductor, and adductor machines), and duration (12 weeks) of the study differed markedly from ours. Likewise, utilizing the same training duration and frequency, Ramírez-Campillo et al. (2014) have revealed significant differences in favor of the high-velocity resistance training group in dynamic balance, measured by the TUG test (18% vs 10%). In this case, the power strength group exercised at 40%–75% of 1RM, while the traditional resistance training was performed at 75% of 1RM. Both groups performed 3 sets of 8 repetitions in the six resistance exercises prescribed (bench press, standing upper row, biceps curl, leg press, prone leg curl, and leg extension). As we observed, the differences in the training design between the studies that have reported the superiority of power training and our training interventions are notable. The higher intensities utilized in our traditional resistance training strategy and conversely, the lower intensities applied in the high-velocity resistance training modality have led to greater specific improvements for each type of training in the physical function of the older women studied. Thus, based on our results, it seems that there is more than one effective way to improve physical function in older adults and that positive results in physical function can be produced by different adaptations generated through different training modalities.

In fact, some reviews and meta-analyses have reported with moderate-level evidence that power strength training is more effective for enhancing the physical performance of older adults than progressive resistance training in some physical function components (Byrne et al., 2016; da Rosa Orssatto, Cadore et al., 2019; Steib et al., 2010; Tschopp et al., 2011), although our results align with the findings reported by da Rosa Orssatto, de la Rocha Freitas et al. (2019), which is probably the most comprehensive meta-analysis to date. The authors, after analyzing 15 studies, have concluded that there is inconclusive evidence to support the superiority of high-velocity resistance training to improve functional capacity when

compared to traditional resistance training due to the lack of high-quality and pre-registered studies, high heterogeneity, and small-studies' publication bias. The authors have not found significant differences between training modalities on muscle strength (30sec-CS), muscle power (5STS), balance (TUG), and aerobic capacity (6MWT). In this sense, our study provides high-quality evidence about the lack of significant differences between both training modalities, with the exception of lower-limb power strength (as measured by the 5STS test), since the study was pre-registered and featured a high sample size for each group as well as a longer duration of study, which are characteristics that have not been previously grouped in any study to date. In fact, the main characteristics of the studies that compared both training modalities are as follows: short-term duration (≤ 12 weeks), not pre-registered, low quality, small sample sizes (~ 10 subjects per group), training frequency of 1–3 sessions, 2–4 sets per exercise, and 6–15 repetitions per set. Regarding intensity, some studies adopted higher loads in traditional resistance training, as did our study (Balachandran et al., 2014; Gray et al., 2018; Henwood et al., 2008; Lopes et al., 2016; Miszko et al., 2003; Ramírez-Campillo et al., 2014; Richardson, Duncan, Jimenez, Juris et al., 2018; Yoon et al., 2017), while others utilized the same training load in both training groups (Bean et al., 2009; Bottaro et al., 2007; Correa et al., 2012; Englund et al., 2017; Marsh et al., 2009; Tiggemann et al., 2016; Zech et al., 2012).

In agreement with our results, Drey et al. (2012) and Yoon et al. (2016) have found no statistical difference among power strength and traditional resistance training groups; theirs are the only previous studies in which both intervention programs were performed with elastic bands alone (Yoon et al., 2016) or in combination with machines and free weights (Drey et al., 2012) in older adults. Contrary to our findings, Yoon et al. (2016), have found significant improvements in the SPPB in both training groups but no significant improvements in the TUG tests after 12 weeks (twice weekly) in older women with mild

cognitive impairment. The high-velocity resistance training consisted of 2–3 sets of 12–15 repetitions at an RPE of 12–13 ("somewhat hard") with green elastic bands (low tension). For the traditional resistance training intervention, participants were instructed to perform 2–3 sets of 8–10 repetitions at an RPE of 15–16 ("hard") with blue elastic band (moderate tension). As we observed, the short duration of the training period and the low intensity at which both training groups exercised probably explain the lack of significant changes in dynamic balance.

Focusing on the specific adaptations achieved by the P group in physical function, the findings reported in our second study align with a significant number of studies that analyzed the effect of power strength training on physical function among the elderly population in the past decade and have suggested that muscle power and physical function can be improved by power strength training across a wide range of combinations in training parameters (Balachandran et al., 2014; Bean et al., 2004, 2009; Beijersbergen et al., 2017; Beltran Valls et al., 2014; Bottaro et al., 2007; Cadore et al., 2014; Coelho-Junior et al., 2017; Conlon et al., 2016; Correa et al., 2012; de Vreede et al., 2005; de Vos et al., 2005; Drey et al., 2012; Earles et al., 2001; Englund et al., 2017; Fielding et al., 2002; Gianoudis et al., 2014; Glenn et al., 2015; Henwood & Taaffe, 2006; Henwood et al., 2008; Hruda et al., 2003; Katula et al., 2008; Lohne-Seiler et al., 2013; Lopes et al., 2015; Macaluso et al., 2003; Marsh et al., 2009; Miszko et al., 2003; Nogueira et al., 2009; Onambele et al., 2008; Orr et al., 2006; Pamukoff et al., 2014; Paul et al., 2014; Pereira et al., 2012; Portegijs et al., 2008; Radaelli et al., 2018; Ramírez-Campillo et al., 2014, 2016, 2018; Ramsbottom et al., 2004; Reid, Martin et al., 2008, 2014; Richadson et al., 2018; Sayers et al., 2003, 2012, 2016; Signorile et al., 2002, 2005; Valls et al., 2014; Van Roie et al., 2013; Vasconcelos et al., 2016; Wilhelm et al., 2014).

Specifically, in absolute and relative values, the P group improved by 4.80 repetitions (+24.44%) the number of sit-to-stand cycles performed in the 30sec-CS, achieving the greatest improvements in lower-limb muscle strength and endurance among the training groups. These gains are similar to those revealed by Katsoulis et al. (2018), who have reported significant improvements of 23.5% (ranging from 12.7%–43%) in muscle strength assessed by the 30sec-CS test after power strength exercise interventions in older adults. Additionally, the P group exceeded the MDC of 3.49 and 1.64 sit-to-stand cycles that have previously been reported in the literature regarding older people with dementia (Blankevoort et al., 2013) and end-stage hip or knee osteoarthritis (Gill et al., 2008). Baseline values reported were above the cutoff point of 10 sit-to-stand cycles, which is the determining factor for an increased risk of falls in older women, and above the reference value for maintaining physical independence that has been proposed by Rikli and Jones (2013b). Furthermore, baseline values for the P group were within and above a typical range when compared to the normative values reported by Rikli and Jones (2013b) for the age group of 65–69 (11–16). The initial values were additionally above the mean reference values reported by Chen et al. (2009) and McKay et al. (2017) of 15.8 and 15.9 repetitions, respectively. At the end of the training program, the average final value recorded of 24 sit-to-stand cycles in 30 s in the P group was equivalent to values relative to populations under 60 years of age. Moreover, the magnitude of the changes was moderate.

Regarding muscle strength and endurance in upper limbs, in absolute values, the P group improved by 4.53 repetitions (+ 22.68%) the number of bicep curls (elbow flexion-extension cycle) performed in 30 s. As with the lower limbs, baseline values for this group were high and were above the reference value for maintaining physical independence proposed by Rikli and Jones (2013b), which is 17 repetitions for women between 65 and 69 years of age. Additionally, initial values were above the typical range when compared with

the average values reported by Rikli and Jones (2013b) for the 30sec-AC test (12–18 repetitions for the age group of 65–69 years). Similar to the behavior demonstrated in lower-limb power strength and endurance after 20 weeks, the average final value recorded of 24 elbow flexion-extension cycles in 30 s in the P group is equivalent to values relative to populations under 60 years of age. Moreover, the magnitude of the ES reported was large.

In line with the improvements observed in muscle strength and endurance in lower and upper limbs, the P group additionally significantly increased muscle power in lower limbs. The P group achieved a significant reduction of 2.24 s (-25.68%) in the time required to perform the 5STS test. This improvement is within the range of significant positive changes of 12.8%–44% in the 5STS reported by Katsoulis et al. (2018). This test has been previously determined to be more purely a muscle power test than the stair-climbing test, since the peak angular velocities for knee and hip extensor are 186°/s and 224°/s, respectively, when sit-to-stand movements are performed quickly (Gross et al., 1998; Hortobagyi et al., 2003; Schenkman et al., 1996), which implies a high demand of muscle power in lower-limb muscles. The baseline values exhibited by the P group in this test were far above the cutoff value of 17 s, which is a valid predictor score of poor health conditions, such as hospitalization events, lower-limb limitations, and death in older adults (Cawthon, 2015; Cesari et al., 2009). Additionally, the absolute and relative changes obtained by the P group were similar to and greater than the absolute and relative MDC of 2.5 s and 17.5% established for the 5STS test (Goldberg et al., 2012). Moreover, the ES reported for the changes obtained in this test was large.

With the intention to provide more detailed, complete, and direct information of muscle power, the following formulas are included: sit-to-stand mean velocity ($m \cdot s^{-1}$) [vertical distance (m) covered by the center of mass divided by the mean time (s) spent to complete the concentric phase of 1 STS repetition], STS mean force (N; the body mass

displaced during the test multiplied by gravity), absolute STS mean power (W; the product of STS mean velocity and STS mean force), relative STS mean power ($W \cdot kg^{-1}$; absolute STS power normalized to body mass, which denotes the ability to produce mechanical power per unit of body mass), and allometric STS mean power ($W \cdot m^2$; absolute STS power normalized to height^2, which is a scaled measure of mechanical power). These formulas have been proposed by Alcazar, Losa-Reyna et al. (2018) and Losa-Reyna et al. (2020). At the baseline, the STS mean velocity as well as the absolute, relative, and allometric STS mean power were 0.34 $m \cdot s^{-1}$, 201.07 W, 3.03 $W \cdot kg^{-1}$, and 86.53 $W \cdot m^2$, respectively. After 20 weeks, the P group achieved an improvement of 34.14% in these parameters [post-training values and absolute changes from baseline values follow: 0.46 $m \cdot s^{-1}$ (+ 0.11 $m \cdot s^{-1}$), 269.74 W (+ 68.66 W), 4.06 $W \cdot kg^{-1}$ (+ 1.03 $W \cdot kg^{-1}$), and 116.07 $W \cdot m^2$ (+ 29.54 $W \cdot m^2$) for STS mean velocity as well as absolute, relative, and allometric STS mean power, respectively)]. As we can appreciate, the P group improved both velocity and muscle power outputs, increasing the ability to produce higher mechanical power per unit of body mass. Additionally, gains in STS mean velocity and absolute STS mean power reached the MDC of 0.06 $m \cdot s^{-1}$ and 40.5 W, respectively, which have been established to detect important velocity and power gains in elderly populations (Alcaraz et al., 2018). These clinically significant changes achieved by the P group are increasingly important if we consider that this group exhibited high levels of relative (≥ 2.2 $W \cdot kg^{-1}$) and allometric (≥ 67.1 $W \cdot m^2$) muscle power at the beginning of the study, according to the classification levels proposed by Losa-Reyna et al. (2020).

Analyzing the results obtained in the other lower-limb muscle power tests, the P group demonstrated significant improvements of -1.25 s (-9.38%), -0.11 steps/s (-9.38%), and + 19.39 W (+ 9.83%) in stair-climbing time, SCS, and SCP, respectively. In this case, the P group obtained lower gains compared with the other training modalities studied due to the higher requirements of maximal muscle strength compared with the 5STS test. The

improvements obtained in stair-climbing time were higher than the range of significant positive changes of 7.1%–8% reported by Katsoulis et al. (2018). It is important to note that stair ascent and descent are essential ADLs that contribute to functional independence and quality of life and that previous studies have registered both tasks; however, we decided to assess only stair ascent to avoid unnecessary risks, as previous studies have concluded that stair descent is particularly hazardous and has been implicated in three times more accidents than stair ascent (Hemenway et al., 1994; Tinetti, 1988). Additionally, 75% of the falls reported on stairs occur during descent, and the 37% hospitalization rate is associated with falls on stairs, particularly in women who live alone (Hemenway et al., 1994; Tinetti, 1988). The initial and final values of the SCS were within the average speed for older adults, which has previously been established at .1 to 1.7 steps/s (Hinman et al., 2014). Nevertheless, the MDC, established at 5.5 s and 2.6 s (Almeida et al., 2010; Kennedy et al., 2005), for stair-climbing time was not reached. The main reason is that these MDCs have been proposed for samples of people with end-stage hip or knee osteoarthritis and with lower-extremity osteoarthritis following knee arthroplasty rather than for healthy older adults. In fact, typical values and the MDC for this test in older adults have not yet been developed.

The improvements achieved in proactive and dynamic balance by the P group were also statistically significant, increasing by 3.21 cm (+ 14.02%) and reducing by 0.71 s (-11.60%) the distance in the FRT and the time in the TUG test, respectively. The walking speed (m/s) during the TUG also improved from 0.81 m/s to 0.91m/s. When results obtained in the FRT regarding the risk of falling were transformed to a gradable scale from 0 to 3 (Duncan et al., 1990), the subjects in the P group reduced the risk of falling from two times more likely to fall (2 = reach between 15.3 and 25.4 cm) to not likely to fall (3 = reach ≥ 25.4 cm) after the training study period. The ESs obtained in this test were moderate (ANOVA)

and small (ANCOVA). The significant positive changes obtained in the TUG test were within the range for significant positive changes (10.2%–17.3%) reported by Katsoulis et al. (2018).

Despite the significant improvements, the MDC of 1.09 s, which has been established by Mangione, Miller & Naughton (2010) for the elderly population, or from 0.8 to 1.4 s, which has been determined for individuals with hip osteoarthritis by Wright et al. (2011), was not reached, although it was close. With a longer duration of the training program, these MDCs would probably have been reached. The initial and final values of the P group in this test were within a normal range when compared with the normative values reported by Rikli and Jones (2013b; 6.4–4.8 s for the age group of 65–69 years). However, the initial values were far from the normative values for Spanish women between 65 and 69 years of age, which has been established as 5.20 s (Gusi et al., 2012), and also from the reference value for maintaining physical independence proposed by Rikli and Jones (2013b), which is 5.3 s. However, at the end of the training period, individuals in the P group were close to reaching these reference values.

Finally, regarding the changes in aerobic capacity, the P group improved by 21.41 m (+ 3.99%) the distance covered in the 6MWT, reaching a small MCID for this test, which has been established at 20 m (Perera et al., 2006). However, the changes obtained in this test were slightly lower than the 5% reported by Katsoulis et al. (2018). The walking speed (m/s) during this long-walk task also improved from 1.49 m/s to 1.55 m/s. The initial and final scores were above the cutoff point of 300 m or less, which is associated with increased risk of morbidity and mortality (Rostagno et al., 2003; Salzman, 2009). The baseline values were within the typical range for women between 65 and 69 years, as proposed by Rikli and Jones (2001), but below the reference value for maintaining physical independence, also proposed by Rikli and Jones (2013b), which is 605 m for the same age group. Conversely, after 20 weeks of training, the distance covered in the P group was closer to that cutoff point.

However, after utilizing the regression formula proposed by Mänttäri et al. (2018) to calculate the VO_2max through the distance in the 6MWT, we determined that the P group achieved an improvement of 1.09 mL/min/kg (+ 3.97%; pre: 27.50 mL/min/kg; post: 28.59 mL/min/kg). Additionally, the initial and final values of VO_2max presented by the P group were above the reference values proposed by Myers et al. (2017) for women aged 60–69 and 70–79 years, which are 20.7 ± 5.0 mL/min/kg and 18.3 ± 3.6 mL/min/kg, respectively.

This second study demonstrates that an elastic high-velocity resistance training strategy performed over 20 weeks is effective in improving the general physical function in healthy older women, as the individuals in this group achieved significant improvements with moderate to large ESs in all physical function parameters tested. Additionally, despite the typical and high baseline physical functioning of the older women analyzed, the MDCs were reached in almost all physical function field tests, which denotes the considerably positive impact that this kind of training modality can have not only in the disabled population, but also in healthy elders.

The results obtained in our second study further support the effectiveness of the traditional high-intensity resistance training modality for the improvement of physical function in older women. Our second study confirms the findings reported in our first study after 32 weeks but also provides evidence that only 20 weeks are necessary to significantly improve, with a moderate to large ES, the main physical function components in healthy older women. Our findings align with previous reviews and meta-analyses that have found that progressive resistance training is a successful strategy for improving functional outcomes in older adults (Beckwée et al., 2019; Borde et al., 2015; Byrne et al., 2016; Csapo & Alegre, 2015; Fiatarone et al., 1990; Jadczak et al., 2018; Liu & Latham, 2009; Mangione, Miller & Naughton, 2010; da Rosa Orssatto, Cadore et al., 2019; Papa et al., 2017; Skelton et al., 1995; Steib et al., 2010; Theodorakopoulos et al., 2017; Tschopp et al., 2011; Yoshimura et al.,

2017). However, it is important to note that the ES reported in all parameters analyzed by the T group were higher than the SMD reported in the Cochrane review by Liu and Latham (2009), who have indicated a small effect (SMD = 0.14) in favor of progressive resistance training for improving physical function and decreasing physical disability in older adults. Thus, our results suggest that progressive elastic resistance training applied over 20 weeks can play a fundamental role in improving physical function in older adults.

Focusing on the results obtained in each physical function component, the T group improved by 3.32 repetitions (+ 16.63%) the number of sit-to-stand cycles performed in the 30sec-CS, obtaining lower improvements than the P and MT groups. However, despite the lower gains, the MDC established for this test was reached. Regarding muscle strength and endurance of upper limbs, in absolute values, the T group improved by 4.7 repetitions (+ 23.05%) the number of bicep curls (elbow flexion-extension cycle) performed in 30 s. As with the P group, individuals within the T group presented baseline physical function levels within the typical range compared to the average values reported for an age group of women between 65 and 69 years (Chen et al., 2009; Mckay et al., 2017; Rikli & Jones, 2001) or even above this range. These typical and high levels of physical functioning reported by the T group were common in the other physical function tests. Therefore, with the exception of the 6MWT distance, the initial values in the other tests were also above the reference value for maintaining physical independence proposed by Rikli and Jones (2013b). At the end of the training program, the average final values recorded in almost all tests were equivalent to values relative to populations under 60 years of age.

In line with the improvements observed in muscle strength and endurance in lower and upper limbs, the T group also significantly increased muscle power in lower limbs. The T group achieved a significant reduction of 1.22 s (-14.14%) in the time required to perform the 5STS test. However, the absolute and relative changes obtained by the T group were lower

than the absolute and relative MDC of 2.5 s and 17.5% established for the 5STS test (Goldberg et al., 2012). The dominance of the muscle power component in this test caused the T group to obtain lower gains than the P group. In the STS mean velocity as well as absolute, relative, and allometric STS mean power, the T group demonstrated a baseline level of 0.36 $m \cdot s^{-1}$, 219.07 W, 3.20 $W \cdot kg^{-1}$, and 91.85 $W \cdot m^2$, respectively. After the training period, the T group achieved an improvement of 16.48% in these parameters [post-training values and absolute changes from baseline values follow: 0.42 $m \cdot s^{-1}$ (+ 0.05 $m \cdot s^{-1}$), 255.44 W (+ 36.15 W), 3.72 $W \cdot kg^{-1}$ (+ 0.52 $W \cdot kg^{-1}$), and 106.99 $W \cdot m^2$ (+ 15.14 $W \cdot m^2$) for STS mean velocity as well as absolute, relative, and allometric STS mean power, respectively)], which is approximately half of the gain obtained by the P group. The gains in STS mean velocity and absolute STS mean power were close to reaching the MDC of 0.06 $m \cdot s^{-1}$ and 40.5 W, which have been established to detect important velocity and power gains in elderly populations (Alcaraz et al., 2018). It is necessary to consider that this group revealed considerable levels of relative ($\geq$ 2.2 $W \cdot kg^{-1}$) and allometric ($\geq$ 67.1 $W \cdot m^2$) muscle power at the beginning of the study, according to the classification levels proposed by Losa-Reyna et al. (2020). These high initial values increased the difficulty of reaching notable differences.

However, a striking observation that emerged from the data analysis was the significant improvement obtained by the T group in stair-climbing time (-1.65 s; -12.34%), SCS (-0.15 steps/s; -12.34%), and SCP (+ 29.69 W; + 14.43%) parameters. In fact, the T group achieved the greatest lower-limb muscle power gains in this test due to the higher requirements of maximal muscle strength compared with the 5STS test. The initial and final values of the SCS were within the average speed for older adults, which has previously been established at 1.1 to 1.7 steps/s (Hinman et al., 2014).

The results in the second study also corroborate the findings of a significant portion of the first study in relation to the physical function component of balance. The T group

reported significant improvements in proactive and dynamic balance, increasing by 2.54 cm (+ 10.35%) and reducing by 0.7 s (-11.61%) the distance in the FRT and the time in the TUG test, respectively. The walking speed (m/s) during the TUG also improved from 0.82 m/s to 0.93 m/s. At the end of the training period, the subjects of the T group were close to reaching the normative and reference values reported by Gusi et al. (2012) and Rikli and Jones (2013b) for the TUG test, although the MDC proposed by Mangione, Miller & Naughton (2010) was not achieved. Additionally, according to the score reported in the FRT, the T group reduced the risk of falling from two times more likely to fall to not likely to fall.

In terms of aerobic capacity, the T group improved by 31 m (+ 5.69%) the distance covered in the 6MWT, reaching between small and substantial MCIDs for this test, which has been established as between 20 and 50 m (Perera et al., 2006). The walking speed (m/s) during this long-walk task also improved from 1.51 m/s to 1.59 m/s, being the highest speed registered among the experimental groups. The baseline values were within the normative range for women between 65 and 69 years, which has been proposed by Rikli and Jones (2001), but below the reference value for maintaining physical independence, also proposed by Rikli and Jones (2013b). However, at the end of the study period, the average 6MWT distance reached by the T group was only 30 m below this cutoff point. Additionally, this group achieved an improvement of 1.58 mL/min/kg (+ 5.55%; pre: 27.39 mL/min/kg; post: 28.98 mL/min/kg). Furthermore, the initial and final values of VO_2max presented by the T group were above the reference values proposed by Myers et al. (2017).

The results obtained by the T group broadly support the work of other studies that utilized elastic bands as training devices in traditional resistance training protocols and have reported significant improvements in physical function parameters in older adults (Frantke et al., 2015; Fritz et al., 2018; Hoffman et al., 2016; Kwak et al., 2016; Liao et al., 2018;

Martins, Safons et al., 2015; Oesen et al., 2015; Oh et al., 2016; Oliveira et al., 2018; Park et al., 2016; Silva et al., 2020; So et al., 2013; Straight et al., 2012; Yamauchi et al., 2005).

Regarding the results obtained by the MT group, our findings agree with several reviews and meta-analyses that have certified, with a satisfactory level of evidence, the effectiveness of this kind of exercise strategy on the functional status of older adults (Baker, Atlantins & Fiatore, 2007; Bouaziz et al., 2016;, Cadore et al., 2013; Cadore & Izquierdo, 2013; de Labra et al., 2015; de Vries et al., 2012; Gine-Garriga et al., 2014; Howe, Rochester et al., 2011; Jadczak et al., 2018; Lopez et al., 2017; Mcleod et al., 2018; Theou et al., 2011). Consistent with the literature, our research finds that participants who trained different components of physical function, such as balance, strength, and cardiorespiratory capacity, in the same session significantly improved all components after 20 weeks, with no significant advantage over power strength or traditional resistance training modalities.

Additionally, our positive results align with previous studies that have reported significant positive adaptations in all or at least one physical function component after applying multi-component training interventions in older adults (Ansai et al., 2015; Arai et al., 2007; Baker, Kennedy et al., 2007; Barnett et al., 2003; Beyer et al., 2007; Binder et al., 2002; Bird et al., 2011; Campbell et al., 1997; Carvalho et al., 2009, 2010a, 2010b; Casas-Herrero et al., 2019; Clemson et al., 2012; Freiberger et al., 2012; Justine et al., 2012; Hara et al., 2007; Iwamoto 2009; Jessup et al., 2003; Kamide et al., 2009; Karikanta et al., 2007; King et al., 2002; Kovacs et al., 2013; Levy et al., 2012; Lin et al., 2007; Liu-Ambrose et al., 2008; Lord et al., 1995, 2003, 2005; Losa-Reyna et al., 2019; McMurdo & Rennie, 1993; Marques et al., 2009; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Means et al., 2005; Nakamura et al., 2007; Nelson et al., 2004; Oliveira et al., 2019; Otero et al., 2017; Park et al., 2008; Pope et al., 2019; Ramsbottom et al., 2004; Rubenstein et al., 2000; Shubert et al., 2010; Suzuki et al., 2004, 2012, 2013; Sykes & Ling, 2004; Taguchi et al., 2010;

Toraman et al., 2004; Toraman & Sahin, 2004; Tolomio et al., 2010; Toto et al., 2012; Trape et al., 2017; Vaughan et al., 2014; Villareal, Erman & Agyar, 2011; Worm et al., 2001).

As in our study, some studies have reported positive effects in lower- or upper-limb muscle strength assessed through the 30sec-CS and 30sec-AC tests (Justine et al., 2012; Marques et al., 2011, 2013; Nakamura et al., 2007; Oliveira et al., 2019; Otero et al., 2017; Tolomio et al., 2010; Toraman et al., 2004; Toto et al., 2012; Trape et al., 2017; Losa-Reyna et al., 2019); others have reported positive effects on proactive and dynamic balance (Ansai et al., 2015; Bird et al., 2011; Justine et al., 2012; Marques et al., 2011; Marques et al., 2013; Nakamura et al., 2007; Oliveira et al., 2019; Otero et al., 2017; Pope et al., 2019; Toraman et al., 2004; Toto et al., 2012) measured by FRT and TUG tests, and still others have demonstrated positive effects in aerobic capacity assessed by the 6MWT (Carvalho et al., 2010b; Justine et al., 2012; Marques et al., 2009; Marques, Mota, Machado et al.,2011; Nakamura et al., 2007; Toraman et al., 2004; Toto et al., 2012; Trape et al., 2017; Losa-Reyna et al., 2019). Additionally, our study supports evidence from previous RCTs performed in older women (Carvalho et al., 2010b; Marques et al., 2009; Marques, Mota, Machado et al., 2011; Nakamura et al., 2007; Otero et al., 2017; Trape et al., 2017).

For example, Marques, Mota, Machado et al. (2011) have found a significant reduction of 0.8 s in the TUG test and a significant improvement of 11 m in the 6MWT distance in older women after 8 months of multi-component exercise intervention performed twice per week. Sessions were composed of weight-bearing activities, muscular endurance exercises, balance training, agility training, and stretching exercises. Likewise, Traped et al. (2017) have reported an improvement of 47 m in the 6MWT in elderly women after applying a multi-component training program over 12 weeks (twice weekly). Sessions included strength, aerobic, stretching, balance, and coordination exercises. Similarly, Otero et al. (2017) have found significant improvements in older women in dynamic balance (TUG: + -

36%) and strength of upper (30sec-AC: 80%) and lower limbs (30sec-CS: 47%) after 6 months. Each session consisted of warm-up exercises (10 min), balance training (20 min), strength training (20 min), and cool-down (10 min). Differences in the physical function gains between studies are reasonable due to the high heterogeneity in the multi-component training program parameters applied as well as the differences in the population and duration of the multi-component interventions.

We analyzed the results obtained in each physical function component; regarding muscle strength and endurance in lower limbs, the M group improved by 3.32 repetitions (+ 18.49%) the number of sit-to-stand cycles performed in the 30sec-CS, obtaining lower improvements than the P group and similar improvements to the T group. Additionally, the MDC established for this test was reached along with a moderate ES. Regarding muscle strength and endurance in upper limbs, in absolute values, the MT group improved by 3.64 repetitions (+ 17.82%) the number of bicep curls (elbow flexion-extension cycle) performed in 30 s, achieving lower gains than the P and T groups. However, the improvements reported by the MT group in both muscle strength and endurance tests align with the muscle strength gains reported in the meta-analysis by Bouaziz et al. (2016), which ranged from 1.4%–95.0% in the multi-component training interventions compared with control groups. As with the P and T groups, the baseline physical function levels presented by the individuals in the MT group were within the normal range compared to the normative values reported for an age group of women between 65 and 69 years (Chen et al., 2009; Mckay et al., 2017; Rikli & Jones, 2001) or even above this range. These typical and high levels of physical functioning reported by the MT group were also common in the other physical function tests. Therefore, with the exception of the 6MWT distance, the initial values in the other tests were also above the reference value proposed by Rikli and Jones (2013b) for maintaining physical

independence. At the end of the training program, the average final values recorded in almost all tests were equivalent to values relative to populations under 60 years of age.

Of note is that the multi-component training modality also significantly improved lower-limb muscle power after 20 weeks of intervention. These results suggest that, although the multi-component training program prescribed was not specifically designed to improve this physical function component, the improvements observed in force production at low and high velocities in the isokinetic dynamometer transfer to ADLs, such as chair stands and stair-climbing, in which muscle power is highly determinant. It seems that muscle strength adaptations produced mainly by exercises in the strength block but also probably by the aerobic, balance, flexibility, and coordination training components result in significant improvements in lower-limb muscle power. These data are particularly important because no previous studies have analyzed the effects of multi-component training programs on muscle power in older women. Specifically, the MT group achieved a significant reduction of 1.23 s (-14.42%) in the time required to perform the 5STS test. These gains were similar to the T group but lower than the P group. The absolute and relative changes obtained by the MT group in this test were lower than the absolute and relative MDCs of 2.5 s and 17.5%, which have been established for the 5STS test (Goldberg et al., 2012).

In the STS mean velocity as well as absolute, relative, and allometric STS mean power, the MT group presented baseline levels of 0.36 $m \cdot s^{-1}$, 241.06 W, 3.46 $W \cdot kg^{-1}$, and 95.67 $W \cdot m^2$, respectively. After the training period, the MT group achieved an improvement of 16.89% in these parameters [post-training values and absolute changes from baseline values follow: 0.42 $m \cdot s^{-1}$ (+ 0.06 $m \cdot s^{-1}$), 281.79 W (+ 40.72 W), 4.04 $W \cdot kg^{-1}$ (+ 0.58 $W \cdot kg^{-1}$), and 111.84 $W \cdot m^2$ (+ 16.16 $W \cdot m^2$) for STS mean velocity as well as absolute, relative, and allometric STS mean power, respectively)], which were approximately half of the gains obtained by the P group. The gains in STS mean velocity and absolute STS mean

power reached the MDCs of 0.06 $m \cdot s^{-1}$ and 40.5 W, which have been established to detect important velocity and power gains in elderly populations (Alcaraz et al., 2018). It is necessary to consider that this group also demonstrated high levels of relative ($\geq$ 2.2 $W \cdot kg^{-1}$) and allometric ($\geq$ 67.1 $W \cdot m^2$) muscle power at the beginning of the study, according to the classification levels proposed by Losa-Reyna et al. (2020). Additionally, the MT group obtained a significant improvement of 1.47 s (-10.59%), 0.13 steps/s (-10.59%), and 22.32 W (+ 11.26%) in stair-climbing time, SCS, and SCP, respectively. The MT group achieved the second highest improvements in these parameters, placing only behind the T group. The ESs were small (SCP) to moderate (stair-climbing and SCS). The initial and final values the SCS were within the average speed for older adults, which has previously been established as 1.1 to 1.7 steps/s (Hinman et al., 2014).

The results obtained by the MT group in balance parameters corroborate the positive findings revealed in the other physical function components. The MT group reported significant improvements in proactive and dynamic balance, increasing by 2.38 cm (+ 8.96%) and reducing by 0.74 s (-12.40%) the distance in the FRT and the time in the TUG test, respectively. The walking speed (m/s) during the TUG also improved from 0.84 m/s to 0.96 m/s. Unlike the P and T groups, at the end of the training period, the subjects in the MT group reached the typical and reference values reported by Gusi et al. (2012) and Rikli and Jones (2013b) for the TUG test, although the MDC proposed by Mangione, Miller & Naughton. (2010) was not achieved. Additionally, according to the score reported in the FRT, the MT group also reduced the risk of falling from two times more likely to fall to not likely to fall. The improvements reported by the MT group in both balance tests align with the estimated balance gains of 5.3%–88.9% reported in the meta-analysis by Bouaziz et al. (2016) for multi-component interventions. However, the changes observed in the MT group were lower than the statistically significant reduction in time to perform the TUG test (1.63 s) and the

significant improvement of 5.77 cm in FRT reported by Howe, Rochester et al. (2011). It seems possible that these greater results in Howe, Rochester et al.'s (2011) study are because the majority of the interventions included in the meta-analysis were conducted with older adults with low to very low physical function levels, such as prefrail, frail, or community-dwelling older adults. In our study, despite the high physical functioning levels at baseline, the ESs obtained were moderate and large for FRT and TUG, respectively.

Finally, in terms of aerobic capacity, the MT group improved by 17.32 m (+ 3.18 %) the distance covered in the 6MWT, being close to reaching the small MCID for this test, which has been established at 20 m (Perera et al., 2006). The walking speed (m/s) during this long-walk task also improved from 1.51 m/s to 1.56 m/s. The baseline values were within the typical range proposed by Rikli and Jones (2001) for women between 65 and 69 years of age but below the reference value for maintaining physical independence, which has also been proposed by Rikli and Jones (2013b). Despite the MT group achieving lower gains in this test compared to the other training modalities, at the end of the study period, the average 6MWT distance reached by the MT group was close to the cutoff point for maintaining physical independence. It is necessary to consider that the initial values of the MT group were the highest at the beginning of the study, which may explain the lower gains obtained by this group. Additionally, the MT group achieved an improvement of 0.88 mL/min/kg (+ 3.28%; pre: 26.91 mL/min/kg; post: 27.80 mL/min/kg). Furthermore, the initial and final values of VO_2max presented by the MT group were above the reference values proposed by Myers et al. (2017) for older women.

One of the main objectives of the second project was to assess the efficacy for older adults of a multi-component training program performed with elastic bands since no previous data were found on the effectiveness of this kind of exercise modality conducted entirely with variable resistance on physical function parameters in older adults. Our study demonstrates

that multi-component training interventions performed with elastic bands are at least equally effective for improving muscle strength and endurance in upper and lower limbs, muscle power in lower limbs, proactive and dynamic balance, and aerobic capacity in older women as multi-component programs performed with machines and free weights. Previously, few studies have utilized this kind of training device in multi-component training interventions, but they are typically employed in combination with machines or free weights (Brouwer et al., 2003; Carvalho et al., 2010b; Kamide et al., 2009; Nakamura et al., 2007). For instance, Carvalho et al. (2010b) have illustrated that a multi-component training program utilizing elastic bands and free weights performed 3 times per week for 8 months had a significant effect on aerobic capacity in older women, improving by 6.07% the distance covered in the 6MWT. Nevertheless, Nakamura et al. (2007) compared three training frequencies (1, 2, or 3 days per week) of a multi-component training program consisting of a 10-min warm-up, 20 min of walking, 30 min of recreational activities, 20 min of resistance training, and a 10-min cool-down in older women and have found that only the multi-component program performed 3 days per week improved the 30sec-CS (+ 4.4%), 30sec-AC (+ 7.5%), FRT (+ 9.6%), and 6MWT (+ 4.1%) after 12 weeks.

As noted in the literature review, the high heterogeneity in the multi-component training protocols prescribed between studies makes comparisons difficult. Generally, our positive findings in the MT group corroborate the broad evidence about the efficacy of multi-component exercise strategies in improving physical functioning in older adults, regardless of whether the training program was composed of three, four, or five training components or what kind of training intensity, frequency, or training device was applied (Taguchi et al., 2010; Toto et al., 2012; Vaughan et al., 2014; Villareal, Erman & Agyar, 2011).

However, the efficacy of the multi-component training modality on physical function compared directly with other training strategies has rarely been studied. In fact, no previous

studies have compared the multi-component and high-velocity resistance training modalities in older adults; our second study is the first to compare these two training strategies. Additionally, few studies have compared the effectiveness of multi-component training with traditional resistance training modalities on physical function parameters (Marques et al., 2009; Leite et al., 2015). Our results align with the studies of Marques et al. (2009) and Leite et al. (2015), finding no significant differences between multi-component and traditional resistance training modalities after 32 and 12 weeks, respectively. Specifically, Marques et al. (2009) compared the effects of these two training modalities over 8 months in older women and have found significant, similar improvements in aerobic capacity in both training groups (26 and 25 m for the MT and T groups, respectively). The multi-component intervention was composed of aerobic exercises, muscular endurance exercises performed in a circuit utilizing elastic bands and free weights, static and dynamic balance exercises, and flexibility exercises. Two sets of 10–12 repetitions at 70% of 1RM for seven exercises performed on machines (leg press, leg extension, seated leg curl, double chest press, lateral raise, overhead press, and abdominal machine) were performed in the traditional resistance training strategy. Both training modalities were performed twice weekly. Compared with our results, our T group achieved greater improvements, which are probably due to the higher intensities applied, while the lower gains observed in our MT group may be related to the shorter duration of the intervention (32 vs 20 weeks).

Similarly, Leite et al. (2015) have found similar improvements in the 5STS test between multi-component (pre: 8.7 s; post: 7.5 s, -1.2 s) and resistance training (pre: 8.5 s; post: 7.47 s, -1.03 s) interventions after 12 weeks (twice weekly) in healthy elderly adults. As we observed, the improvements in this test were similar in both groups compared with the gains achieved by the MT and T groups of our study. However, contrary to our results, Leite et al. (2015) have found only non-significant improvements in the VO_2max of the traditional

resistance training group (from 28 mL/min/kg to 31 mL/min/kg) and a non-significant decrease in the multi-component modality (from 24.4 mL/min/kg to 23.6 mL/min/kg). A possible explanation for these results may be that the intensity, duration, and type of exercises prescribed in the different blocks of the multi-component program were not appropriate to produce enough stimuli to generate muscle and aerobic adaptations in the sample studied.

This second study has demonstrated that a multi-component training modality performed over 20 weeks is effective to improve the general physical function in apparently healthy older women, as the individuals in this group achieved significant improvements with moderate to large ESs in all physical function parameters tested. Furthermore, the positive adaptations among the physical function components achieved by the multi-component training strategy were similar to the other training modalities studied, revealing only a significant disadvantage compared to the power strength modality in the lower-limb muscle power measured by the 5STS test. Additionally, despite the normal and high baseline physical functioning of the older women analyzed, the MDCs were reached in almost all physical function field tests, which denotes the high positive impact that this kind of training modality can have in a wide range of populations, such as disabled and healthy elders.

Several factors may account for the beneficial effects on physical function obtained by the three training groups. For instance, the type of exercises selected in the main parts of the P and T groups as well as those performed in the different blocks by the MT group involved the main muscle groups of the lower and upper limbs. Additionally, the high intensity in the T group has been widely demonstrated as effective for improving physical function in older adults, especially muscle strength and aerobic capacity. Conversely, low-to-moderate intensities when performing resistance exercises at maximal speed are most effective in producing muscle power improvements in activities that allow the power component to dominate the maximal strength component in the force-power relationship. In

the MT group, the type of exercises proposed in the strength block (squat plus upright rowing and lunge) as well as the volume of series and repetitions performed in the same block seems to produce enough stimuli to generate positive impacts in physical function components. Additionally, the exercises and the volume prescribed in the other blocks (balance, aerobic, coordination, and flexibility) also favor the positive results reported by the MT group. The time under tension, rest between sets, and type of training device utilized could additionally impact the results achieved in physical function by the three training groups. Furthermore, for the T group and for the strength block in the MT group, rather than being exposed to high loads or high volumes, achieving maximal effort was an important factor in the gains achieved. As in our first study, the RPE was moderate but typically high during the majority of the training program. This close-to-maximal effort could maximize the neuromuscular adaptations to enhance the muscle strength response (Goto et al., 2005; Carpinelli, 2008) and therefore, the positive physical function responses.

The underlying mechanisms by which these training modalities induced improvements in the physical function components may be related to the same structural, neural, and musculotendinous or connective tissue factors previously mentioned for muscle strength and power adaptations. The neural factors could be significant in the three modalities due to the high-velocity muscle contractions performed in the P group, the high intensity applied in the resistance exercises in the T group, and the variety of stimuli prescribed through the balance, aerobic, strength, and coordination components in the multi-component training modality. Especially important are the neural mechanisms in the high-velocity resistance training since high-velocity contractions diminish motor unit recruitment thresholds and increase discharge rates as the rates of force and power development increase (Budingen & Freund, 1976; Del Vecchio et al., 2019; Desmedt & Godaux, 1977, 1978; Tanji & Kato, 1973). These changes in the recruitment patterns produce training adaptations, such

as muscle power and strength improvements, consequently increasing functional performance in older adults.

Additionally, the rapid contractions induced by power strength training increase the Type II fibers' CSA, pennation angle, and fascicle length (Aagaard et al., 2001; Kawakami et al., 1995), which have direct implications in the improvement of physical function. However, structural and musculotendinous factors could have greater weight in the improvements obtained in the MT and T groups. In fact, the improvements in the different components of physical function obtained in our second study by the MT and T groups could be related to the improvements observed in neuromuscular function and specifically to the increase in muscle strength and muscle power as well as to the increase in muscle mass and reduction of body fat mass.

Overall, the results obtained in our second study regarding the effects on physical function could be considered highly relevant, as the reported findings illuminate the effectiveness of multi-component, high-velocity resistance training and traditional high-intensity resistance training modalities on different components of physical function in older women. Contrary to expectations, all training modalities improved by similar amounts the lower and upper muscle and endurance strength, lower-limb muscle power, proactive and dynamic balance, and aerobic capacity. Only the power strength training modality produced significant differences from the other training modalities in the 5STS, achieving the greatest improvements in the lower-limb muscle power. Additionally, the results obtained in the second project are interesting since, for the first time, the effectiveness of the most relevant training strategies in reversing or at least reducing the effects of aging on physical function in older women was compared, and all three training interventions utilized elastic bands as the main training device.

As in our first study, the three training programs proposed in the second study also favored healthy aging through the development of functional ability and optimized the intrinsic capacity of the older women studied by improving their capacity to produce force and power in their lower limbs, maintain balance, and walk long distances, all of which are basic components necessary for ADLs in the elderly population and goals that the WHO considers essential in its new paradigm of healthy aging as of 2015 (WHO, 2015). However, the improvements achieved in physical function in our second study have additional merit since, unlike our first study, the older women studied presented physical function values according to the typical range for their age. These findings suggest that, with an appropriate prescription of training parameters, the three training modalities can improve the physical function of healthy older women with normal levels of physical function; therefore, these strategies are effective in the prevention stage of frailty and dysmobility syndromes.

In summary, in our second study, the training modality had no effect on the gains of physical function for the majority of the physical function components studied, since all training modalities achieved significant improvements in the physical function parameters analyzed. However, the modality training utilized was decisive for the improvements in muscle power in lower limbs for power-predominant tasks in which high-velocity resistance training is more effective than multi-component and traditional high-intensity resistance training modalities. Therefore, these data suggest that in well-functioning older women, the three training modalities studied could prevent and delay the appearance of disability and frailty syndromes. However, it is necessary to consider the velocity of contractions as an important factor if the goal of the program is the improvement of muscle power in lower limbs. These findings in muscle power measured by field tests corroborate the greatest improvements observed by the P group in force production at high velocities. Consequently, power resistance training to increase physical function and particularly muscle power in older

people may be an alternative to traditional resistance training, because lower intensities achieved similar results in physical function with lower RPEs, which may increase the adherence of participants. Nevertheless, it is also necessary to highlight as one of the main findings reported in our second study that the muscle power in lower limbs can be improved by multi-component and traditional high-intensity resistance training modalities. Thus, in women who cannot or do not want to perform high-velocity resistance training, these strategies can be an alternative. In fact, if the characteristics of the elderly population do not allow performance of contractions at high speed or with high loads, then a multi-component training modality could be an appropriate exercise modality to improve physical function.

Additionally, the second project demonstrates that the three training modalities can attenuate age-related changes in physical function and improve ADLs, such as stair-climbing, chair stands, or walking long distances, even when elastic bands are utilized as the main training device in all training modalities analyzed. Finally, the high quality of the study, the duration of the training period, and the specific older female population analyzed provide useful knowledge and insights into the field of healthy aging through exercise.

V.XIV. DISCUSSION ON POTENTIAL CONFOUNDING VARIABLES

Regarding the influence of the potential confounding variables in both studies, we hypothesized in H9 (Chapter III, Sections III.I.III and III.II.III) that the potential confounding variables analyzed do not influence the rest of the parameters in any experimental group.In the first study, our findings largely confirm this hypothesis, as we found that age, basic physical function reflected in the BADLs and IADLs questionnaires, and cognitive status collected by the MMSE revealed no significant differences between experimental groups at baseline. However, in the second study, our findings partially confirm this hypothesis since variables such as age, basic physical function reflected in the BADLs and IADLs questionnaires, cognitive status collected by the MMSE, and anxiety or depression state

recorded by the OASIS and ODSIS scales, respectively, presented no significant differences between groups at baseline. Additionally, no significant differences were found between groups at the beginning of the study in physical activity levels. However, significant nutrional differences were found between groups at baseline in protein, magnesium, and vitamin H intake but not in the other parameters. Furthermore, significant differences in time were found in total energy intake, protein, magnesium, and selenium intake in some groups.

Our results in the first and second studies are in accordance with previous studies that have found no significant differences or only minor differences in the potential confounding variables analyzed, and these were mainly in nutrition intake and physical activity levels (Barnett et al., 2003; Stotl et al., 2019; Coelho-Júnior et al., 2019; Nabuco, Tomeleri, Fernandes, Sugihara Junior, Venturini et al., 2019; Hamaguchi et al., 2017; Ribero et al., 2015; Richardson, Duncan, Jimenez, Juris et al., 2018; Tomeleri et al., 2016; Torres et al., 2017).

V.XV. DISCUSSION ON PROGRAM FEASIBILITY AND SAFETY

Regarding the feasibility and safety of the exercise programs designed in the first study, we hypothesized in H11 (Chapter III, Section III.I.III) that both training programs are effective and safe due to their positive effects on all parameters analyzed, the high rates of attendance and compliance of the participants, and the low level of adverse events reported. Our findings largely confirm this hypothesis, as we found that both training intensities were effective in significantly improving the majority of the parameters analyzed and were concurrently feasible due to the high attendance and compliance rates in both training groups, which were above 75% after 8 months of intervention. Additionally, both exercise programs were also safe, given the following factors: 1) the attrition rate was low (approximately 15%); 2) none of the drop-outs left the program as a result of injuries or adverse responses to the

intervention; and 3) only a small number of mild or moderate adverse events were recorded, with no serious adverse events collected.

Regarding the feasibility and safety of the exercise programs designed in the second study, we hypothesized in H11 (Chapter III, Section III.II.III) that all the training modalities studied (multi-component, power, and traditional high-intensity resistance training) are effective and safe due to their positive effects on all parameters analyzed, the high rate of attendance and compliance of the participants, and the low level of reported adverse events. Our findings largely confirm this hypothesis, as we found that the three training modalities were effective in significantly improving the majority of the parameters analyzed and were concurrently feasible due to the high attendance and compliance rates in both training groups, which were above 80% after 5 months of intervention. Additionally, both exercise programs were safe, given the following factors: 1) the attrition rate was low (below 15%); 2) none of the drop-outs left the program as a result of injuries or adverse responses to the intervention; and 3) only a small number of mild or moderate adverse events were recorded, with no serious adverse events collected.

Long-term adherence to physical activity is essential for the health of older adults to be realized. Previous research has demonstrated that, despite the widespread usage of conventional devices and the benefits to health-related parameters in the elderly population, 50% of people who adopt this type of training quit during the first year of practice (Lopes et al., 2019). However, the results obtained in both of our studies regarding feasibility and safety demonstrate that an elastic-based exercise program, regardless of the training modality or intensity applied, could be an interesting alternative to increase long-term adherence in older adults, as attendance and compliance rates in the medium- and long-term in our studies were high. These results align with previous research that also applied elastic resistance

training, although the durations of the interventions were shorter than our two studies (Colado et al., 2010; Flandez et al., 2017; Fritz et al., 2018).

Moderate- and high-intensity resistance training programs in the first study reported similar attendance and compliance rates, contrary to what has previously been reported by some authors. Previous research has stated that training with heavier loads is related to a higher RPE, even when the total training load is carefully matched (Alegre et al., 2015), and consequently, the greater the sensation of effort, the more adherence rates decrease, which indicates an inverse relationship between exercise adherence and intensity (Perri et al., 2002)**.** Nevertheless, in our first study, the results reflect that both training intensities were well-received by the participants, as attrition rates and adverse events were similar. While adherence and engagement present challenges in elderly populations, we have demonstrated that it is possible to successfully apply progressive resistance training programs at moderate and high intensities with high levels of effort in this population. Thus, not only the usage of elastic bands, but also the effectiveness of the RPE method to control intensity and to monitor correct progression in volume, exercises, and intensity could favor the high rates of attendance and compliance achieved in both studies. In fact, our results align with previous studies that have indicated that the usage of RPE could increase adherence, mainly in novice subjects in the early stages of training (Gearhart et al., 2002; Tiggemann et al., 2016). At these ages, the main challenge is to combine the efficiency and safety of the training programs, as older adults often present chronic health problems and comorbidities that can compromise both the efficiency and safety of the exercise programs designed.

It is important to note that our second study is the first to contribute regarding the effectiveness, feasibility, and safety of training modalities other than resistance training, such as multi-component and power strength training when performed with elastic bands in older adults. Our results demonstrate that elastic bands are a safe training device to increase

adherence to resistance, multi-component, and power strength training in older adults. Regardless of the type of training tool utilized, the results presented by the P group are similar and even better than those reported in previous studies that analyzed this training modality in older adults via weight machines (Balachandran et al., 2017; Coelho-Júnior et al., 2019; De Vos et al., 2008; Gray et al., 2018; Hamaguchi et al., 2017; Marsh et al., 2009) or elastic bands (Drey et al., 2012). Furthermore, in terms of safety, the results obtained by the P group align with previous research that has reported no serious adverse events after applying this training modality in older adults (Balanchandran et al., 2017; De Vos et al., 2008; Marsch et al., 2009; Ramírez-Campillo et al., 2018; Richardson, Duncan, Jimenez, Juris et al., 2018). Additionally, the attendance and compliance rates observed in the M group are similar to previous studies that analyzed this training modality in elderly populations (Grossman et al., 2016; Karikanta et al., 2007; Leite et al., 2015; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Otero et al., 2017). Likewise, previous studies have confirmed our results in terms of safety, reporting few or no adverse events for this training modality (Karikanta et al., 2007; Marín-Cascales et al., 2015, 2017; Marques, Mota, Machado et al., 2011; Marques et al., 2013; Oliveira et al., 2019).

However, it is important to remark that the majority of studies do not report on whether there have been adverse events in the training interventions. In this sense, both studies presented in this PhD dissertation reveal the most complete information collected to date regarding the safety of different training programs performed in older adults. Therefore, and considering that the training programs studied are characterized by applied high intensities in load (65%–85% of 1RM) or effort (6–9 RPE), high-velocity contractions (power strength training), or multiple stimuli (multi-component training), the results obtained in both studies are highly relevant since these strategies may allow greater adherence and accessibility with similar results and high levels of safety for older adults.

CHAPTER VI

Strengths and limitations

VI.I. STRENGTHS

The present PhD dissertation has several strengths that should be mentioned and considered that add robustness to the main findings:

Regarding design, novelty, and effectiveness aspects:

1. The prospective randomized controlled trial design used in both projects;
2. The pre-registration of the second project in ClinicalTrials.gov;
3. The blinding of data collectors and data analysts along with the codification of participants in both projects;
4. The inclusion and comparison of three (project one) and four (project two) experimental groups in the same study;
5. The novel data combining the effects of training intensity and modality in elastic-based exercise interventions on all the variables collected has been examined in older women for the first time, providing an important contribution to the current body of literature;
6. The positive effects of all the elastic-based exercise interventions studied for most of the parameters analyzed in apparently healthy older women, which implies that they are effective strategies not only to treat but also to prevent future disabilities and frailty syndromes.

Regarding the sample:

7. The successful recruitment strategy since a large number of well-characterized older women were recruited;
8. The type of sample studied due to the lack of studies analyzing the effects of elastic-based exercise interventions in older adults;
9. The large sample size of both projects, especially the second;

10. The groups of participants well balanced in characteristics and number at baseline, especially in the second project.

Regarding the parameters assessed:

11. The type and number of variables analyzed in both projects that have never been included together in previous studies, allowing for the visualization of a larger map of the adaptations produced by different elastic-based interventions among older women;
12. The use of gold-standard oxidative stress and bone biomarkers;
13. The use of gold standards and effective equipment such as DXA, an isokinetic dynamometer, and field tests to assess body composition, neuromuscular strength, and physical function in older adults;
14. The rigorous assessment of the parameters analyzed following the standardized protocols, especially for the assessment of oxidative stress and BTMs where their clinical variability was taken into account;
15. The use of specialists to collect and analyze some data, such as dietitians for the nutrition assessment or laboratory technicians for the oxidative stress and bone biomarkers. The DXA assessment and interpretation was also performed by a specialist;
16. The assessment of oxidative stress products from the three main macromolecules, DNA, lipids, and proteins, while previous studies have only reported the results of oxidative products from one or two macromolecules;
17. The assessment of multiple oxidative stress, antioxidant biomarkers, and thiol redox state, whereas previous studies have only reported few oxidative products or antioxidants;

18. The assessment of aBMD of multiple bone sites, whereas previous studies reported results from fewer bone areas;
19. The assessment of neuromuscular strength for hip and elbow muscle groups because no previous studies have analyzed the effects of elastic-based exercise intervention on these two joints;
20. The use of two velocities in the assessment of neuromuscular strength with the isokinetic dynamometer since no previous studies have done so using elastic-based exercise interventions;
21. The consideration of potential confounding variables, especially in the second project.

Regarding the training programs:

22. The relatively long-term duration of the training programs, especially the first project, since most previous studies were short-term (<12 weeks);
23. The location of the training programs since all sessions were conducted in MACOPs, allowing greater accessibility to older adults and also indirectly promoting the interest and participation of older adults in physical activity and exercise activities;
24. The training frequency, due to higher frequencies could represent a barrier to the initiation or adherence to training, especially among older women, whereas lower frequencies could limit the adaptations achieved;
25. The close supervision of the training sessions by qualified exercise personnel in both projects;

26. The use of safe, low-cost, easy, accessible, non-time-consuming training equipment such as elastic bands that allow for the training programs studied in both projects to be applied in multiple environments with few resources;
27. The high applicability of the training programs analyzed in both studies thanks to previous aspects mentioned (duration, location, frequency, supervision, and equipment), which eliminate important barriers to exercise participation for older adults.

Regarding the training parameters:

28. The intensity of training carefully defined and supervised by the level of both load and effort;
29. The equalization of intensity in terms of effort in the first study, although the intensity for load was different, whereas in previous studies that compare intensities, only load has been used to account for intensity;
30. The use of a valid, reliable, objective, and quantitative methods to control intensity when elastic bands are used as a training device in resistance-training interventions in older adults, such as the OMNI-RES perceived exertion scale;
31. The use of a method to control the velocity displacement of the load when elastic bands are used through the use of OMNI-RES perceived exertion and perception of velocity scales;
32. The design of the training programs following the training principles of individualization, periodization, and progression as well as the specific principles for producing adaptations in certain structures, as in the case of bone.

Regarding the safety and feasibility:

33. The high adherence and compliance rate throughout the elastic-based training programs studied in both projects;
34. The low attrition rate in both projects;
35. The low number of mild and moderate adverse events reported in both projects;
36. The lack of serious adverse events in both projects;

Regarding the statistical methods:

37. The ITT analysis performed in both projects, which is considered the best analysis for providing unbiased estimates of the efficacy of the intervention;
38. The PPA performed as a secondary and supportive analysis of the ITT analysis;
39. The control of potential confounders using the baseline values and age as covariates, although there were no statistical differences between groups at baseline for most of the variables examined in both studies;
40. The calculation of ICC (test-retest, intra-rater, and inter-rater reliability), short-term CV, and intra-assay variation for most of the variables assessed in our laboratory;
41. The sample size estimation with the G*Power program.

Regarding how the data is displayed:

42. The detailed results reported with the mean, SD, ES within and between groups, and the Δ% from the ANOVA and ANCOVA.

43. The depth and detail of the literature review that allows the reader to fully understand not only the current evidence regarding exercise and the different parameters analyzed but also the physiology and pathology of the tissues and biomarkers analyzed, the most effective methods for their assessment, definitions of key concepts, and the effects of aging.

Regarding other aspects:

44. The contributions by professors Dr. Mike Rogers and Dr. Travis Triplett from the international universities of Wichita State (Kansas, USA) and Appalachian State (North Carolina, USA), respectively.

VI.II. LIMITATIONS

Despite this dissertation's relevant results and strengths, the present PhD dissertation is not exempt from limitations and, therefore, a number of limitations must be considered when interpreting the findings:

Regarding the research design:

1. The non-blinding of participants in both projects;
2. The blinding of the research staff and data collectors was not possible for the entire experimental period in both projects because the same staff sometimes conducted the baseline and post-intervention assessment sessions, which may have led to measurement bias; however, potential bias was counteracted by providing different codes to participants and also providing identical assessment procedures and motivation to all participants;
3. Lack of pre-registration of the first project.

Regarding the sample:

4. The population analyzed in both studies included only apparently healthy, well-functioning, independently living, urban, Caucasian older women. Thus, our findings may not be applicable to older adults with functional limitations and chronic-diseases, high-risk populations, men, older adults living in extended care facilities, institutionalized individuals, older adults with specific conditions (e.g., sarcopenia, frailty), other ethnic groups, or rural areas;
5. The participants in both studies were motivated women who volunteered to exercise, which perhaps limits the generalizability of the findings to other older women with similar characteristics. In this sense, the Hawthorne effect

should be considered since exercise intervention studies appeal to healthier and better-motivated individuals;

6. Despite the strict screening and recruitment process, there were older women with some pathologies such as obesity and osteoporosis;
7. The small sample size in some groups of the first project possibly increases the risk of type two errors;
8. The unequal sample size in the first project may have affected the between-group analyses, may have introduced bias in the statistical analysis, and may have consequently reduced the power of the study.

Regarding the parameters assessed:

9. Some tests used have a ceiling effect, which may limit the ability to detect subtle changes in response to an exercise intervention in relatively healthy older women;
10. The absence of more physiological measurements and additional biomarkers to better understand underlying mechanisms of training-induced adaptation, although the array of biomarkers used is capable of characterizing the oxidative stress and bone status;
11. The absence of measures of bone quality;
12. The lack of devices that directly assess muscle power output such as the Nottingham power rig or linear position transducer;
13. Not having measured oxidative stress and bone turnover rate in all participants in both projects and in all the assessment sessions (baseline, middle, and final) in the first project;

14. Possible effect of other confounding variables or unknown measures not assessed, such as psychological or genetic factors;
15. Omission of seasonal and behavioral confounding factors that could have occurred due to the duration of both projects;
16. Lack of control of nutritional status and physical activity levels in the first study, although participants were encouraged to maintain their regular activities of daily living and nutritional habits and to abstain from any dietary supplements or new exercises programs throughout the experimental period. Although subjects were instructed to maintain their dietary and physical activity routines, it should be noted that their involvement in the training programs could have promoted behavioral changes affecting, above all, diet.;
17. Lack of monitoring of nutritional status and physical activity levels outside of the study environment in the second study;
18. Physical activity levels in the second project were measured at the beginning of the study but not at the end, and therefore, changes in dependent variables could be affected by potential variations in participants' habitual physical activity levels;
19. Physical activity levels in the second project were measured through a questionnaire rather than objective methods such as accelerometry;
20. All the assessments except the collection of blood and urine samples were conducted on the same day, meaning some assessments may have been affected by fatigue; however, all assessments were performed in the same order with appropriate rest times and accounted for the effects of one test over the next.

Regarding the training program and training parameters:

21. The highly supervised training sessions in both projects is a positive aspect of the research, but our findings may not be applicable and extrapolated to sessions without supervision or those that are self-controlled;
22. Although the duration of the training interventions in both projects was longer than 12 weeks, a longer intervention (>one year) might have allowed for the detection of significant differences between exercise strategies. However, the duration of both projects reflects the likely scenario in clinical or real practice, where it may not be feasible to introduce interventions of greater duration;
23. The results are not generalizable to weight machines due to their differences compared with the elastic resistance device;
24. The absence of objective movement velocity measurement (e.g., using accelerometers) during the power strength exercises despite instructing participants to move the resistance "as fast as possible" could have resulted in considerable variability among participants regarding self-selected movement velocity given the broad range of characteristics of the sample. Therefore, there is a lack of objective control of the velocity movement of the resistance exercises in the power strength intervention of the second project despite having ensured that all participants exercise at the same RPE;
25. Despite the efforts to use a valid and reliable method for controlling the intensity and velocity of movement with RPE and elastic bands, to date there is no validated scale of RPE and velocity control with elastic bands in samples of older people.

Regarding the statistical methods:

26. Although study populations were similar at baseline and adjusted for several known confounders (baseline values and age), results may be influenced by other influential covariates;
27. The lack of comparisons between groups based on some basic characteristics such as age, body mass index, physical activity levels, and muscle strength;
28. The lack of associations and predictions between dependent variables.

CHAPTER VII

Implications for practice

There are important clinical implications related to our PhD dissertation findings. The elastic-based exercise programs proposed in both projects are useful working tools for health and sport professionals such as strength and conditioning coaches, sports physicians, physiotherapists, gerontologists, and occupational therapists who work with physical exercise and older people. They further contribute to prolonging functional independence and quality of life in the older population.

The results obtained in both projects should be considered when designing appropriate elastic-based exercise programs for older adults because coaches and clinicians have the information to tailor their exercise prescriptions regarding exercise intensity and modality for resistance, power strength, and multi-component training for older women. Depending on which health parameters are to be improved, our results indicate that coaches and clinicians will have to select the most appropriate training intensity and modality to achieve their proposed objective. In this sense, for most of the health parameters we analyzed, the choice of training intensity or modality might be more related to individual and logistical aspects than to training factors mainly because all the proposed training programs achieved positive effects in older women with no significant differences between them.

Given the difficulties to motivate older adults to take part in vigorous training programs due to the numerous barriers that exists, we believe that the elastic-based power strength training may have important implications for exercise prescription strategies for older adults, as the use of lighter loads moved more rapidly at a lower RPE may be a more practical and tolerable form of resistance training for older adults compared with other modalities, which may increase the adherence of participants. This may be of particular relevance for older adults with chronic conditions, whose reaction to high-intensity exercise may be contraindicated or poorly tolerated. In addition, our findings highlight the effectiveness, feasibility, and safety of this type of training strategy, particularly for the

improvement of oxidative stress, bone health, and the muscle power of the upper and lower limbs relative to other training modalities. Therefore, although further research is needed, the application of this kind of training modality in the older population could have widespread public health implications since muscle power determines the ability to develop force rapidly and the ability to proficiently execute daily tasks, such as walking or climbing stairs. Therefore, this exercise regimen conserves functional capacity and ultimately prolongs an independent lifestyle at a higher quality of life among older women.

However, despite the wide benefits of the power strength training using elastic bands in older adults, another important practical implication extracted from our results is that a multi-component training strategy could be a good alternative for older women who cannot or do not want to perform high-speed or high-load contractions since multi-component training is also able to increase muscle strength and muscle power in older women. Furthermore, from a practical point of view, a multi-component training program using easily administrable and cost-effective equipment such as elastic bands might be recommended as a primary training intervention. This program can improve oxidative stress levels and physical function in older women, but moreover it can especially improve the body composition and lower the cardiovascular risk of this population. If the characteristics of the older population do not allow for high-speed or high-load contractions, multi-component training modalities could be the most appropriate exercise modalities for improving physical function and general health in this population.

Because primary prevention is crucial, the data obtained in the present PhD dissertation also suggest that, in well-functioning older women, the three training modalities studied along with both elastic-based resistance training protocols at different intensities could prevent and delay the appearance of disability and frailty syndromes in this population. In this sense, the large improvements observed in physical function have previously been

associated with a lower risk of falls, hip fractures, dependence and institutionalization, cognitive decline, chronic diseases, and early all-cause mortality.

The clinical implications of the present PhD dissertation are also related to the importance that elastic-based resistance training performed at moderate intensity could have compared with high-intensity resistance training since the former can produce similar improvements in physical function and muscle strength without negative effects in oxidative stress. In fact, elastic resistance training has a positive effect on the oxidative stress levels in older women. It is important for exercise coaches and clinicians to consider this outcome because, despite the benefits of high-intensity resistance training reported in the literature, which are also observed in our studies, a chronic increase in oxidative stress produces advanced aging, which increases the probability of suffering from important pathologies such as cancer or dementia. It is important that health professionals consider not only the load but also the exercise effort when prescribing resistance-training intensity in order to achieve the positive effects of moderate-intensity resistance training using elastic bands in older women.

However, despite the apparent negative effects of high-intensity resistance training on oxidative stress, it is important to recognize that this exercise strategy is highly effective in improving the bone health of older women, improving bone formation and the aBMD of both spine and hip sites and reducing fracture risk to a greater extent than the moderate-intensity resistance training in the short and long term. Therefore, exercise professionals should choose the training modality and exercise intensity based on the target population and the main training goal, being the elastic-based high-intensity resistance training especially interesting for older adults with a low BMD or with a high risk of fracture.

The use of easy, portable, and low-cost training equipment such as elastic bands is another favorable aspect of the proposed exercise interventions. This equipment might offer

health-care providers and practitioners the opportunity to develop exercise interventions in community centers, sport fields, outdoors, or even at home. Moreover, due to the excellent adherence and safety observed in both studies, the use of this training device, regardless of whether the training modality or intensity applied could help promote adherence to physical activity in older adults, eliminates the classic barriers reported by this population regarding training equipment.

Another practical aspect of the present PhD dissertation that deserves attention is the prescription of training intensity according to the RPE methods validated for resistance exercise performed with elastic resistance in older adults. Due to the limited used of traditional methods for prescribing intensity based on maximal tests or repetitions (e.g., 1RM, 8RM) in clinical practice, our method using validated RPE scales for prescribing exercise intensity and the velocity of contraction can be highly useful for health professionals implementing exercise programs using elastic bands in this population.

Moreover, due to the detailed and well-designed exercise interventions we conducted, the same methodology can be easily extrapolated to other clinical settings and scenarios like daycare centers, nursing homes, community centers, and hospitals. Furthermore, all the exercise interventions proposed were time-efficient since they achieved significant positive effects for most of the health parameters analyzed with only two sessions a week.

In summary, we believe our findings constitute a relevant contribution to the existing literature due to their novelty and their high translatability to the clinical setting and other health-related settings. Our results thus allow exercise science to contribute to improving the health of older people and their integration into society by helping them stay or become mentally and physically “strong.”

CHAPTER VIII
Future perspectives

To overcome the abovementioned limitations and to extend our findings, this PhD dissertation leaves open questions and highlights several future actions and new challenges that may contribute to the knowledge in the fields of exercise, health, and aging.

First, future studies are needed to identify the dose-response relationship between different training intensities and exercise modalities using elastic resistance on the parameters analyzed in the present PhD dissertation and also in other older adults.

Second, more research is needed to elucidate the optimal combination of training parameters (intensity, volume, frequency, duration, and rest) in multi-component, power strength, and resistance training exercise interventions performed with elastic resistance in older adults used to improve the health-related parameters studied in the present PhD dissertation and other literature.

Third, further investigations that combine different types of exercise modalities, such as multi-component and power strength, should be performed to find which of them, alone or in combination, is more effective in improving the health of the older population.

Fourth, it is unknown how much the dosage and intensity of each component of multi-component training actually contributes to the improvement of each studied outcome. Therefore, future studies are needed to compare different multi-component training programs performed with elastic bands in older adults.

Fifth, since the power strength training program performed in the second project was the first to use elastic bands among older adults following an appropriate method of velocity and intensity control, more studies are needed to investigate the effects of applying different intensities with this training modality.

Sixth, due to both projects being highly supervised, further research should compare the effect of supervised vs self-directed or home elastic-based exercise interventions in older adults.

Seventh, future studies could consider replicating the current studies with larger samples to detect small ES and increase statistical power.

Eighth, due to the general low methodological quality of the studies that have analyzed the effects of multi-component and power strength training in the older population, futures pre-registered RCTs that compare the effects of these two training modalities on different parameters are needed.

Ninth, future research might investigate the effect of different elastic-based exercise interventions using higher or lower weekly training frequencies and increased research durations to look for a larger impact and to investigate the long-term effects of our proposed exercise programs.

Tenth, further studies should aim to replicate current projects among other older populations such as those at a greater risk of developing functional disabilities, pre-frail or frail individuals, older adults with chronic diseases, men, or institutionalized older adults. In addition, future studies could include older adults from various ethnic groups and rural regions.

Eleventh, it should be noticed that, despite the high number of health parameters and biomarkers analyzed, future research may focus on the effects of the studied elastic-based exercise intervention on additional variables such as inflammatory, metabolic, or immune biomarkers. Furthermore, psychological, social, and cognitive measures can also add useful information regarding additional benefits of these training strategies. In addition, futures

studies should analyze participants' perceptions of these programs. Moreover, the incorporation of bone-quality metrics regarding bone geometry, microarchitecture, and vBMD changes should be further explored.

Twelfth, future studies could investigate the acute changes produced by the studied elastic-based exercise interventions on different health-related parameters in older adults.

Thirteenth, future studies could consider analyzing the effects of detraining to better understand to what extent the benefits obtained are maintained over time.

Fourteenth, although the maximal muscle power output determined by isokinetic dynamometry was assessed at a high and safe velocity for older adults (180°/s), it may have been underestimated compared with the velocity at which explosive movements are performed in daily life. Therefore, future studies could analyze the muscle power output at higher velocities, such as 240°/s or more, although the safety of participants could be compromised.

Fifteenth, future studies could include some technological devices such as accelerometers to measure the movement velocity in elastic-based power strength training or heart-rate monitors to prescribe the aerobic threshold in the multi-component training modality.

Finally, future research should concentrate on clarifying the effects of moderating variables such as the characteristics of individuals, age, level of physical activity, or body mass index on the health parameters analyzed. In addition, future studies should employ more statistical techniques such as regression analysis to identify which variables can predict the behavior of the changes achieved by the elastic-based exercise interventions proposed for older adults.

CHAPTER IX

Conclusions

The main conclusions regarding the objectives and hypothesis of this PhD dissertation are presented below.

IX.I. PROJECT ONE

IX.I.I. General conclusion

A 32-week elastic-based resistance training program done at a high or moderate intensity is effective in improving the bone health, body composition, neuromuscular strength, and physical function of older women. In addition, a 16-week progressive resistance training program using elastic bands at a moderate intensity improved oxidative stress levels while, in the same period, high-intensity resistance training was more effective in increasing the bone-formation rate among older women. Furthermore, both elastic-based exercise programs can be performed safely and effectively among older women.

IX.I.II. Specific conclusions

1. Regarding oxidative stress (SO 1, SO9; H1, H2 and H10):

- A 16-week moderate-intensity progressive resistance-training program with elastic bands elicited positive effects on oxidative stress by significantly decreasing DNA damage (urine 8-oxo-dG) and lipid peroxidation (8-iso-P, MDA) and by not producing negative changes in protein oxidation (protein carbonyls). The moderate-intensity elastic-based resistance-training intervention significantly improved antioxidant defenses in older women by increasing the endogenous enzymatic antioxidants (CAT) without changing the thiol redox state (GSH, GSSG, and GSSG/GSH ratio).

- A 16-week high-intensity progressive resistance-training program with elastic bands produced the opposite effect, eliciting negative effects on oxidative stress by significantly increasing DNA damage (urine 8-oxo-dG) and lipid

peroxidation (8-iso-P) and also the levels of MDA and protein carbonyls, although not significantly. In addition, the elastic-based high-intensity resistance-training intervention significantly impaired antioxidant defenses in older women by significantly decreasing the antioxidant tripeptide GSH and GPx enzymes.

2. Regarding bone health (SO 2 to SO4 and SO9; H3 to H5 and H10):

- Both high- and moderate-intensity resistance training with elastic bands improved the bone turnover rate in older women by significantly increasing the concentrations of bone-formation biomarkers (P1NP and bALP) and reducing the values of bone resorption biomarkers (β-CTx) after 16 and 32 weeks of training. The high-intensity elastic-based resistance training was significantly more effective than the moderate-intensity resistance training in improving the bALP in the short (16 weeks) and long (32 weeks) term and in improving the bALP /β-CTx ratio in the short term.

- Both high-and moderate-intensity resistance training with elastic bands improved the aBMD in older women by significantly increasing most of the RoI at the lumbar spine and proximal femur after 32 weeks of training. Although there were no significant differences between the training intensities, the high-intensity resistance training produced greater effects at the total lumbar spine, trochanter, and total hip, while the moderate-intensity progressive resistance training resulted in a higher increase of aBMD at the femoral neck and Ward's triangle.

- Both high-and moderate-intensity resistance training with elastic bands reduced the risk of fracture in older women by significantly decreasing the

major osteoporotic and hip-fracture probabilities for the following 10 years after 32 weeks of training . However, the elastic-based high-intensity resistance training was significantly more effective than moderate-intensity resistance training in reducing both fracture risk parameters (10-year probability of a major osteoporotic fracture and 10-year probability of a hip fracture).

3. Regarding body composition (SO5 and SO9; H6 and H10):

- Both high- and moderate-intensity resistance training with elastic bands produced significant changes in body composition in older women by increasing total fat-free mass and by decreasing total body fat percentage after 32 weeks of training.

- Although there were no significant differences between both training intensities for any parameter, progressive moderate-intensity elastic resistance training resulted in greater changes in both adipose and skeletal muscle body components and achieved significant reductions in total fat mass.

4. Regarding neuromuscular strength (SO6 and SO9; H7 and H10):

- Both high-and moderate-intensity resistance training with elastic bands significantly increased neuromuscular strength in older women at low and high velocities of the upper limbs, which is reflected in strength gains in elbow flexor and extensor muscles, and also the lower limbs by improving the strength of knee flexor and extensor muscles and the hip abductor and adductor muscles after 32 weeks of training.

- Although there were no significant differences between both training intensities for any parameter, high-intensity progressive elastic resistance training resulted in greater neuromuscular strength at hip, knee, and elbow joints for most of the concentric movements analyzed at both velocities, while moderate-intensity progressive elastic resistance training resulted in a greater strength increase at the elbow flexion muscles when the task was performed at a high velocity.

5. Regarding physical function (SO7 and SO9; H8 and H10):

- Both high-and moderate-intensity resistance training with elastic bands significantly increased physical function in older women in terms of muscle strength and the endurance of the upper and lower limbs, dynamic balance, and aerobic capacity after 32 weeks of training.

- Although there were no significant differences between both training intensities for any parameter, high-intensity progressive elastic resistance training achieved better results for muscle strength and endurance for the upper limbs and aerobic capacity, while moderate-intensity progressive elastic resistance training resulted in a higher increase in lower extremity muscle strength and endurance and in a greater improvement in dynamic balance.

6. Regarding potential confounding variables and program feasibility and safety (SO8 and SO10; H9 and H11):

- The possible confounding variables studied (BADLs, IADLs, and MMSE) had no influence on the parameters analyzed at the beginning of the study.

- Both elastic-based resistance-training interventions were feasible, effective, and safe for older women because of 1) their positive effects on the analyzed parameters using easy-to-use training devices such as elastic bands; 2) the high rates of adherence and compliance of the participants; 3) the low level of mild and moderate adverse events reported; 4) the lack of serious adverse events; and 5) the low attrition rate, with no drop-outs due to injuries or adverse responses to the intervention after 32 weeks of training.

IX.II. PROJECT TWO

IX.II.I. General conclusion

Twenty-week elastic-based multi-component, power strength, and traditional high-intensity resistance training programs are effective in improving bone health, body composition, neuromuscular strength and physical function in older women. In addition, multi-component training and especially power strength training are effective in improving oxidative stress and bone turnover rate in older women after a 20-week training period. Moreover, the power strength exercise strategy seems to be the most appropriate for producing power adaptations, while multi-component training is best for reducing adipose tissue in older women after a 20-week period of training. Furthermore, the three elastic-based training modalities can be performed safely and effectively by older women.

IX.II.II. Specific conclusions

1. Regarding oxidative stress (SO1, SO10; H1and H10):

- Both multi-component and power strength training elicited positive effects on oxidative stress in older women by significantly decreasing DNA damage (urine 8-oxo-dG) and lipid peroxidation (8-iso-P) after an intervention period of 20 weeks using elastic resistance.

- The elastic-based power strength training modality elicited positive effects on oxidative stress levels in older women by significantly improving antioxidant enzymes, especially SOD, and the thiol redox state. This modality further shows greater effectiveness than the multi-component training strategy particularly regarding total glutathione and GSH parameters after 20 weeks of training.

2. Regarding bone health (SO2 to SO4 and SO9; H2 to H4 and H10):

- Both multi-component and power strength training improved the bone turnover rate in older women by significantly increasing the concentrations of bone-formation biomarkers (OC) and reducing the values of bone resorption biomarkers (β-CTx); moreover, no difference was found between both training strategies after an intervention period of 20 weeks using elastic resistance.

- Multi-component, power strength, and traditional high-intensity resistance training improved the aBMD and T-score of the lumbar spine and proximal femur areas in older women. Although there were no significant differences between the training modalities, the elastic-based power strength exercise strategy was the most effective, as it was the only one that achieved significant changes in total lumbar spine, intertrochanteric, and total hip aBMD after an intervention period of 20 weeks.

- Multi-component, power strength, and traditional high-intensity resistance training all reduced the risk of fracture by significantly decreasing the major osteoporotic and hip-fracture probabilities in older women after an intervention period of 20 weeks using elastic resistance. In addition, the high-intensity resistance-training modality was more effective than the multi-component exercise strategy in reducing the 10-year risk probability of hip fracture in older women.

3. Regarding anthropometry and body composition (SO5, SO6 and SO9; H5, H6 and H10):

- Multi-component, power strength, and traditional high-intensity resistance training elicited improvements in anthropometric parameters in older women by significantly reducing the WC, HC, and WHtR after an intervention period of 20 weeks using elastic resistance. Therefore, these are effective strategies for reducing cardiovascular risk in this population.

- The multi-component training modality seemed to be the most effective exercise strategy because it produced the largest effects among all anthropometric parameters and achieved significant differences in HC compared with the traditional high-intensity resistance training modality in older women after an intervention period of 20 weeks using elastic resistance.

- Multi-component, power strength, and traditional high-intensity resistance training significantly improved the body composition of older women by decreasing the total body fat and total body fat percentage, but only the multi-component and traditional high-intensity resistance training significantly improved total fat-free mass after an intervention period of 20 weeks using elastic resistance.

- Although there were no significant differences among the training modalities, the multi-component one resulted in greater changes in the fat-mass parameters, while the elastic-based high-intensity resistance training modality resulted in the greatest changes in fat-free mass in older women after an intervention period of 20 weeks.

4. Regarding neuromuscular strength (SO7 and SO9; H7 and H10):

- Multi-component, power strength, and traditional high-intensity resistance improved neuromuscular strength at low and high velocities of upper and lower limbs in older women by significantly increasing the muscle strength of the elbow and knee flexor and extensor muscles along with the strength of the hip abductor and adductor muscles after an intervention period of 20 weeks using elastic resistance.

- Power strength training seemed to be the most useful training strategy for older women regarding improving neuromuscular strength at high speeds for all assessed muscle groups, especially for hip and elbow muscles, since significant differences were found compared with the other training modalities after an intervention period of 20 weeks using elastic resistance.

- Traditional high-intensity resistance training seemed to be the most effective training modality for improving neuromuscular strength at low speeds for hip, knee, and elbow muscle groups among all the concentric movements analyzed in older women after an intervention period of 20 weeks using elastic resistance; this result was especially true for the elbow extensor muscles, as significant differences were found compared with the other training modalities.

5. Regarding physical function (SO8 and SO9; H8 and H10):

- Multi-component, power strength, and traditional high-intensity resistance improved physical function in older women by significantly enhancing the muscle strength of the upper and lower limbs, the muscle power of lower

limbs, proactive and dynamic balance, and aerobic capacity after an intervention period of 20 weeks using elastic resistance.

- Elastic-based power strength training seemed to be the most useful strategy for improving lower-limb muscle power in older women compared with multi-component and traditional high-intensity resistance training after an intervention period of 20 weeks, especially for tasks where the velocity component was predominant over the force component, such as with the 5STS test.

- Elastic-based traditional high-intensity resistance training produced the greatest adaptations in the muscle strength of the upper and lower limbs for tasks where the force component predominated (e.g., stair-climbing), and for aerobic capacity in older women after an intervention period of 20 weeks; however, this result is not significantly better than those for the multi-component and power strength training modalities.

- The multi-component training modality produced the highest adaptations in dynamic balance in older women after an intervention period of 20 weeks, although this result is not significantly better than those for the power strength and traditional high-intensity resistance training modalities.

6. Regarding potential confounding variables and program feasibility and safety (SO9 and SO11; H9 and H11):

- The possible confounding variables studied (age, basic physical functions [BADLs and IADLs], cognitive status [MMSE], anxiety [OASIS], depression [ODSIS]) and the levels of physical activity (GPAQ) had no influence on the

parameters analyzed at the beginning of the study, while nutritional status may have slightly influenced the results.

- Multi-component, power strength, and traditional high-intensity resistance training were feasible, effective, and safe for older women due to 1) their positive effects on the parameters analyzed in conjunction with easy-to-use training devices such as elastic bands; 2) the high rates of attendance and compliance of the participants; 3) the low level of mild and moderate adverse events reported; 4) the lack of serious adverse events; and 5) the low attrition rate, with no drop-outs due to injuries or adverse responses to the intervention after 20 weeks of training.

CHAPTER X

Summary of key findings

Take-home messages

- To lower oxidative stress levels in older women, the best options seem to be elastic-based resistance training at a moderate intensity, power strength training, and multi-component exercise interventions.

- To enhance bone health in older women, the best exercise strategy seems to be high-intensity resistance training and power strength training using elastic bands.

- To improve body composition and cardiovascular health in older women, the most effective training modality seems to be elastic-based multi-component training.

- To improve neuromuscular strength in older women, all training modalities are effective, but power strength training seems to be the best exercise strategy for increasing force production at high velocities, while high-intensity resistance training seems to be the best option for increasing force produced closer to maximal strength at lower velocities.

- All training modalities are effective for improving physical function in older women; however, to enhance lower-limb muscle power for tasks requiring the predominance of velocity over force, the elastic-based power strength training seems to be the best exercise strategy.

- Older women may not need access to specialized weight machines or free-weight equipment and facilities to maintain physical health since multi-component, power strength and resistance training performed with elastic bands have all been shown to be feasible, effective, and safe for this population.

- Adaptations related to oxidative stress, bone health, body composition, neuromuscular strength, and physical function are training-intensity and modality dependents since one of these two key exercise programming parameters determined that will achieve significant better results with some exercise interventions than others.

- Two weekly sessions is enough training frequency to produce positive effects in older women participating in medium- and long-term training periods with respect to oxidative stress, bone health, body composition, neuromuscular strength, and physical function.

- Prescribed training intensity should account for both load and effort by using the appropriate methods specific to elastic bands and older adults.

- Adherence to physical activity and exercise training can be increased by implementing the elastic-based exercise modalities prescribed in this dissertation.

- Multi-component, power strength, and resistance training at moderate and high intensities using elastic resistance are effective primary prevention strategies, as they improve the health of well-functioning older women.

CHAPTER XI
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CHAPTER XII

Supplementary material

SUPPLEMENTARY MATERIAL A. PPA RESULTS ON NUTRITION INTAKE

Table A.1. *Daily macronutrients and total energy intake from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
CHO intake (g/d)	MT	140.86	141.33 ± 35.43 (128.44–154.21)	140.13 ± 32.86 (127.13–153.12)	-0.85	0.666 (0.04)	0.644 (0.04)	MT vs P: 1.000 (0.38) MT vs T: 1.000 (0.18)	MT vs P: 0.336 (0.23) MT vs T: 1.000 (0.15)
	P		147.13 ± 38.18 (133.79–160.46)	153.01 ± 34.43 (139.57–166.46)	4.00	**0.043** (0.16)	**0.028** (0.18)	MT vs C: 1.000 (0.23)	MT vs C: 1.000 (0)
	T		143.01 ± 34.53 (129.67–156.34)	146.60 ± 38.52 (133.15–160.05)	2.51	0.213 (0.1)	0.171 (0.11)	P vs T: 1.000 (0.18)	P vs T: 1.000 (0.07)
	C		132.54 ± 34.26 (119.66–145.42)	131.93 ± 37.62 (118.94–144.92)	-0.46	0.825 (0.02)	0.636 (0.04)	P vs C: 0.165 (0.58) T vs C: 0.737 (0.39)	P vs C: 0.341 (0.21) T vs C: 1.000 (0.14)
Protein intake (g/d)	MT	71.66	75.82 ± 15.87 (70.15–81.48)	75.84 ± 16.38 (70.05–81.63)	0.04	0.953 (0)	0.914 (0)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.25)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.01)
	P		73.38 ± 18.14 (67.51–79.24)	72.64 ± 17.87 (66.65–78.63)	-1.00	0.115 (0.04)	0.110 (0.04)	MT vs C: 0.136 (0.67)	MT vs C: 1.000 (0.02)
	T		71.51 ± 16.35 (65.65–77.37)	71.65 ± 17.60 (65.65–77.64)	0.19	0.770 (0.01)	0.768 (0.01)	P vs T: 1.000 (0.06) P vs C: 0.804 (0.06)	P vs T: 1.000 (0.05) P vs C: 0.625 (0.05)
	C		66.03 ± 11.80 (60.36–71.69)	66.30 ± 11.57 (60.51–72.08)	0.41	0.547 (0.02)	0.480 (0.03)	T vs C: 1.000 (0.42)	T vs C: 1.000 (0.07)
Lipids intake (g/d)	MT	58.3	61.35 ± 14.39 (55.85–66.85)	61.63 ± 14.19 (56.2–67.05)	0.45	0.500 (0.02)	0.434 (0.02)	MT vs P: 1.000 (0.34) MT vs T: 1.000 (0.12)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.03)
	P		57.53 ± 13.02 (51.84–63.23)	57.07 ± 12.77 (51.45–62.69)	-0.81	0.275 (0.04)	0.243 (0.04)	MT vs C: **0.041** (0.77)	MT vs C: 0.350 (0.08)
	T		63.01 ± 19.17 (57.32–68.7)	63.69 ± 18.94 (58.07–69.31)	1.08	0.112 (0.04)	0.052 (0.04)	P vs T: 0.610 (0.41) P vs C: 0.735 (0.41)	P vs T: 0.171 (0.08) P vs C: 1.000 (0.08)
	C		51.57 ± 13.60 (46.07–57.07)	50.94 ± 13.49 (45.51–56.36)	-1.23	0.124 (0.05)	0.055 (0.06)	T vs C: 0.010 (0.47)	T vs C: **0.047** (0.02)

Table A.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total energy intake (Kcal/d)	MT	1425.42	1465.30 ± 272 (1357.57–1573.02)	1432.30 ± 243.90 (1325.74–1538.85)	-2.25	**0.018** (0.13)	**0.020** (0.13)	MT vs P: 1.000 (0.13)	MT vs P: 0.328 (0.14)
	P		1464.14 ± 298.71 (1352.63–1575.64)	1468.64 ± 301.16 (1358.34–1578.94)	0.31	0.753 (0.02)	0.680 (0.02)	MT vs T: 1.000 (0.16)	MT vs T: 0.365 (0.12)
	T		1480.60 ± 361.24 (1369.1–1592.11)	1481.75 ± 377.38 (1371.45–1592.04)	0.08	0.936 (0)	0.709 (0.01)	MT vs C: 0.360 (0.59)	MT vs C: 1.000 (0.07)
	C		1297.90 ± 252.81 (1190.17–1405.62)	1287.83 ± 242.03 (1181.27–1394.39)	-0.78	0.467 (0.04)	0.258 (0.06)	P vs T: 1.000 (0.04)	P vs T: 1.000 (0)
								P vs C: 0.128 (0.66)	P vs C: 1.000 (0.08)
								T vs C: 0.082 (0.62)	T vs C: 1.000 (0.07)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30).MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CHO: carbohydrates; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

Table A.2. *Daily macronutrients and total energy intake relative to body mass from PPA.*

Variables	Group	Baseline	Post-test	Variables	Group	Baseline	Post-test
CHO intake (g/Kg/d)	MT	1.98 (50.74%)	1.98 (50.47%)	Lipids intake (g/Kg/d)	MT	0.86 (22.02%)	0.87 (22.2%)
	P	2.22 (52.91%)	2.33 (54.12%)		P	0.87 (20.69%)	0.86 (20.18%)
	T	2.12 (51.52%)	2.17 (51.99%)		T	0.93 (22.7%)	0.94 (22.58%)
	C	1.87 (52.98%)	1.86 (52.94%)		C	0.73 (20.61%)	0.71 (20.44%)
Protein intake (g/Kg/d)	MT	1.06 (27.22%)	1.07 (27.31%)	Total energy intake (Kcal/Kg/d)	MT	20.59	20.25
	P	1.10 (26.39%)	1.10 (25.69%)		P	22.14	22.37
	T	1.06 (25.76%)	1.06 (25.41%)		T	21.99	22
	C	0.93 (26.39%)	0.93 (26.6%)		C	18.39	18.16

Note. In parentheses, the percentage that each macronutrient represents from the total energy intake. Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30).MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CHO: carbohydrates.

Table A.3. *Daily minerals intake from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Calcium intake (mg/d)	MT	667.10	696.40 ± 165.49 (631.70–761.09)	689.36 ± 169.84 (622.26–756.46)	-1.01	0.206 (0.04)	0.174 (0.05)	MT vs P: 1.000 (0.13) MT vs T: 1.000 (0.14) MT vs C: 1.000 (0.29) P vs T: 1.000 (0.01) P vs C: 1.000 (0.01) T vs C: 1.000 (0.15)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.04) MT vs C: 1.000 (0.06) P vs T: 1.000 (0.06) P vs C: 1.000 (0.04) T vs C: 1.000 (0.05)
	P		672.75 ± 173.14 (605.78–739.71)	665.46 ± 184.74 (596.01–734.91)	-1.08	0.206 (0.04)	0.200 (0.04)		
	T		663.64 ± 194.80 (596.68–730.60)	663.28 ± 200.29 (593.83–732.74)	-0.05	0.950 (0)	0.937 (0)		
	C		635.77 ± 181.32 (571.08–700.46)	637.77 ± 186.81 (570.67–704.87)	0.31	0.718 (0.01)	0.620 (0.01)		
Ferrous intake (mg/d)	MT	11.29	11.08 ± 2.67 (9.71–12.45)	11.22 ± 2.96 (9.84–12.60)	1.26	0.654 (0.05)	0.487 (0.07)	MT vs P: 1.000 (0.3) MT vs T: 1.000 (0.24) MT vs C: 1.000 (0.28) P vs T: 1.000 (0) P vs C: 0.443 (0.56) T vs C: 0.457 (0.43)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.02) MT vs C: 1.000 (0.1) P vs T: 1.000 (0.01) P vs C: 1.000 (0.13) T vs C: 1.000 (0.08)
	P		12.30 ± 3.72 (10.88–13.71)	12.25 ± 3.81 (10.82–13.68)	-0.35	0.895 (0.01)	0.818 (0.02)		
	T		12.04 ± 5.54 (10.63–13.46)	12.24 ± 5.42 (10.81–13.67)	1.63	0.544 (0.04)	0.669 (0.02)		
	C		9.85 ± 2.55 (8.48–11.22)	10.44 ± 2.56 (9.06–11.82)	6.02	0.060 (0.23)	0.112 (0.19)		
Iodine intake (mg/d)	MT	92.18	93.63 ± 32.44 (82.12–105.14)	92.63 ± 31.55 (81.23–104.03)	-1.07	0.188 (0.03)	0.210 (0.03)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.12) MT vs C: 1.000 (0.01) P vs T: 1.000 (0.11) P vs C: 1.000 (0.11) T vs C: 1.000 (0.0)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.02) P vs C: 1.000 (0.02) T vs C: 1.000 (0.01)
	P		92.58 ± 37.37 (80.67–104.49)	92.58 ± 36.81 (80.78–104.38)	0.00	1.000 (0)	0.987 (0)		
	T		89.65 ± 26.34 (77.73–101.56)	89.15 ± 26.76 (77.35–100.94)	-0.56	0.524 (0.02)	0.467 (0.02)		
	C		92.73 ± 30.16 (81.22–104.24)	92.43 ± 30.16 (81.09–103.83)	-0.32	0.692 (0.01)	0.704 (0.01)		
Magnesium intake (mg/d)	MT	256.05	268.90 ± 53.77 (245.06–292.73)	272.00 ± 63.11 (246.79–297.2)	1.15	0.575 (0.05)	0.479 (0.07)	MT vs P: 1.000 (0.1) MT vs T: 1.000 (0.14) MT vs C: 0.200 (0.58) P vs T: 1.000 (0.23) P vs C: 0.469 (0.5) T vs C: **0.049** (0.64)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.09) MT vs C: 1.000 (0) P vs T: 1.000 (0.02) P vs C: 1.000 (0.08) T vs C: 1.000 (0.08)
	P		256.39 ± 53.77 (231.71–281.06)	265.78 ± 58.46 (239.69–291.87)	3.66	0.103 (0.17)	0.100 (0.17)		
	T		272.21 ± 92.17 (247.53–296.89)	282.57 ± 84.28 (256.47–308.66)	3.80	0.072 (0.12)	0.069 (0.12)		
	C		227.79 ± 57.25 (203.95–251.63)	233.22 ± 70.53 (208.01–258.43)	2.39	0.327 (0.08)	0.462 (0.07)		

Table A.3. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Zinc intake (mg/d)	MT	7.76	8.08 ± 1.52 (7.32–8.83)	8.24 ± 1.19 (7.63–8.85)	2.06	0.478 (0.12)	0.170 (0.19)	MT vs P: 0.987 (0.43) MT vs T: 0.863 (0.42)	MT vs P: 0.812 (0.29) MT vs T: 0.857 (0.26)
	P		7.77 ± 2.08 (6.98–8.55)	7.62 ± 1.65 (6.99–8.25)	-1.84	0.557 (0.08)	0.453 (0.08)	MT vs C: 0.230 (0.57)	MT vs C: 0.439 (0.3)
	T		7.77 ± 2.16 (6.99–8.55)	7.59 ± 1.85 (6.96–8.22)	-2.30	0.463 (0.09)	0.467 (0.07)	P vs T: 1.000 (0.02)	P vs T: 1.000 (0)
	C		7.43 ± 2.49 (6.68–8.19)	7.33 ± 1.92 (6.72–7.94)	-1.34	0.670 (0.04)	0.239 (0.1)	P vs C: 1.000 (0.02) T vs C: 1.000 (0.16)	P vs C: 1.000 (0) T vs C: 1.000 (0.04)
Selenium intake (mg/d)	MT	93.83	92.17 ± 22.26 (80.65–103.68)	90.77 ± 21.07 (79.4–102.13)	-1.52	0.289 (0.06)	0.311 (0.06)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.1)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.02)
	P		97.56 ± 33.34 (85.65–109.48)	95.99 ± 33.65 (84.23–107.75)	-1.61	0.250 (0.05)	0.303 (0.04)	MT vs C: 1.000 (0.02)	MT vs C: 0.747 (0.09)
	T		89.85 ± 31.21 (77.93–101.76)	88.20 ± 31.52 (76.44–99.96)	-1.83	0.230 (0.05)	0.146 (0.06)	P vs T: 1.000 (0.24) P vs C: 1.000 (0.13)	P vs T: 1.000 (0.02) P vs C: 0.835 (0.08)
	C		95.74 ± 38.38 (84.23–107.25)	91.48 ± 37.23 (80.11–102.84)	-4.46	**0.002** (0.11)	**0.002** (0.11)	T vs C: 1.000 (0.09)	T vs C: 1.000 (0.06)
Sodium intake (mg/d)	MT	1331.78	1426.63 ± 493.15 (1270.11–1583.14)	1435.00 ± 496.01 (1272.08–1597.91)	0.59	0.700 (0.02)	0.711 (0.02)	MT vs P: 1.000 (0.11) MT vs T: 0.883 (0.36)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.08)
	P		1366.07 ± 476.14 (1204.06–1528.08)	1380.21 ± 483.73 (1211.58–1548.84)	1.04	0.529 (0.03)	0.536 (0.03)	MT vs C: 0.595 (0.45)	MT vs C: 1.000 (0.01)
	T		1294.21 ± 407.22 (1132.2–1456.22)	1262.25 ± 466.70 (1093.61–1430.88)	-2.47	0.157 (0.07)	0.161 (0.07)	P vs T: 1.000 (0.25)	P vs T: 0.924 (0.1)
	C		1240.00 ± 338.09 (1083.48–1396.51)	1241.66 ± 341.50 (1078.75–1404.58)	0.13	0.939 (0)	0.923 (0.01)	P vs C: 1.000 (0.25) T vs C: 1.000 (0.33)	P vs C: 1.000 (0.1) T vs C: 1.000 (0.03)
Potassium intake (mg/d)	MT	2776.51	2856.10 ± 519.53 (2623.40–3088.79)	2848.93 ± 530.96 (2611.87–3085.98)	-0.25	0.566 (0.01)	0.465 (0.02)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.02)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.02)
	P		2839.35 ± 603.89 (2598.49–3080.22)	2833.07 ± 630.43 (2587.69–3078.44)	-0.22	0.626 (0.01)	0.567 (0.01)	MT vs C: 0.571 (0.51)	MT vs C: 1.000 (0.02)
	T		2854.64 ± 826.41 (2613.77–3095.50)	2860.60 ± 837.17 (2615.23–3105.98)	0.21	0.644 (0.01)	0.616 (0.01)	P vs T: 1.000 (0.04) P vs C: 0.727 (0.44)	P vs T: 1.000 (0.02) P vs C: 1.000 (0.01)
	C		2565.36 ± 593.93 (2332.66–2798.06)	2564.16 ± 594.94 (2327.11–2801.22)	-0.05	0.923 (0)	0.919 (0)	T vs C: 0.527 (0.41)	T vs C: 1.000 (0.01)

Table A.3. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Phosphorus intake (mg/d)	MT	1190.86	1245.50 ± 219.34 (1144.82–1346.17)	249.06 ± 73.65 (1142.47–1344.59)	-80.00	0.857 (0.01)	0.882 (0.01)	MT vs P: 1.000 (0.08)	MT vs P: 1.000 (0.05)
	P		1228.28 ± 278.73 (1144.82–1346.17)	256.00 ± 98.68 (1142.47–1344.59)	-79.16	0.995 (0)	0.967 (0)	MT vs T: 1.000 (0.21)	MT vs T: 1.000 (0.04)
	T		1175.78 ± 318.43 (1071.57–1279.99)	264.75 ± 77.84 (1072.21–1281.42)	-77.48	0.927 (0.01)	0.860 (0.01)	MT vs C: 0.635 (0.58)	MT vs C: 1.000 (0.04)
	C		1115.36 ± 290.30 (1014.69–1216.04)	203.57 ± 81.76 (1024.87–1226.99)	-81.75	0.335 (0.03)	0.427 (0.03)	P vs T: 1.000 (0.1)	P vs T: 1.000 (0)
								P vs C: 0.998 (0.1)	P vs C: 1.000 (0)
								T vs C: 1.000 (0.58)	T vs C: 1.000 (0)
Fluoride intake (mg/d)	MT	239.76	242.89 ± 71.67 (213.41–272.36)	249.06 ± 73.65 (218.91–279.20)	2.54	0.171 (0.08)	0.148 (0.09)	MT vs P: 1.000 (0.08)	MT vs P: 1.000 (0.05)
	P		254.53 ± 93.08 (224.02–285.04)	256.00 ± 98.68 (224.79–287.20)	0.58	0.753 (0.02)	0.692 (0.07)	MT vs T: 1.000 (0.21)	MT vs T: 1.000 (0.01)
	T		258.03 ± 79.36 (227.52–288.54)	264.75 ± 77.84 (233.54–295.95)	2.60	0.150 (0.09)	0.169 (0.08)	MT vs C: 0.220 (0.58)	MT vs C: 0.745 (0.11)
	C		205.80 ± 81.05 (176.32–235.27)	203.57 ± 81.76 (173.42–233.71)	-1.09	0.619 (0.03)	0.538 (0.03)	P vs T: 1.000 (0.1)	P vs T: 1.000 (0.05)
								P vs C: 0.110 (0.58)	P vs C: 1.000 (0.05)
								T vs C: **0.037** (0.77)	T vs C: 0.676 (0.11)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30). MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

Table A.4. *Daily vitamins intake from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin B1 intake (mg/d)	MT	1.12	1.17 ± 0.29 (1.05–1.30)	1.19 ± 0.29 (1.06–1.32)	1.13	0.609 (0.04)	0.402 (0.07)	MT vs P: 1.000 (0.2) MT vs T: 1.000 (0.16) MT vs C: 0.333 (0.59) P vs T: 1.000 (0.03) P vs C: 1.000 (0.3) T vs C: 1.000 (0.34)	MT vs P: 0.900 (0.15) MT vs T: 1.000 (0.04) MT vs C: 1.000 (0.13) P vs T: 1.000 (0.09) P vs C: 1.000 (0.09) T vs C: 1.000 (0.04)
	P		1.15 ± 0.45 (1.02–1.29)	1.12 ± 0.40 (0.99–1.25)	-3.08	0.187 (0.08)	0.234 (0.07)		
	T		1.12 ± 0.35 (0.99–1.25)	1.13 ± 0.40 (1–1.26)	0.95	0.691 (0.03)	0.814 (0.02)		
	C		1.02 ± 0.30 (0.89–1.15)	1.01 ± 0.29 (0.88–1.14)	-0.97	0.701 (0.03)	0.484 (0.06)		
Vitamin B2 intake (mg/d)	MT	1.41	1.43 ± 0.27 (1.29–1.58)	1.43 ± 0.28 (1.28–1.58)	-0.23	0.865 (0.01)	0.903 (0.01)	MT vs P: 1.000 (0.32) MT vs T: 1.000 (0.33) MT vs C: 1.000 (0.4) P vs T: 0.127 (0.51) P vs C: 0.090 (0.51) T vs C: 1.000 (0.55)	MT vs P: 0.893 (0.09) MT vs T: 1.000 (0.07) MT vs C: 1.000 (0.01) P vs T: 0.169 (0.13) P vs C: 0.724 (0.09) T vs C: 1.000 (0.06)
	P		1.54 ± 0.57 (1.39–1.69)	1.58 ± 0.62 (1.42–1.74)	2.54	0.055 (0.07)	0.061 (0.06)		
	T		1.34 ± 0.39 (1.19–1.50)	1.32 ± 0.37 (1.16–1.48)	-1.85	0.220 (0.07)	0.205 (0.07)		
	C		1.32 ± 0.32 (1.17–1.46)	1.31 ± 0.31 (1.16–1.46)	-0.50	0.734 (0.02)	0.756 (0.02)		
Vitamin B3 (niacin) intake (mg/d)	MT	30.62	32.40 ± 7.33 (29.59–35.20)	32.57 ± 7.43 (29.62–35.51)	0.51	0.699 (0.02)	0.691 (0.02)	MT vs P: 1.000 (0.04) MT vs T: 0.845 (0.41) MT vs C: 0.335 (0.56) P vs T: 1.000 (0.31) P vs C: 0.515 (0.43) T vs C: 1.000 (0.12)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.03) MT vs C: 1.000 (0.03) P vs T: 1.000 (0.02) P vs C: 1.000 (0.02) T vs C: 1.000 (0.03)
	P		32.07 ± 9.86 (29.16–34.97)	32.21 ± 9.91 (29.16–35.26)	0.45	0.749 (0.01)	0.761 (0.01)		
	T		29.42 ± 6.99 (26.52–32.33)	29.39 ± 8.03 (26.34–32.44)	-0.12	0.936 (0)	0.893 (0.01)		
	C		28.60 ± 6.49 (25.79–31.40)	28.50 ± 7.05 (25.55–31.45)	-0.35	0.817 (0.01)	0.858 (0.01)		
Vitamin B6 intake (mg/d)	MT	1.88	2.00 ± 0.41 (1.81–2.18)	2.02 ± 0.53 (1.81–2.22)	1.00	0.677 (0.04)	0.700 (0.04)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.33) MT vs C: 0.154 (0.59) P vs T: 1.000 (0.28) P vs C: 0.204 (0.28) T vs C: 1.000 (0.52)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.07) MT vs C: 1.000 (0.06) P vs T: 1.000 (0.05) P vs C: 1.000 (0.05) T vs C: 1.000 (0)
	P		1.99 ± 0.63 (1.80–2.18)	2.00 ± 0.65 (1.79–2.22)	0.72	0.774 (0.02)	0.798 (0.02)		
	T		1.86 ± 0.47 (1.67–2.05)	1.84 ± 0.50 (1.63–2.06)	-0.96	0.719 (0.04)	0.719 (0.04)		
	C		1.70 ± 0.48 (1.51–1.88)	1.68 ± 0.59 (1.47–1.89)	-1.17	0.677 (0.04)	0.727 (0.03)		

Table A.4. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin B9 (folic acid) intake (µg/d)	MT	249.03	248.23 ± 65.44 (221.25–275.21)	250.26 ± 73.60 (220.49–280.03)	0.82	0.683 (0.03)	0.718 (0.03)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.28)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.01)
	P		256.03 ± 79.83 (228.11–283.95)	250.96 ± 89.21 (220.15–281.77)	-1.98	0.326 (0.06)	0.291 (0.06)	MT vs C: 1.000 (0.37)	MT vs C: 1.000 (0.04)
	T		271.46 ± 94.49 (243.54–299.38)	274.96 103.51 (244.15–305.77)	1.29	0.497 (0.04)	0.576 (0.03)	P vs T: 1.000 (0.25)	P vs T: 1.000 (0.09)
	C		222.37 ± 54.27 (195.39–249.35)	225.50 ± 57.88 (195.73–255.27)	1.41	0.529 (0.06)	0.402 (0.08)	P vs C: 1.000 (0.34) T vs C: 0.144 (0.6)	P vs C: 1.000 (0.09) T vs C: 1.000 (0.13)
Vitamin B12 intake (µg/d)	MT	4.23	4.31 ± 1.30 (3.45–5.17)	4.34 ± 1.33 (3.48–5.19)	0.70	0.424 (0.02)	0.380 (0.03)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.18)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.03)
	P		4.86 ± 3.85 (3.97–5.75)	4.86 ± 3.76 (3.98–5.74)	0.15	0.854 (0)	0.675 (0)	MT vs C: 1.000 (0.39)	MT vs C: 1.000 (0)
	T		4.03 ± 2.21 (3.14–4.93)	4.02 ± 2.19 (3.14–4.90)	-0.44	0.645 (0.01)	0.546 (0.01)	P vs T: 1.000 (0.27)	P vs T: 1.000 (0.01)
	C		3.77 ± 1.34 (2.91–4.63)	3.81 ± 1.39 (2.96–4.66)	1.06	0.287 (0.03)	0.367 (0.02)	P vs C: 0.546 (0.27) T vs C: 1.000 (0.38)	P vs C: 1.000 (0.01) T vs C: 1.000 (0.03)
Vitamin C intake (mg/d)	MT	129.12	128.98 ± 60.33 (109.16–148.81)	129.52 ± 62.53 (81.87–177.16)	0.41	0.981 (0.01)	0.940 (0.03)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.14)	MT vs P: 1.000 (0) MT vs T: 1.000 (0.14)
	P		130.33 ± 56.37 (109.81–150.86)	129.19 ± 55.04 (79.88–178.51)	-0.88	0.960 (0.02)	0.939 (0.03)	MT vs C: 1.000 (0.2)	MT vs C: 1.000 (0.24)
	T		135.03 ± 56.25 (114.51–155.55)	138.17 ± 57.37 (88.86–187.49)	2.33	0.891 (0.06)	0.766 (0.12)	P vs T: 1.000 (0.16) P vs C: 1.000 (0.2)	P vs T: 1.000 (0.15) P vs C: 1.000 (0.15)
	C		122.60 ± 45.31 (102.77–142.42)	163.97 ± 239.14 (116.32–211.61)	33.74	0.063 (0.24)	0.069 (0.24)	T vs C: 1.000 (0.15)	T vs C: 1.000 (0.24)
Vitamin A intake (µg/d)	MT	769.72	856.13 ± 369.37 (733.29–978.96)	853.93 ± 363.09 (731.40–976.46)	-0.26	0.602 (0.01)	0.685 (0)	MT vs P: 1.000 (0.17) MT vs T: 1.000 (0.37)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.01)
	P		796.17 ± 359.13 (669.02–923.31)	792.42 ± 356.80 (665.59–919.25)	-0.47	0.392 (0.01)	0.413 (0.01)	MT vs C: 0.336 (0.46)	MT vs C: 1.000 (0)
	T		735.89 ± 238.29 (608.74–863.03)	737.17 ± 247.80 (610.35–864)	0.17	0.769 (0.01)	0.812 (0)	P vs T: 1.000 (0.18) P vs C: 1.000 (0.3)	P vs T: 0.747 (0.02) P vs C: 1.000 (0.02)
	C		690.20 ± 368.66 (567.36–813.03)	685.07 ± 368.15 (562.54–807.59)	-0.74	0.225 (0.01)	0.200 (0)	T vs C: 1.000 (0.16)	T vs C: 1.000 (0.01)

Table A.4. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Vitamin H intake (B8 or biotin) (µg/d)	MT	25.64	28.20 ± 8.90 (25.37–31.02)	28.03 ± 8.48 (25.33–30.73)	-0.59	0.697 (0.02)	0.855 (0.01)	MT vs P: 0.316 (0.5) MT vs T: 1.000 (0.07)	MT vs P: 1.000 (0.09) MT vs T: 1.000 (0.01)
	P		24.68 ± 7.33 (21.76–27.61)	24.18 ± 6.67 (21.39–26.98)	-2.03	0.260 (0.07)	0.179 (0.08)	MT vs C: **0.019** (0.79)	MT vs C: 1.000 (0.06)
	T		27.42 ± 8.57 (24.5–30.35)	27.46 ± 8.32 (24.66–30.26)	0.13	0.936 (0)	0.711 (0.02)	P vs T: 0.622 (0.43)	P vs T: 1.000 (0.1)
	C		22.32 ± 6.13 (19.49–25.14)	22.22 ± 6.13 (19.52–24.94)	-0.45	0.815 (0.02)	0.360 (0.06)	P vs C: 1.000 (0.31) T vs C: 0.052 (0.72)	P vs C: 1.000 (0.1) T vs C: 1.000 (0.03)
Vitamin D intake (µg/d)	MT	2.19	2.64 ± 1.91 (1.93–3.35)	2.72 ± 1.95 (1.99–3.44)	3.03	0.370 (0.04)	0.390 (0.04)	MT vs P: 1.000 (0.08) MT vs T: 0.769 (0.45)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.04)
	P		2.52 ± 2.23 (1.79–3.26)	2.55 ± 2.20 (1.80–3.3)	1.13	0.757 (0.01)	0.754 (0.01)	MT vs C: 0.714 (0.39)	MT vs C: 1.000 (0)
	T		1.77 ± 1.49 (1.03–2.5)	1.91 ± 1.62 (1.15–2.66)	7.86	0.133 (0.09)	0.130 (0.09)	P vs T: 1.000 (0.33)	P vs T: 1.000 (0.06)
	C		1.82 ± 2.13 (1.11–2.53)	1.90 ± 2.19 (1.17–2.63)	4.57	0.351 (0.049	0.374 (0.04)	P vs C: 1.000 (0.33) T vs C: 1.000 (0.29)	P vs C: 1.000 (0.02) T vs C: 1.000 (0.03)
Vitamin E intake (mg/d)	MT	6.65	6.80 ± 2.35 (5.91–7.69)	6.65 ± 1.98 (5.83–7.48)	-2.16	0.387 (0.07)	0.443 (0.06)	MT vs P: 1.000 (0.17) MT vs T: 1.000 (0.31)	MT vs P: 1.000 (0.08) MT vs T: 0.975 (0.13)
	P		7.00 ± 2.25 (6.08–7.92)	7.00 ± 2.15 (6.15–7.86)	0.00	1.000 (0)	0.760 (0.02)	MT vs C: 0.271 (0.62)	MT vs C: 1.000 (0.07)
	T		7.33 ± 3.25 (6.41–8.25)	7.44 ± 3.01 (6.59–8.30)	1.56	0.515 (0.04)	0.227 (0.06)	P vs T: 1.000 (0.17) P vs C: 0.068 (0.77)	P vs T: 1.000 (0.06) P vs C: 1.000 (0.06)
	C		5.56 ± 1.80 (4.67–6.45)	5.46 ± 1.84 (4.63–6.28)	-1.80	0.555 (0.05)	0.121 (0.14)	T vs C: **0.008** (0.8)	T vs C: 0.336 (0.15)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30). MT: multi-component training group; P: power training group; T: traditional high-intensity resistance training group; C: control group; CIs: coefficient intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate= 67.97.

SUPPLEMENTARY MATERIAL B. PPA RESULTS ON OXIDATIVE STRESS OF PROJECT ONE

Table B.1. *Intervention effects on oxidative stress of DNA, lipid protein biomarkers from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Urinary 8-oxo-dG (nmol/mmol creatinine)	M	2.87	3.91 ± 1.10 (3.36–4.47)	2.90 ± 1.15 (2.30–3.50)	-25.87	**0.001** (0.9)	0.077 (0.49)	M vs HI: 0.216 (0.61)	M vs HI: **0.001** (1.46)
	HI		2.12 ± 1.02 (1.63–2.62)	3.64 ± 1.23 (3.10–4.18)	71.49	**0.000** (1.34)	**0.000** (1.06)	M vs C: 1.000 (0.13)	M vs C: 0.727 (0.41)
	C		2.75 ± 1.18 (2.19–3.30)	2.75 ± 1.18 (2.19–3.30)	0.00	1.000 (0)	0.806 (0.06)	HI vs C: 0.092 (0.74)	HI vs C: **0.004** (1.04)
8-iso-P (nmol/mmol creatinine)	M	37.64	45.01 ± 16.19 (37.47–52.54)	37.08 ± 12.57 (30.35–43.82)	-17.60	**0.038** (0.55)	0.248 (0.26)	M vs HI: 0.701 (0.41)	M vs HI: 0.067 (0.79)
	HI		33.34 ± 16.25 (26.46–40.21)	42.57 ± 14.22 (36.42–48.72)	27.69	**0.009** (0.6)	**0.021** (0.45)	M vs C: 1.000 (0.11)	M vs C: 1.000 (0.15)
	C		35.31 ± 18.18 (27.58–43.03)	35.31 ± 18.18 (27.58–43.03)	0.00	1.000 (0)	0.655 (0.08)	HI vs C: 0.365 (0.45)	HI vs C: 0.170 (0.52)
MDA (nmol/mg protein)	M	0.20	0.21 ± 0.10 (0.17–0.24)	0.16 ± 0.04 (0.13–0.19)	-21.41	**0.022** (0.55)	**0.018** (0.41)	M vs HI: 1.000 (0.28)	M vs HI: 1.000 (0.3)
	HI		0.17 ± 0.06 (0.14–0.21)	0.18 ± 0.06 (0.15–0.20)	2.09	0.833 (0.06)	0.182 (0.28)	M vs C: **0.031** (0.85)	M vs C: **0.045** (0.78)
	C		0.22 ± 0.07 (0.18–0.25)	0.22 ± 0.07 (0.18–0.25)	0.00	1.000 (0)	0.292 (0.2)	HI vs C: 0.169 (0.55)	HI vs C: 0.301 (0.47)
Protein carbonyls (nmol/mg protein)	M	19.60	20.49 ± 3.85 (19.15–21.83)	20.52 ± 1.86 (19.51–21.53)	0.12	0.972 (0.01)	0.326 (0.15)	M vs HI: 0.750 (0.35)	M vs HI: 1.000 (0.03)
	HI		18.96 ± 2.71 (17.74–20.19)	19.72 ± 2.55 (18.80–20.64)	4.00	0.256 (0.29)	0.226 (0.2)	M vs C:0.465 (0.51)	M vs C: 1.000 (0.31)
	C		19.47 ± 2.22 (18.09–20.85)	19.47 ± 2.22 (18.09–20.85)	0.00	1.000 (0)	0.716 (0.08)	HI vs C: 1.000 (0.1)	HI vs C: 0.837 (0.29)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size in 8-oxo-dG: M = 16; HI = 20; C = 16. Sample size in the rest of the parameters: M = 20; HI= 24; C = 19.M: moderate-intensity group; HI: high-intensity group; C: control group; DNA: deoxyribonucleic acid; 8-oxo-dG: 8-oxo-2-deoxyguanosine; 8-iso-P: 8-isoprostane; MDA: malonaldehyde; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17 (70.12 for the analysis of 8-oxo-dG).

Table B.2. *Intervention effects on antioxidants enzymes from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
CAT (U/mg protein)	M	204.88	201.41 ± 26.78 (190.35–212.48)	214.07 ± 28.98 (201.49–226.65)	6.28	**0.025** (0.45)	**0.042** (0.4)	M vs HI: 1.000 (0.28)	M vs HI: 0.860 (0.29)
	HI		202.41 ± 19.20 (192.31–212.51)	206.36 ± 27.09 (194.87–217.84)	1.95	0.435 (0.17)	0.518 (0.14)	M vs C: 1.000 (0.08)	M vs C: 0.760 (0.31)
	C		211.65 ± 28.48 (200.29–223.00)	211.65 ± 28.48 (200.29–223.00)	0.00	1.000 (0)	0.665 (0.08)	HI vs C: 1.000 (0.19)	HI vs C: 1.000 (0.03)
GPx (U/mg protein)	M	57.55	55.01 ± 10.26 (49.76–60.26)	54.67 ± 6.01 (50.82–58.51)	-0.62	0.885 (0.04)	0.205 (0.27)	M vs HI: 0.615 (0.54)	M vs HI: 0.426 (0.59)
	HI		57.31 ± 12.15 (52.52–62.10)	51.33 ± 6.20 (47.83–54.84)	-10.43	**0.008** (0.62)	**0.000** (0.61)	M vs C: 0.113 (0.6)	M vs C: 0.313 (0.42)
	C		60.52 ± 12.59 (55.14–65.91)	60.52 ± 12.59 (55.14–65.91)	0.00	1.000 (0)	0.291 (0.15)	M vs C: **0.003** (0.96)	M vs C: **0.006** (0.81)
SOD (U/mg protein)	M	4.94	5.00 ± 0.43 (4.75–5.25)	5.08 ± 0.49 (4.82–5.34)	1.65	0.555 (0.18)	0.380 (0.24)	M vs HI: 1.000 (0.31)	M vs HI: 1.000 (0.16)
	HI		4.83 ± 0.52 (4.60–5.06)	4.92 ± 0.52 (4.69–5.16)	1.85	0.482 (0.17)	0.794 (0.06)	M vs C: 1.000 (0.09)	M vs C: 1.000 (0.1)
	C		5.03 ± 0.70 (4.77–5.28)	5.03 ± 0.70 (4.77–5.28)	0.00	1.000 (0)	0.702 (0.07)	HI vs C: 1.000 (0.17)	HI vs C: 1.000 (0.03)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (n = 20), HI (n = 24), C (n = 19). M: moderate-intensity group; HI: high-intensity group; C: control group; CAT: catalase; GPx: glutathione peroxidase; SOD: superoxide dismutase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17

Table B.3. *Intervention effects on thiol state from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
GSH (nmol/mg protein)	M	22.04	20.84 ± 3.15 (19.36–22.33)	20.69 ± 4.22 (19.12–22.25)	-0.74	0.857 (0.04)	0.221 (0.26)	M vs HI: 1.000 (0.12)	M vs HI: 0.988 (0.28)
	HI		22.71 ± 3.83 (21.36–24.07)	20.23 ± 3.35 (18.81–21.66)	-10.92	**0.002** (0.69)	**0.006** (0.56)	M vs C: 0.353 (0.5)	M vs C: 0.822 (0.34)
	C		22.46 ± 2.72 (20.94–23.99)	22.46 ± 2.72 (20.94–23.99)	0.00	1.000 (0)	0.748 (0.09)	HI vs C: 0.125 (0.72)	HI vs C: 0.099 (0.73)
GSSG (nmol/mg protein)	M	0.24	0.25 ± 0.07 (0.21–0.29)	0.23 ± 0.09 (0.18–0.28)	-7.16	0.525 (0.21)	0.697 (0.12)	M vs HI: 1.000 (0.14)	M vs HI: 1.000 (0.19)
	HI		0.23 ± 0.08 (0.19–0.26)	0.25 ± 0.13 (0.20–0.29)	7.91	0.479 (0.17)	0.608 (0.11)	M vs C: 1.000 (0.06)	M vs C: 1.000 (0.1)
	C		0.23 ± 0.10 (0.19–0.28)	0.23 ± 0.10 (0.19–0.28)	0.00	1.000 (0)	0.984 (0)	HI vs C: 1.000 (0.09)	HI vs C: 1.000 (0.1)
GSSG/GSH Ratio	M	1.12	1.25 ± 0.40 (1.03–1.47)	1.19 ± 0.57 (0.89–1.49)	-4.63	0.717 (0.12)	0.840 (0.06)	M vs HI: 1.000 (0.15)	M vs HI: 1.000 (0.22)
	HI		1.05 ± 0.48 (0.85–1.26)	1.29 ± 0.79 (1.02–1.57)	22.74	0.104 (0.36)	0.182 (0.28)	M vs C: 1.000 (0.19)	M vs C: 1.000 (0.10)
	C		1.08 ± 0.58 (0.85–1.30)	1.08 ± 0.58 (0.85–1.30)	0.00	1.000 (0)	0.865 (0.04)	HI vs C: 0.897 (0.3)	HI vs C: 0.911 (0.3)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (n = 20), HI (n = 24), C (n = 19). M: moderate-intensity group; HI: high-intensity group; C: control group; GSH: reduced glutathione; GSSG: oxidized glutathione; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 70.17.

SUPPLEMENTARY MATERIAL C. PPA RESULTS ON BONE HEALTH OF PROJECT ONE

Table C.1. *Intervention effects on BMD at lumbar spine from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L1vertebra aBMD (g/cm^2)	M	0.79	0.77 ± 0.13 (0.73–0.82)	0.79 ± 0.13 (0.74–0.84)	1.61	**0.046** (0.09)	0.051 (0.09)	M vs HI: 1.000 (0.06) M vs C: 1.000 (0.02) HI vs C: 1.000 (0.02)	M vs HI: 1.000 (0.02) M vs C: 0.088 (0.15) HI vs C: 0.154 (0.15)
	HI		0.78 ± 0.10 (0.74–0.83)	0.79 ± 0.10 (0.75–0.84)	1.21	0.075 (0.09)	0.092 (0.08)		
	C		0.80 ± 0.14 (0.74–0.86)	0.79 ± 0.14 (0.73–0.85)	-1.15	0.206 (0.07)	0.229 (0.06)		
L1 vertebra T-score (SD)	M	-1.84	-1.92 ± 1.19 (-2.36 to -1.49)	-1.81 ± 1.20 (-2.24 to -1.37)	-6.02	**0.011** (0.1)	**0.014** (0.1)	M vs HI: 1.000 (0.04) M vs C: 1.000 (0.05) HI vs C: 1.000 (0.03)	M vs HI: 1.000 (0.03) M vs C: **0.049** (0.14) HI vs C: 0.099 (0.14)
	HI		-1.86 ± 0.87 (-2.23 to -1.48)	-1.77 ± 0.90 (-2.14 to -1.39)	-4.74	**0.024** (0.1)	**0.030** (0.1)		
	C		-1.68 ± 1.31 (-2.19 to -1.16)	-1.74 ± 1.26 (-2.25 to -1.23)	3.63	0.249 (0.05)	0.284 (0.04)		
L2 vertebra aBMD (g/cm^2)	M	0.83	0.82 ± 0.13 (0.77–0.87)	0.83 ± 0.13 (0.78–0.88)	1.00	0.194 (0.06)	0.133 (0.07)	M vs HI: 1.000 (0.23) M vs C: 1.000 (0.02) HI vs C: 1.000 (0.26)	M vs HI: 1.000 (0) M vs C: 0.291 (0.12) HI vs C: 0.253 (0.12)
	HI		0.85 ± 0.13 (0.80–0.89)	0.86 ± 0.12 (0.81–0.90)	1.24	0.055 (0.08)	0.086 (0.07)		
	C		0.83 ± 0.12 (0.77–0.89)	0.82 ± 0.11 (0.77–0.88)	-0.86	0.333 (0.06)	0.371 (0.05)		
L2 vertebra T-score (SD)	M	-1.68	-1.69 ± 1.37 (-2.18 to -1.21)	-1.74 ± 1.17 (-2.19 to -1.29)	2.83	0.630 (0.04)	0.798 (0.02)	M vs HI: 1.000 (0.15) M vs C: 1.000 (0.03) HI vs C: 1.000 (0.19)	M vs HI: 1.000 (0.07) M vs C: 1.000 (0.01) HI vs C: 1.000 (0.08)
	HI		-1.64 ± 1.15 (-2.05 to -1.22)	-1.56 ± 1.12 (-1.95 to -1.18)	-4.65	0.372 (0.07)	0.475 (0.05)		
	C		-1.73 ± 1.08 (-2.30 to -1.16)	-1.77 ± 1.06 (-2.30 to -1.24)	2.24	0.740 (0.04)	0.738 (0.03)		

Table C.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L3 vertebra aBMD (g/cm^2)	M	0.88	0.87 ± 0.14 (0.81–0.93)	0.87 ± 0.15 (0.82–0.93)	0.72	0.419 (0.04)	0.317 (0.05)	M vs HI: 1.000 (0.2) M vs C: 1.000 (0.14) HI vs C: 0.754 (0.34)	M vs HI: 1.000 (0.01) M vs C: 0.649 (0.1) HI vs C: 0.466 (0.11)
	HI		0.89 ± 0.15 (0.84–0.95)	0.90 ± 0.15 (0.85–0.95)	1.12	0.130 (0.07)	0.168 (0.06)		
	C		0.86 ± 0.14 (0.79–0.93)	0.85 ± 0.12 (0.79–0.92)	-0.78	0.460 (0.05)	0.444 (0.05)		
L3vertebra T-score (SD)	M	-1.81	-1.91 ± 1.34 (-2.45 to -1.37)	-1.84 ± 1.36 (-2.37 to -1.32)	-3.55	0.261 (0.05)	0.235 (0.05)	M vs HI: 1.000 (0.22) M vs C: 1.000 (0.14) HI vs C: 0.646 (0.37)	M vs HI: 1.000 (0.01) M vs C: 0.514 (0.1) HI vs C: 0.325 (0.11)
	HI		-1.64 ± 1.36 (-2.10 to -1.17)	-1.55 ± 1.35 (-2.00 to -1.10)	-5.38	0.091 (0.06)	0.094 (0.06)		
	C		-1.98 ± 1.33 (-2.61 to -1.34)	-2.03 ± 1.16 (-2.65 to -1.41)	2.52	0.482 (0.04)	0.437 (0.04)		
L4 vertebra aBMD (g/cm^2)	M	0.88	0.86 ± 0.15 (0.80–0.92)	0.87 ± 0.14 (0.81–0.93)	1.07	0.300 (0.06)	0.196 (0.08)	M vs HI: 1.000 (0.25) M vs C: 1.000 (0.08) HI vs C: 0.820 (0.31)	M vs HI: 1.000 (0.01) M vs C:0.723 (0.1) HI vs C: 0.829 (0.09)
	HI		0.90 ± 0.15 (0.84–0.95)	0.91 ± 0.15 (0.85–0.96)	1.29	0.133 (0.07)	0.204 (0.06)		
	C		0.86 ± 0.15 (0.79–0.94)	0.86 ± 0.16 (0.78–0.93)	-0.57	0.638 (0.03)	0.671 (0.02)		
L4 vertebra T-score (SD)	M	-1.67	-1.80 ± 1.43 (-2.37 to -1.22)	-1.72 ± 1.35 (-2.28 to -1.15)	-4.44	0.238 (0.06)	0.145 (0.07)	M vs HI: 1.000 (0.21) M vs C: 1.000 (0.05) HI vs C: 1.000 (0.25)	M vs HI: 1.000 (0.01) M vs C: 0.598 (0.09) HI vs C: 0.640 (0.08)
	HI		-1.53 ± 1.44 (-2.03 to -1.04)	-1.43 ± 1.40 (-1.91 to -0.95)	-6.69	0.078 (0.07)	0.127 (0.09)		
	C		-1.75 ± 1.44 (-2.43 to -1.07)	-1.79 ± 1.49 (-2.45 to -1.13)	2.22	0.625 (0.03)	0.669 (0.05)		

Table C.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total lumbar spine aBMD (g/cm^2)	M	0.85	0.83 ± 0.13 (0.78–0.89)	0.84 ± 0.13 (0.79–0.90)	1.10	**0.032** (0.07)	**0.024** (0.07)	M vs HI: 1.000 (0.2) M vs C: 1.000 (0.09) HI vs C: 0.949 (0.3)	M vs HI: 1.000 (0.01) M vs C: **0.038** (0.12) HI vs C: **0.018** (0.13)
	HI		0.86 ± 0.13 (0.81–0.90)	0.87 ± 0.12 (0.83–0.92)	1.30	**0.003** (0.09)	**0.005** (0.09)		
	C		0.84 ± 0.13 (0.78–0.90)	0.83 ± 0.12 (0.77–0.89)	-0.82	0.165 (0.05)	0.175 (0.05)		
Total lumbar spine T-score (SD)	M	-1.80	-1.89 ± 1.22 (-2.37 to -1.42)	-1.83 ± 1.24 (-2.29 to -1.36)	-3.38	0.076 (0.05)	0.070 (0.05)	M vs HI: 1.000 (0.17) M vs C: 1.000 (0.06) HI vs C: 1.000 (0.23)	M vs HI: 1.000 (0.02) M vs C: 0.114 (0.1) HI vs C: **0.032** (0.12)
	HI		-1.72 ± 1.16 (-2.13 to -1.31)	-1.63 ± 1.13 (-2.03 to -1.23)	-5.12	**0.005** (0.08)	**0.006** (0.08)		
	C		-1.85 ± 1.18 (-2.40 to -1.29)	-1.90 ± 1.11 (-2.44 to -1.35)	2.70	0.236 (0.04)	0.237 (0.04)		
L2-L4 lumbar spine segment aBMD (g/cm^2)	M	0.87	0.85 ± 0.13 (0.80–0.91)	0.86 ± 0.14 (0.80–0.92)	0.96	0.108 (0.06)	0.079 (0.06)	M vs HI: 0.780 (0.29) M vs C: 1.000 (0.1) HI vs C: 0.552 (0.39)	M vs HI: 1.000 (0.01) M vs C: 0.166 (0.11) HI vs C: 0.100 (0.11)
	HI		0.89 ± 0.15 (0.84–0.94)	0.90 ± 0.14 (0.85–0.95)	1.19	**0.016** (0.07)	**0.025** (0.07)		
	C		0.85 ± 0.13 (0.79–0.92)	0.85 ± 0.12 (0.78–0.91)	-0.71	0.307 (0.05)	0.310 (0.05)		
L2-L4 lumbar spine segment T-score (SD)	M	-1.76	-2.03 ± 1.26 (-2.58 to -1.49)	-1.97 ± 1.28 (-2.51 to -1.43)	-3.02	0.170 (0.05)	0.123 (0.05)	M vs HI: 0.242 (0.45) M vs C: 1.000 (0.07) HI vs C: 0.220 (0.52)	M vs HI: 1.000 (0.01) M vs C: 0.243 (0.1) HI vs C: 0.137 (0.1)
	HI		-1.43 ± 1.51 (-1.90 to -0.96)	-1.34 ± 1.50 (-1.80 to -0.88)	-6.16	**0.023** (0.06)	**0.035** (0.05)		
	C		-2.01 ± 1.20 (-2.65 to -1.36)	-2.06 ± 1.11 (-2.69 to -1.42)	2.49	0.343 (0.04)	0.337 (0.04)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (n = 25), HI (n = 34), C (n = 18). M: moderate-intensity group; HI: high-intensity group; C: control group; BMD: bone mineral density; aBMD: areal bone mineral density; CIs: confidence intervals;
ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table C.2. *Intervention effects on BMD at proximal femur from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Femoral neck aBMD (g/cm^2)	M	0.66	0.67 ± 0.08 (0.63–0.71)	0.68 ± 0.09 (0.65–0.72)	1.93	**0.003** (0.14)	**0.001** (0.17)	M vs HI: 1.000 (0.25) M vs C: 1.000 (0.23) HI vs C: 1.000 (0.01)	M vs HI: 0.925 (0.07) M vs C: **0.028** (0.19) HI vs C: 0.204 (0.13)
	HI		0.65 ± 0.09 (0.62–0.68)	0.66 ± 0.09 (0.63–0.69)	1.61	**0.005** (0.11)	**0.018** (0.1)		
	C		0.66 ± 0.09 (0.62–0.71)	0.66 ± 0.10 (0.62–0.70)	-0.50	0.512 (0.03)	0.604 (0.03)		
Femoral neck T-score (SD)	M	-1.66	-1.59 ± 0.80 (-1.92 to -1.25)	-1.48 ± 0.79 (-1.82 to -1.15)	-6.53	**0.011** (0.13)	**0.005** (0.14)	M vs HI: 1.000 (0.17) M vs C: 1.000 (0.16) HI vs C: 1.000 (0)	M vs HI: 1.000 (0.01) M vs C: 0.153 (0.14) HI vs C: 0.151 (0.13)
	HI		-1.74 ± 0.83 (-2.03 to -1.46)	-1.62 ± 0.84 (-1.91 to -1.33)	-6.90	**0.001** (0.14)	**0.002** (0.13)		
	C		-1.61 ± 0.90 (-2.01 to -1.22)	-1.62 ± 0.92 (-2.02 to -1.23)	0.69	0.813 (0.01)	0.896 (0.01)		
Trochanter aBMD (g/cm^2)	M	0.64	0.67 ± 0.09 (0.63–0.70)	0.67 ± 0.09 (0.63–0.71)	0.90	0.091 (0.06)	**0.047** (0.07)	M vs HI: 0.797 (0.3) M vs C: 0.476 (0.44) HI vs C:1.000 (0.14)	M vs HI: 0.925 (0.02) M vs C: **0.028** (0.11) HI vs C: 0.204 (0.13)
	HI		0.63 ± 0.09 (0.60–0.67)	0.64 ± 0.09 (0.61–0.68)	1.60	**0.001** (0.11)	**0.004** (0.1)		
	C		0.63 ± 0.09 (0.59–0.68)	0.63 ± 0.09 (0.59–0.67)	-0.52	0.424 (0.04)	0.477 (0.03)		
Trochanter T-score (SD)	M	-0.56	-0.39 ± 0.90 (-0.75 to -0.03)	-0.34 ± 0.88 (-0.70 to 0.02)	-13.27	0.139 (0.06)	0.103 (0.07)	M vs HI: 1.000 (0.24) M vs C: 0.772 (0.36) HI vs C: 1.000 (0.11)	M vs HI: 1.000 (0.04) M vs C: 0.153 (0.11) HI vs C: 0.151 (0.15)
	HI		-0.66 ± 0.88 (-0.97 to -0.35)	-0.56 ± 0.91 (-0.87 to -0.25)	-15.49	**0.001** (0.11)	**0.002** (0.11)		
	C		-0.61 ± 0.94 (-1.04 to -0.19)	-0.66 ± 0.92 (-1.08 to -0.23)	7.21	0.282 (0.05)	0.307 (0.05)		

Table C.2. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Intertro-chanteric area aBMD (g/cm^2)	M	0.99	1.00 ± 0.16 (0.94–1.05)	1.00 ± 0.15 (0.95–1.06)	0.60	0.344 (0.04)	0.240 (0.05)	M vs HI: 1.000 (0.22) M vs C: 1.000 (0.07) HI vs C: 0.938 (0.33)	M vs HI: 1.000 (0.03) M vs C: 0.695 (0.07) HI vs C: 1.000 (0.06)
	HI		0.97 ± 0.11 (0.92–1.02)	0.97 ± 0.11 (0.93–1.02)	0.64	0.247 (0.05)	0.440 (0.03)		
	C		1.02 ± 0.16 (0.95–1.09)	1.01 ± 0.13 (0.95–1.08)	-0.65	0.369 (0.04)	0.575 (0.02)		
Intertro-chanteric area T-score (SD)	M	-0.69	-0.69 ± 0.98 (-1.05 to -0.33)	-0.64 ± 0.94 (-0.99 to -0.30)	-6.36	0.275 (0.05)	0.220 (0.05)	M vs HI: 1.000 (0.09) M vs C: 1.000 (0.08) HI vs C: 1.000 (0.18)	M vs HI: 1.000 (0) M vs C: 0.733 (0.08) HI vs C: 0.718 (0.08)
	HI		-0.78 ± 0.82 (-1.08 to -0.47)	-0.72 ± 0.81 (-1.02 to -0.43)	-7.14	0.108 (0.07)	0.176 (0.06)		
	C		-0.54 ± 0.90 (-0.96 to -0.12)	-0.57 ± 0.83 (-0.98 to -0.17)	6.12	0.482 (0.04)	0.634 (0.03)		
Ward's triangle aBMD (g/cm^2)	M	0.50	0.52 ± 0.10 (0.48–0.56)	0.53 ± 0.09 (0.49–0.58)	3.17	**0.006** (0.17)	**0.001** (0.2)	M vs HI: 0.494 (0.36) M vs C: 0.904 (0.35) HI vs C: 1.000 (0.05)	M vs HI: 0.636 (0.09) M vs C: 0.055 (0.22) HI vs C: 0.526 (0.1)
	HI		0.48 ± 0.11 (0.45–0.52)	0.50 ± 0.11 (0.46–0.53)	2.84	**0.007** (0.12)	**0.028** (0.1)		
	C		0.50 ± 0.10 (0.45–0.55)	0.50 ± 0.09 (0.45–0.55)	-0.33	0.809 (0.02)	0.955 (0.01)		
Ward's triangle T-score (SD)	M	-1.97	-1.80 ± 0.87 (-2.18 to -1.42)	-1.66 ± 0.81 (-2.02 to -1.30)	-7.54	**0.007** (0.16)	**0.001** (0.2)	M vs HI: 0.537 (0.35) M vs C: 0.920 (0.35) HI vs C: 1.000 (0.04)	M vs HI: 0.888 (0.07) M vs C: **0.043** (0.21) HI vs C: 0.305 (0.12)
	HI		-2.11 ± 1.01 (-2.44 to -1.79)	-1.99 ± 0.99 (-2.30 to -1.68)	-5.97	**0.003** (0.13)	**0.014** (0.1)		
	C		-1.93 ± 0.88 (-2.37 to -1.49)	-1.95 ± 0.83 (-2.38 to -1.53)	1.15	0.699 (0.03)	0.830 (0.01)		

Table C.2. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total hip aBMD (g/cm^2)	M	0.83	0.85 ± 0.12 (0.81–0.90)	0.86 ± 0.13 (0.82–0.91)	1.38	**0.000** (0.09)	**0.000** (0.1)	M vs HI: 0.671 (0.33)	M vs HI: 1.000 (0.02)
	HI		0.82 ± 0.09 (0.78–0.85)	0.83 ± 0.09 (0.79–0.87)	1.41	**0.000** (0.12)	**0.000** (0.11)	M vs C: 1.000 (0.22)	M vs C: **0.018** (0.1)
	C		0.84 ± 0.11 (0.78–0.89)	0.84 ± 0.11 (0.787–0.89)	-0.09	0.840 (0.01)	0.927 (0)	HI vs C: 1.000 (0.09)	HI vs C: 0.051 (0.11)
Total hip T-score (SD)	M	-0.85	-0.77 ± 0.97 (-1.14 to -0.40)	-0.68 ± 0.96 (-1.04 to -0.32)	-11.86	**0.004** (0.09)	**0.003** (0.1)	M vs HI: 1.000 (0.17)	M vs HI: 1.000 (0.01)
	HI		-0.93 ± 0.85 (-1.24 to -0.61)	-0.83 ± 0.83 (-1.14 to -0.52)	-10.09	**0.001** (0.11)	**0.001** (0.11)	M vs C: 1.000 (0.15)	M vs C: 0.069 (0.12)
	C		-0.81 ± 0.97 (-1.25 to -0.38)	-0.83 ± 0.96 (-1.26 to -0.40)	2.04	0.650 (0.02)	0.693 (0.01)	HI vs C: 1.000 (0.01)	HI vs C: 0.078 (0.12)
10-year probability of a major osteoporotic fracture (%)	M	0.10	0.12 ± 0.05 (0.11–0.14)	0.12 ± 0.04 (0.10–0.13)	-6.05	**0.013** (0.16)	0.110 (0.08)	M vs HI: **0.019** (0.93)	M vs HI: 0.278 (0.22)
	HI		0.09 ± 0.03 (0.08–0.11)	0.08 ± 0.02 (0.07–0.10)	-11.29	**0.000** (0.34)	**0.000** (0.37)	M vs C: 0.336 (0.57)	M vs C: 1.000 (0.07)
	C		0.09 ± 0.04 (0.07–0.11)	0.09 ± 0.04 (0.07–0.11)	0.58	0.881 (0.01)	0.677 (0.02)	HI vs C: 1.000 (0.24)	HI vs C: 0.058 (0.32)
10-year probability of a hip fracture (%)	M	0.02	0.02 ± 0.01 (0.01–0.03)	0.02 ± 0.01 (0.01–0.02)	-5.60	**0.035** (0.09)	**0.050** (0.06)	M vs HI: 0.085 (0.92)	M vs HI: 1.000 (0.09)
	HI		0.01 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.01–0.01)	-12.58	**0.001** (0.37)	**0.001** (0.4)	M vs C: 1.000 (0.24)	M vs C: 0.917 (0.13)
	C		0.01 ± 0.01 (0.01–0.02)	0.01 ± 0.01 (0.01–0.02)	1.17	0.769 (0.02)	0.833 (0.07)	HI vs C: 0.907 (0.72)	HI vs C: 0.151 (0.33)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (n = 25), HI (n = 34), C (n = 18).M: moderate-intensity group; HI: high-intensity group; C: control group; BMD: bone mineral density; aBMD: areal bone mineral density; CIs: confidence intervals;
ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table C.3. *Intervention effects on bone biomarkers at pre and midpoint (16 weeks) from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
P1NP (µg/L)	M	36.62	34.60 ± 12.78 (29.56–39.64)	38.99 ± 14.30 (34.01–43.96)	12.68	**0.002** (0.32)	**0.003** (0.31)	M vs HI: 1.000 (0.07) M vs C: 1.000 (0.11) HI vs C: 1.000 (0.2)	M vs HI: 0.814 (0.15) M vs C:0.095 (0.28) HI vs C: 0.598 (0.18)
	HI		35.03 ± 12.03 (30.59–39.48)	38.13 ± 10.84 (33.75–42.52)	8.84	**0.011** (0.27)	**0.018** (0.25)		
	C		41.12 ± 16.23 (35.30–46.94)	40.64 ± 15.34 (34.90–46.38)	-1.17	0.760 (0.03)	0.967 (0)		
β-CTx (pg/mL)	M	311.76	300.57 ± 107.12 (253.64–347.50)	276.85 ± 111.93 (232.24–321.46)	-7.89	**0.007** (0.22)	**0.003** (0.23)	M vs HI: 1.000 (0.02) M vs C: 0.110 (0.6) HI vs C: 0.070 (0.62)	M vs HI: 1.000 (0.01) M vs C: **0.042** (0.27) HI vs C: **0.022** (0.28)
	HI		300.00 ± 135.17 (258.61–341.38)	274.27 ± 116.41 (234.93–313.62)	-8.57	**0.001** (0.2)	**0.001** (0.21)		
	C		346.85 ± 128.13 (292.66–401.04)	349.61 ± 130.77 (298.10–401.13)	0.80	0.781 (0.02)	0.481 (0.05)		
bALP (U/L)	M	34.75	31.87 ± 7.21 (28.87–34.87)	32.71 ± 7.07 (29.62–35.80)	2.63	0.260 (0.12)	0.436 (0.08)	M vs HI: 0.008 (0.75) M vs C: 1.000 (0.09) HI vs C: **0.036** (0.66)	M vs HI: 0.493 (0.17) M vs C: 0.518 (0.23) HI vs C: **0.018** (0.35)
	HI		37.26 ± 8.75 (34.61–39.91)	39.15 ± 9.65 (36.42–41.87)	5.07	**0.005** (0.21)	**0.003** (0.23)		
	C		34.28 ± 7.55 (30.82–37.75)	33.35 ± 6.81 (29.79–36.92)	-2.71	0.280 (0.13)	0.257 (0.13)		
bALP/ β-CTx ratio	M	137.28	116.39 ± 37.87 (83.97–148.82)	133.89 ± 47.53 (99.86–167.92)	15.03	**0.014** (0.41)	**0.016** (0.41)	M vs HI: 0.092 (0.5) M vs C: 1.000 (0.47) HI vs C: **0.012** (0.7)	M vs HI: 1.000 (0) M vs C: 0.120 (0.45) HI vs C: 0.102 (0.22)
	HI		166.67 ± 121.38 (138.07–195.26)	184.08 ± 126.04 (154.07–214.09)	10.45	**0.006** (0.14)	**0.007** (0.14)		
	C		114.74 ± 52.69 (77.30–152.18)	110.79 ± 52.32 (71.50–150.09)	-3.44	0.626 (0.08)	0.553 (0.09)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 28), HI (*n* = 36), C (*n* = 21).M: moderate-intensity group; HI: high-intensity group; C: control group; P1NP: N-terminal propeptide of type1 procollagen; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); bALP: bone-specific alkaline phosphatase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table C.4. *Intervention effects on bone health related variables at pre and midpoint (16 weeks) from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
25OHD (ng/ml)	M		24.57 ± 8.58 (19.95–29.18)	25.32 ± 11.53 (20.85–29.78)	3.05	0.582 (0.07)	0.556 (0.08)		
	HI	25.29	27.69 ± 15.34 (23.62–31.76)	28.52 ± 14.20 (24.58–32.46)	3.01	0.488 (0.06)	0.316 (0.08)	M vs HI: 0.862 (0.24)	M vs HI: 1.000 (0.03)
	C		22.14 ± 10.27 (16.81–27.47)	22.19 ± 6.77 (17.03–27.34)	0.22	0.976 (0.01)	0.704 (0.07)	M vs C: 1.000 (0.32)	M vs C: 1.000 (0.14)
								HI vs C: 0.166 (0.53)	HI vs C: 1.000 (0.14)
Na (mEq/L)	M		141.00 ± 1.82 (140.27–141.72)	141.21 ± 1.44 (140.55–141.87)	0.15	0.478 (0.13)	0.382 (0.14)		
	HI	140.92	140.44 ± 2.03 (139.80–141.08)	141.27 ± 2.02 (140.69–141.85)	0.59	**0.002** (0.41)	**0.008** (0.31)	M vs HI: 1.000 (0.04)	M vs HI: 0.803 (0.22)
	C		141.66 ± 1.90 (140.82–142.50)	141.76 ± 1.60 (141.00–142.52)	0.07	0.785 (0.05)	0.181 (0.23)	M vs C: 0.846 (0.36)	M vs C: 1.000 (0.12)
								HI vs C: 0.952 (0.26)	HI vs C: 1.000 (0.12)
K (mEq/L)	M		4.68 ± 0.38 (4.54–4.81)	4.50 ± 0.38 (4.38–4.63)	-3.74	**0.004** (0.46)	**0.029** (0.31)		
	HI	4.58	4.58 ± 0.32 (4.47–4.70)	4.46 ± 0.33 (4.35–4.57)	-2.66	**0.022** (0.37)	**0.005** (0.4)	M vs HI: 1.000 (0.11)	M vs HI: 1.000 (0.04)
	C		4.46 ± 0.39 (4.31–4.62)	4.53 ± 0.26 (4.38–4.68)	1.49	0.335 (0.2)	0.871 (0.03)	M vs C: 1.000 (0.08)	M vs C: 0.360 (0.38)
								HI vs C: 1.000 (0.21)	HI vs C: 0.189 (0.46)
Cl (mEq/L)	M		105.60 ± 2.04 (104.65–106.56)	106.21 ± 2.14 (105.31–107.11)	0.57	0.126 (0.29)	**0.013** (0.43)		
	HI	105	104.22 ± 2.78 (103.37–105.06)	104.97 ± 2.59 (104.17–105.77)	0.72	**0.033** (0.28)	0.202 (0.15)	M vs HI: 0.131 (0.52)	M vs HI: 0.937 (0.21)
	C		105.52 ± 2.69 (104.42–106.62)	106.85 ± 2.39 (105.81–107.90)	1.26	**0.004** (0.52)	**0.000** (0.6)	M vs C: 1.000 (0.28)	M vs C: 0.739 (0.28)
								HI vs C: **0.016** (0.75)	HI vs C: 0.099 (0.45)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs. Sample size of each group: M (n = 28), H (n = 36), C (n = 21). M: moderate-intensity group; HI: high-intensity group; C: control group; 25OHD: 25-hydroxy-vitamin D; Na: sodium; K: potassium; Cl: chloride; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table C.5. *Intervention effects on bone biomarkers at pre and post training period (32 weeks) from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
P1NP (µg/L)	M		34.04 ± 12.88 (28.82–39.26)	42.20 ± 11.48 (37.96–46.43)	23.96	**0.000** (0.67)	**0.000** (0.6)		
	HI	35.76	35.20 ± 12.03 (30.73–39.68)	44.44 ± 9.03 (40.80–48.07)	26.22	**0.000** (0.87)	**0.000** (0.88)	M vs HI: 1.000 (0.22)	M vs HI: 1.000 (0.15)
	C		38.12 ± 15.19 (31.97–44.27)	36.88 ± 12.15 (31.88–41.87)	-3.25	0.554 (0.09)	0.820 (0.03)	M vs C: 0.330 (0.45)	M vs C: **0.002** (0.66)
								HI vs C: 0.052 (0.74)	HI vs C: **0.000** (0.91)
β-CTx (pg/mL)	M		284.80 ± 98.22 (238.45–331.14)	258.24 ± 95.47 (214.48–301.99)	-9.33	**0.006** (0.27)	**0.002** (0.31)		
	HI	298.07	297.88 ± 131.39 (258.14–337.62)	268.67 ± 117.24 (231.15–306.19)	-9.80	**0.001** (0.23)	**0.001** (0.22)	M vs HI: 1.000 (0.1)	M vs HI: 1.000 (0.02)
	C		316.88 ± 108.29 (262.27–371.50)	329.55 ± 113.70 (277.98–381.12)	4.00	0.257 (0.11)	0.168 (0.13)	M vs C: 0.117 (0.69)	M vs C: **0.006** (0.43)
								HI vs C: 0.183 (0.52)	HI vs C: **0.006** (0.37)
bALP (U/L)	M		31.44 ± 6.42 (28.35–34.52)	34.40 ± 5.77 (31.41–37.38)	9.41	**0.001** (0.48)	**0.004** (0.42)		
	HI	34.46	36.98 ± 8.93 (34.33–39.63)	40.65 ± 8.67 (38.08–43.21)	9.91	**0.000** (0.42)	**0.000** (0.45)	M vs HI: **0.007** (0.82)	M vs HI: 0.695 (0.19)
	C		33.91 ± 6.93 (30.27–37.55)	33.52 ± 7.19 (30.00–37.05)	-1.15	0.704 (0.06)	0.665 (0.06)	M vs C: 1.000 (0.14)	M vs C: 0.068 (0.47)
								HI vs C: **0.005** (0.87)	HI vs C: **0.002** (0.54)
bALP/ β-CTx ratio	M		120.65 ± 37.60 (85.48–155.82)	149.19 ± 51.79 (109.28–189.10)	23.66	**0.003** (0.63)	**0.002** (0.67)		
	HI	141.06	165.88 ± 122.46 (135.72–196.04)	199.31 ± 137.68 (165.09–233.54)	20.15	**0.000** (0.26)	**0.000** (0.24)	M vs HI: 0.184 (0.46)	M vs HI: 1.000 (0.02)
	C		122.53 ± 52.84 (81.09–163.98)	117.82 ± 55.39 (70.79–164.86)	-3.84	0.664 (0.09)	0.720 (0.07)	M vs C: 0.943 (0.59)	M vs C: 0.060 (0.64)
								HI vs C: **0.020** (0.7)	HI vs C: **0.036** (0.31)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n*=25), HI (*n*= 34), C (*n*=18). M: moderate-intensity group; HI: high-intensity group; C: control group; P1NP: N-terminal propeptide of type1 procollagen; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); bALP: bone-specific alkaline phosphatase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table C.6. *Intervention effects on bone health related variables at pre and post training period (32 weeks) from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group x time)	*P*-value (ES) ANCOVA (group x time)
25OHD (ng/ml)	M	25.50	25.20 ± 8.85 (20.31–30.08)	28.88 ± 12.39 (23.65–34.10)	14.60	**0.020** (0.34)	**0.022** (0.34)	M vs HI: 1.000 (0.08)	M vs HI: 1.000 (0.02)
	HI		26.70 ± 15.13 (22.51–30.89)	29.94 ± 15.16 (25.46–34.42)	12.11	**0.017** (0.21)	**0.014** (0.22)	M vs C: 0.476 (0.52)	M vs C: 0.199 (0.4)
	C		23.66 ± 9.98 (17.90–29.42)	23.11 ± 9.19 (16.95–29.26)	-2.35	0.761 (0.06)	0.666 (0.08)	HI vs C: 0.234 (0.51)	HI vs C: 0.214 (0.31)
Na (mEq/L)	M	140.79	140.84 ± 1.86 (140.06–141.61)	141.40 ± 1.44 (140.75–142.04)	0.40	0.128 (0.34)	0.064 (0.33)	M vs HI: 0.422 (0.4)	M vs HI: 1.000 (0.21)
	HI		140.32 ± 1.93 (139.66–140.98)	140.76 ± 1.70 (140.21–141.31)	0.31	0.161 (0.24)	0.424 (0.11)	M vs C: 1.000 (0.26)	M vs C: 0.399 (0.44)
	C		141.61 ± 2.03 (140.70–142.52)	141.00 ± 1.68 (140.23–141.76)	-0.43	0.158 (0.33)	0.694 (0.07)	HI vs C: 1.000 (0.14)	HI vs C: 1.000 (0.2)
K (mEq/L)	M	4.6	4.72 ± 0.37 (4.58–4.86)	4.68 ± 0.34 (4.53–4.82)	-0.85	0.540 (0.11)	0.998 (0)	M vs HI: 1.000 (0.21)	M vs HI: 1.000 (0.09)
	HI		4.58 ± 0.32 (4.45–4.70)	4.61 ± 0.35 (4.48–4.73)	0.64	0.599 (0.09)	0.567 (0.09)	M vs C: 0.212 (0.56)	M vs C: 1.000 (0.11)
	C		4.46 ± 0.39 (4.29–4.63)	4.47 ± 0.40 (4.30–4.64)	0.37	0.828 (0.04)	0.581 (0.1)	HI vs C: 0.632 (0.36)	HI vs C: 1.000 (0.19)
Cl (mEq/L)	M	104.93	105.52 ± 2.12 (104.49–106.54)	106.76 ± 2.25 (105.71–107.80)	1.18	**0.003** (0.57)	**0.001** (0.63)	M vs HI: 0.198 (0.49)	M vs HI: 1.000 (0.12)
	HI		104.23 ± 2.77 (103.35–105.11)	105.47 ± 2.90 (104.57–106.36)	1.19	**0.001** (0.43)	**0.002** (0.38)	M vs C: 1.000 (0.27)	M vs C: 1.000 (0.24)
	C		105.44 ± 2.72 (104.23–106.65)	106.11 ± 2.51 (104.88–107.34)	0.63	0.168 (0.25)	0.080 (0.31)	HI vs C: 1.000 (0.23)	HI vs C: 1.000 (0.09)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 25), HI (*n* = 34), C (*n* = 18).M: moderate-intensity group; HI: high-intensity group; C: control group; P1NP: N-terminal propeptide of type1 procollagen; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); bALP: bone-specific alkaline phosphatase; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

SUPPLEMENTARY MATERIAL D. PPA RESULTS ON BONE HEALTH OF PROJECT TWO

Table D.1. *Intervention effects on BMD at lumbar spine from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L1vertebra aBMD (g/cm^2)	MT	0.82	0.80 ± 0.12 (0.76–0.84)	0.82 ± 0.12 (0.78–0.87)	3.06	**0.004** (0.2)	**0.008** (0.19)	MT vs P: 1.000 (0.34) MT vs T: 1.000 (0.06) MT vs C: 1.000 (0.09) P vs T: 1.000 (0.27) P vs C: 0.608 (0.45) T vs C: 1.000 (0.16)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.05) MT vs C: 0.397 (0.19) P vs T: 1.000 (0.03) P vs C: 0.640 (0.17) T vs C: 1.000 (0.14)
	P		0.85 ± 0.11 (0.80–0.89)	0.86 ± 0.11 (0.82–0.91)	2.16	**0.034** (0.16)	**0.020** (0.17)		
	T		0.82 ± 0.11 (0.77–0.86)	0.83 ± 0.12 (0.79–0.88)	1.85	0.078 (0.13)	0.057 (0.15)		
	C		0.81 ± 0.10 (0.77–0.85)	0.81 ± 0.10 (0.77–0.86)	0.17	0.866 (0.01)	0.917 (0.01)		
L1 vertebra T-score (SD)	MT	-1.54	-1.69 ± 1.14 (-2.06 to -1.32)	-1.52 ± 1.14 (-1.89 to -1.14)	-10.41	**0.028** (0.15)	0.054 (0.13)	MT vs P: 1.000 (0.32) MT vs T: 1.000 (0.1) MT vs C: 1.000 (0.05) P vs T: 1.000 (0.21) P vs C: 0.977 (0.21) T vs C: 1.000 (0.4)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.01) MT vs C: 0.997 (0.15) P vs T: 1.000 (0.04) P vs C: 0.719 (0.04) T vs C: 1.000 (0.19)
	P		-1.35 ± 0.93 (-1.73 to -0.97)	-1.18 ± 0.93 (-1.57 to -0.80)	-12.14	**0.049** (0.18)	**0.032** (0.19)		
	T		-1.52 ± 1.02 (-1.91 to -1.14)	-1.40 ± 1.09 (-1.79 to -1.01)	-8.18	0.132 (0.12)	0.090 (0.13)		
	C		-1.57 ± 0.96 (-1.94 to -1.20)	-1.57 ± 0.96 (-1.95 to -1.19)	-0.21	0.967 (0)	0.992 (0)		
L2 vertebra aBMD (g/cm^2)	MT	0.86	0.84 ± 0.14 (0.80–0.89)	0.86 ± 0.13 (0.81–0.90)	1.40	0.144 (0.09)	0.213 (0.06)	MT vs P: 1.000 (0.23) MT vs T: 1.000 (0.12) MT vs C: 1.000 (0.03) P vs T: 1.000 (0.12) P vs C: 1.000 (0.3) T vs C: 1.000 (0.16)	MT vs P: 1.000 (0.11) MT vs T: 1.000 (0) MT vs C: 0.954 (0.12) P vs T: 1.000 (0.13) P vs C: 0.076 (0.27) T vs C: 1.000 (0.13)
	P		0.86 ± 0.09 (0.82–0.91)	0.88 ± 0.09 (0.84–0.93)	2.47	**0.012** (0.23)	**0.006** (0.23)		
	T		0.86 ± 0.12 (0.82–0.91)	0.87 ± 0.11 (0.83–0.91)	0.80	0.408 (0.06)	0.262 (0.08)		
	C		0.86 ± 0.11 (0.81–0.90)	0.85 ± 0.11 (0.81–0.89)	-0.67	0.478 (0.05)	0.454 (0.05)		
L2 vertebra T-score (SD)	MT	-1.52	-1.63 ± 1.28 (-2.03 to -1.23)	-1.51 ± 1.21 (-1.89 to -1.13)	-7.54	0.070 (0.1)	0.103 (0.08)	MT vs P: 1.000 (0.2) MT vs T: 1.000 (0.10) MT vs C: 1.000 (0.04) P vs T: 1.000 (0.1) P vs C: 1.000 (0.1) T vs C: 1.000 (0.26)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0.02) MT vs C: 0.672 (0.13) P vs T: 1.000 (0.1) P vs C: 0.118 (0.1) T vs C: 1.000 (0.23)
	P		-1.48 ± 0.90 (-1.89 to -1.06)	-1.30 ± 0.83 (-1.70 to -0.91)	-11.81	**0.013** (0.2)	**0.008** (0.21)		
	T		-1.46 ± 1.13 (-1.88 to -1.04)	-1.39 ± 1.02 (-1.79 to -1.00)	-4.63	0.332 (0.06)	0.220 (0.08)		
	C		-1.51 ± 1.07 (-1.91 to -1.11)	-1.55 ± 1.06 (-1.93 to -1.17)	2.64	0.553 (0.04)	0.538 (0.04)		

Table D.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
L3 vertebra aBMD (g/cm^2)	MT	0.88	0.87 ± 0.12 (0.82–0.92)	0.88 ± 0.12 (0.83–0.92)	0.50	0.614 (0.03)	0.787 (0.02)	MT vs P: 1.000 (0.37) MT vs T: 1.000 (0.17) MT vs C: 1.000 (0.07) P vs T: 1.000 (0.16) P vs C: 1.000 (0.28) T vs C: 1.000 (0.1)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.02) MT vs C: 1.000 (0.05) P vs T: 1.000 (0.01) P vs C: 1.000 (0.06) T vs C: 1.000 (0.06)
	P		0.92 ± 0.09 (0.87–0.96)	0.92 ± 0.09 (0.87–0.96)	0.22	0.823 (0.02)	0.628 (0.04)		
	T		0.89 ± 0.15 (0.85–0.94)	0.90 ± 0.13 (0.85–0.95)	0.44	0.661 (0.03)	0.617 (0.03)		
	CON		0.89 ± 0.13 (0.84–0.93)	0.88 ± 0.13 (0.84–0.93)	-0.26	0.787 (0.02)	0.738 (0.02)		
L3vertebra T-score (SD)	MT	-1.81	-1.89 ± 1.15 (-2.31 to -1.46)	-1.84 ± 1.18 (-2.26 to -1.43)	-2.46	0.548 (0.04)	0.702 (0.02)	MT vs P: 1.000 (0.36) MT vs T: 1.000 (0.17) MT vs C: 1.000 (0.06) P vs T: 1.000 (0.17) P vs C: 1.000 (0.17) T vs C: 1.000 (0.28)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.01) MT vs C: 1.000 (0.04) P vs T: 1.000 (0) P vs C: 1.000 (0) T vs C: 1.000 (0.06)
	P		-1.49 ± 0.82 (-1.93 to -1.05)	-1.46 ± 0.88 (-1.89 to -1.03)	-1.91	0.722 (0.03)	0.546 (0.06)		
	T		-1.68 ± 1.43 (-2.12 to -1.25)	-1.64 ± 1.23 (-2.07 to -1.21)	-2.54	0.594 (0.03)	0.556 (0.04)		
	CON		-1.75 ± 1.19 (-2.18 to -1.33)	-1.77 ± 1.23 (-2.18 to -1.35)	0.76	0.864 (0.01)	0.818 (0.01)		
L4 vertebra aBMD (g/cm^2)	MT	0.88	0.87 ± 0.15 (0.82–0.92)	0.87 ± 0.14 (0.82–0.92)	0.18	0.858 (0.01)	0.978 (0)	MT vs P: 0.374 (0.5) MT vs T: 1.000 (0.33) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.2) P vs C: 0.429 (0.46) T vs C: 1.000 (0.29)	MT vs P: 0.947 (0.12) MT vs T: 1.000 (0.02) MT vs C: 0.327 (0.16) P vs T: 0.668 (0.16) P vs C: **0.007** (0.28) T vs C: 0.551 (0.15)
	P		0.92 ± 0.12 (0.87–0.98)	0.94 ± 0.13 (0.89–0.99)	1.70	0.079 (0.12)	0.052 (0.13)		
	T		0.92 ± 0.14 (0.86–0.97)	0.91 ± 0.12 (0.86–0.97)	-0.36	0.706 (0.03)	0.758 (0.02)		
	CON		0.89 ± 0.14 (0.84–0.95)	0.87 ± 0.15 (0.82–0.92)	-2.59	**0.007** (0.15)	**0.006** (0.16)		
L4 vertebra T-score (SD)	MT	-1.67	-1.71 ± 1.37 (-2.18 to -1.24)	-1.73 ± 1.26 (-2.18 to -1.27)	0.78	0.856 (0.01)	0.630 (0.03)	MT vs P: 0.348 (0.53) MT vs T: 1.000 (0.32) MT vs C: 1.000 (0.05) P vs T: 1.000 (0.21) P vs C: 0.523 (0.21) T vs C: 1.000 (0.44)	MT vs P: 0.685 (0.14) MT vs T: 1.000 (0.01) MT vs C: 0.661 (0.12) P vs T: 0.563 (0.16) P vs C: **0.011** (0.16) T vs C: 0.883 (0.26)
	P		-1.21 ± 1.14 (-1.69 to -0.72)	-1.09 ± 1.11 (-1.56 to -0.61)	-9.73	0.124 (0.1)	0.081 (0.12)		
	T		-1.27 ± 1.29 (-1.75 to -0.78)	-1.33 ± 1.19 (-1.80 to -0.85)	4.78	0.426 (0.05)	0.530 (0.04)		
	CON		-1.47 ± 1.33 (-1.93 to -1.00)	-1.66 ± 1.44 (-2.12 to -1.20)	13.40	**0.008** (0.14)	**0.006** (0.14)		

Table D.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total lumbar spine aBMD (g/cm^2)	MT	0.85	0.85 ± 0.12 (0.81–0.89)	0.85 ± 0.12 (0.81–0.90)	0.84	0.140 (0.06)	0.234 (0.05)	MT vs P: 0.374 (0.43)	MT vs P: 1.000 (0.09)
	P		0.89 ± 0.08 (0.84–0.93)	0.90 ± 0.08 (0.86–0.94)	1.56	**0.006** (0.16)	**0.004** (0.17)	MT vs T: 1.000 (0.22)	MT vs T: 1.000 (0)
	T		0.88 ± 0.12 (0.83–0.92)	0.88 ± 0.11 (0.84–0.92)	0.53	0.353 (0.04)	0.257 (0.05)	MT vs C: 1.000 (0.03)	MT vs C: 0.443 (0.1)
	C		0.86 ± 0.11 (0.82–0.91)	0.86 ± 0.12 (0.82–0.90)	-0.72	0.201 (0.05)	0.179 (0.05)	P vs T: 1.000 (0.19)	P vs T: 1.000 (0.09)
								P vs C: 0.429 (0.39)	P vs C: **0.016** (0.2)
								T vs C: 1.000 (0.18)	T vs C: 0.490 (0.1)
Total lumbar spine T-score (SD)	MT	-1.80	-1.77 ± 1.13 (-2.15 to -1.39)	-1.71 ± 1.09 (-2.08 to -1.34)	-3.20	0.221 (0.05)	0.322 (0.04)	MT vs P: 0.348 (0.45)	MT vs P: 0.774 (0.1)
	P		-1.42 ± 0.82 (-1.81 to -1.03)	-1.28 ± 0.80 -(1.67 to -0.90)	-9.77	**0.004** (0.17)	**0.002** (0.18)	MT vs T: 1.000 (0.21)	MT vs T: 1.000 (0.01)
	T		-1.51 ± 1.12 (-1.90 to -1.12)	-1.48 ± 1.03 (-1.87 to -1.10)	-1.65	0.601 (0.02)	0.518 (0.03)	MT vs C: 1.000 (0.05)	MT vs C: 0.894 (0.08)
	C		-1.61 ± 1.08 (-1.99 to -1.23)	-1.65 ± 1.14 (-2.02 to -1.28)	2.90	0.313 (0.04)	0.292 (0.04)	P vs T: 1.000 (0.22)	P vs T: 0.520 (0.12)
								P vs C: 0.523 (0.22)	P vs C: **0.022** (0.12)
								T vs C: 1.000 (0.37)	T vs C: 1.000 (0.2)
L2-L4 lumbar spine segment aBMD (g/cm^2)	MT	0.87	0.86 ± 0.13 (0.82–0.91)	0.87 ± 0.12 (0.82–0.91)	0.70	0.314 (0.05)	0.456 (0.04)	MT vs P: 1.000 (0.36)	MT vs P: 1.000 (0.04)
	P		0.90 ± 0.09 (0.86–0.95)	0.91 ± 0.09 (0.86–0.95)	0.82	0.239 (0.08)	0.184 (0.1)	MT vs T: 1.000 (0.23)	MT vs T: 1.000 (0.01)
	T		0.89 ± 0.13 (0.85–0.94)	0.90 ± 0.11 (0.85–0.94)	0.30	0.668 (0.02)	0.547 (0.03)	MT vs C: 1.000(0.04)	MT vs C: 0.915 (0.09)
	C		0.88 ± 0.12 (0.84–0.93)	0.87 ± 0.13 (0.83–0.92)	-0.84	0.218 (0.06)	0.200 (0.05)	P vs T: 1.000 (0.12)	P vs T: 1.000 (0.05)
								P vs C: 1.000 (0.3)	P vs C: 0.395 (0.14)
								T vs C: 1.000 (0.18)	T vs C: 1.000 (0.09)
L2-L4 lumbar spine segment T-score (SD)	MT	-1.76	-1.93 ± 1.18 (-2.34 to -1.52)	-1.86 ± 1.16 (-2.26 to -1.46)	-3.79	0.168 (0.06)	0.255 (0.05)	MT vs P: 0.676 (0.44)	MT vs P: 1.000 (0.01)
	P		-1.46 ± 0.91 (-1.88 to -1.03)	-1.39 ± 0.94 (-1.81 to -0.98)	-4.23	0.261 (0.07)	0.173 (0.08)	MT vs T: 1.000 (0.22)	MT vs T: 1.000 (0.02)
	T		-1.65 ± 1.22 (-2.07 to -1.23)	-1.61 ± 1.05 (-2.03 to -1.20)	-2.16	0.515 (0.03)	0.468 (0.03)	MT vs C: 1.000 (0.03)	MT vs C: 0.449 (0.11)
	C		-1.76 ± 1.15 (-2.16 to -1.35)	-1.83 ± 1.22 (-2.23 to -1.43)	3.98	0.188 (0.06)	0.166 (0.06)	P vs T: 1.000 (0.22)	P vs T: 1.000 (0.03)
								P vs C: 0.843 (0.22)	P vs C: 0.319 (0.13)
								T vs C: 1.000 (0.39)	T vs C: 0.837 (0.1)

Note. Data are expressed as mean ± SD and 95% CIs . Sample size of each group: MT (n = 30), P (n = 28), T (n = 28), C (n = 30).MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; aBMD: areal bone mineral density; ES: effect size; Δ%: percentage of change;; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

Table D.2. *Intervention effects on BMD at proximal femur from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Femoral neck aBMD (g/cm^2)	MT	0.68	0.69 ± 0.07 (0.65–0.72)	0.69 ± 0.07 (0.66–0.72)	0.31	0.700 (0.03)	0.576 (0.04)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.03)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.02)
	P		0.68 ± 0.06 (0.65–0.71)	0.68 ± 0.06 (0.65–0.72)	1.06	0.214 (0.11)	0.200 (0.11)	MT vs C: 1.000 (0.25)	MT vs C: 1.000 (0.07)
	T		0.68 ± 0.09 (0.65–0.71)	0.69 ± 0.09 (0.65–0.72)	0.78	0.358 (0.06)	0.406 (0.05)	P vs T: 1.000 (0)	P vs T: 1.000 (0.02)
	C		0.67 ± 0.10 (0.64–0.70)	0.67 ± 0.10 (0.64–0.70)	-0.36	0.669 (0.02)	0.593 (0.03)	P vs C: 1.000 (0.22) T vs C: 1.000 (0.2)	P vs C: 1.000 (0.12) T vs C: 1.000 (0.08)
Femoral neck T-score (SD)	MT	-1.48	-1.42 ± 0.69 (-1.70 to -1.14)	-1.40 ± 0.65 (-1.68 to -1.12)	-1.64	0.609 (0.03)	0.464 (0.05)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.05)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0)
	P		-1.48 ± 0.55 (-1.77 to -1.19)	-1.44 ± 0.62 (-1.73 to -1.15)	-2.65	0.406 (0.07)	0.370 (0.07)	MT vs C: 1.000 (0.2)	MT vs C: 1.000 (0.05)
	T		-1.47 ± 0.81 (-1.76 to -1.18)	-1.43 ± 0.77 (-1.73 to -1.14)	-2.66	0.406 (0.05)	0.532 (0.04)	P vs T: 1.000 (0.01) P vs C: 1.000 (0.01)	P vs T: 1.000 (0.02) P vs C: 1.000 (0.02)
	C		-1.56 ± 0.97 (-1.84 to -1.28)	-1.57 ± 0.99 (-1.85 to -1.29)	0.43	0.884 (0.01)	0.835 (0.01)	T vs C: 1.000 (0.16)	T vs C: 1.000 (0.06)
Trochanter aBMD (g/cm^2)	MT	0.66	0.65 ± 0.10 (0.61–0.68)	0.65 ± 0.10 (0.62–0.69)	0.38	0.457 (0.02)	0.414 (0.03)	MT vs P: 1.000 (0.17) MT vs T: 1.000 (0.11)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.02)
	P		0.67 ± 0.09 (0.63–0.70)	0.67 ± 0.08 (0.63–0.71)	0.14	0.779 (0.01)	0.768 (0.01)	MT vs C: 1.000 (0.07)	MT vs C: 0.635 (0.08)
	T		0.64 ± 0.09 (0.60–0.68)	0.64 ± 0.09 (0.60–0.68)	0.11	0.835 (0.01)	0.921 (0.01)	P vs T: 1.000 (0.32) P vs C: 1.000 (0.1)	P vs T: 1.000 (0) P vs C: 1.000 (0.06)
	C		0.66 ± 0.09 (0.63–0.70)	0.66 ± 0.10 (0.62–0.70)	-0.74	0.136 (0.05)	0.140 (0.05)	T vs C: 1.000 (0.2)	T vs C: 1.000 (0.06)
Trochanter T-score (SD)	MT	-0.42	-0.48 ± 1.04 (-0.82 to -0.13)	-0.47 ± 1.04 (-0.82 to -0.12)	-1.39	0.853 (0.01)	0.804 (0.01)	MT vs P: 1.000 (0.18) MT vs T: 1.000 (0.11)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.01)
	P		-0.29 ± 0.91 (-0.65 to 0.06)	-0.29 ± 0.90 (-0.65 to 0.06)	0.00	1.000 (0)	0.923 (0)	MT vs C: 1.000 (0.11)	MT vs C: 1.000 (0.03)
	T		-0.58 ± 0.89 (-0.94 to -0.22)	-0.58 ± 0.87 (-0.94 to -0.22)	-0.61	0.924 (0)	0.899 (0.01)	P vs T: 1.000 (0.32) P vs C: 1.000 (0.32)	P vs T: 1.000 (0.01) P vs C: 1.000 (0.01)
	C		-0.34 ± 0.96 (-0.69 to 0.00)	-0.36 ± 1.00 (-0.71 to -0.01)	5.83	0.579 (0.02)	0.619 (0.02)	T vs C: 1.000 (0.07)	T vs C: 1.000 (0.02)

Table D.2. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Intertro-chanteric area aBMD (g/cm^2)	MT	0.98	0.99 ± 0.14 (0.94–1.03)	0.98 ± 0.13 (0.94–1.03)	-0.23	0.696 (0.02)	0.731 (0.01)	MT vs P: 1.000 (0.17) MT vs T: 1.000 (0.18) MT vs C: 1.000 (0.03) P vs T: 1.000 (0.39) P vs C: 1.000 (0.12) T vs C: 1.000 (0.2)	MT vs P: 0.147 (0.15) MT vs T: 1.000 (0.04) MT vs C: 1.000 (0.05) P vs T: 0.566 (0.13) P vs C: **0.011** (0.19) T vs C: 0.917 (0.09)
	P		0.99 ± 0.10 (0.94–1.04)	1.01 ± 0.12 (0.96–1.06)	1.70	**0.006** (0.15)	**0.005** (0.16)		
	T		0.96 ± 0.11 (0.91–1.01)	0.96 ± 0.10 (0.91–1.01)	0.36	0.569 (0.03)	0.670 (0.03)		
	C		1.00 ± 0.15 (0.95–1.05)	0.99 ± 0.16 (0.94–1.04)	-0.99	0.089 (0.06)	0.103 (0.06)		
Intertro-chanteric area T-score (SD)	MT	-0.72	-0.71 ± 0.91 (-1.01 to -0.40)	-0.69 ± 0.87 (-0.99 to -0.39)	-2.35	0.586 (0.02)	0.549 (0.02)	MT vs P: 1.000 (0.11) MT vs T: 1.000 (0.24) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.41) P vs C: 1.000 (0.41) T vs C: 1.000 (0.08)	MT vs P: 0.766 (0.08) MT vs T: 1.000 (0.03) MT vs C: 0.833 (0.07) P vs T: 0.274 (0.14) P vs C: **0.020** (0.14) T vs C: 1.000 (0.15)
	P		-0.68 ± 0.69 (-1.00 to -0.36)	-0.60 ± 0.67 (-0.91 to -0.29)	-11.98	**0.011** (0.12)	**0.008** (0.12)		
	T		-0.88 ± 0.73 (-1.20 to -0.56)	-0.87 ± 0.65 (-1.18 to -0.56)	-0.40	0.910 (0.01)	0.870 (0.01)		
	C		-0.62 ± 1.01 (-0.92 to -0.31)	-0.67 ± 1.03 (-0.97 to -0.37)	8.06	0.104 (0.05)	0.135 (0.05)		
Ward's triangle aBMD (g/cm^2)	MT	0.50	0.50 ± 0.09 (0.45–0.54)	0.51 ± 0.09 (0.47–0.56)	3.41	0.068 (0.18)	0.062 (0.18)	MT vs P: 1.000 (0.21) MT vs T: 1.000 (0.29) MT vs C: 1.000 (0.08) P vs T: 1.000 (0.09) P vs C: 1.000 (0.24) T vs C: 1.000 (0.31)	MT vs P: 1.000 (0.13) MT vs T: 1.000 (0.03) MT vs C: 1.000 (0.07) P vs T: 1.000 (0.09) P vs C: 0.564 (0.17) T vs C: 1.000 (0.09)
	P		0.50 ± 0.09 (0.46–0.55)	0.53 ± 0.10 (0.49–0.58)	5.93	**0.002** (0.3)	**0.002** (0.3)		
	T		0.52 ± 0.12 (0.48–0.57)	0.54 ± 0.12 (0.50–0.59)	3.80	**0.038** (0.16)	**0.041** (0.16)		
	C		0.49 ± 0.14 (0.45–0.54)	0.50 ± 0.14 (0.46–0.55)	1.70	0.361 (0.06)	0.385 (0.06)		
Ward's triangle T-score (SD)	MT	-1.89	-2.00 ± 0.76 (-2.39 to -1.62)	-1.83 ± 0.85 (-2.25 to -1.41)	-8.47	0.061 (0.21)	0.063 (0.21)	MT vs P: 1.000 (0.23) MT vs T: 1.000 (0.24) MT vs C: 1.000 (0.02) P vs T: 1.000 (0.03) P vs C: 1.000 (0.03) T vs C: 1.000 (0.21)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0) MT vs C: 1.000 (0.01) P vs T: 1.000 (0.03) P vs C: 1.000 (0.03) T vs C: 1.000 (0.05)
	P		-1.81 ± 1.11 (-2.21 to -1.41)	-1.60 ± 1.19 (-2.03 to -1.16)	-11.81	**0.023** (0.19)	**0.024** (0.19)		
	T		-1.74 ± 1.08 (-2.14 to -1.34)	-1.56 ± 1.34 (-2.00 to -1.13)	-10.22	0.058 (0.15)	0.066 (0.14)		
	C		-2.01 ± 1.23 (-2.39 to -1.62)	-1.85 ± 1.22 (-2.27 to -1.43)	-7.79	0.084 (0.13)	0.089 (0.13)		

Table D.2. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total hip aBMD (g/cm^2)	MT	0.83	0.83 ± 0.11 (0.79–0.87)	0.84 ± 0.11 (0.80–0.87)	0.43	0.385 (0.03)	0.339 (0.03)	MT vs P: 1.000 (0.17) MT vs T: 1.000 (0.17)	MT vs P: 1.000 (0.07) MT vs T: 1.000 (0)
	P		0.84 ± 0.09 (0.80–0.88)	0.85 ± 0.08 (0.81–0.89)	1.27	**0.014 (0.12)**	**0.010** (0.12)	MT vs C: 1.000 (0.06)	MT vs C: 0.604 (0.08)
	T		0.81 ± 0.09 (0.77–0.85)	0.82 ± 0.08 (0.78–0.86)	0.69	0.193 (0.06)	0.329 (0.05)	P vs T: 1.000 (0.4)	P vs T: 1.000 (0.08)
	C		0.85 ± 0.11 (0.81–0.89)	0.84 ± 0.12 (0.80–0.88)	-0.73	0.134 (0.05)	0.170 (0.05)	P vs C: 1.000 (0.1) T vs C: 1.000 (0.22)	P vs C: **0.031** (0.16) T vs C: 0.604 (0.09)
Total hip T-score (SD)	MT	-0.84	-0.85 ± 0.95 (-1.17 to -0.54)	-0.81 ± 0.86 (-1.11 to -0.51)	-5.06	0.202 (0.05)	0.194 (0.05)	MT vs P: 1.000 (0.14) MT vs T: 1.000 (0.21)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.02)
	P		-0.77 ± 0.74 (-1.10 to -0.44)	-0.70 ± 0.68 (-1.01 to -0.38)	-9.22	**0.043** (0.1)	**0.028** (0.1)	MT vs C: 1.000 (0.07)	MT vs C: 1.000 (0.06)
	T		-1.01 ± 0.76 (-1.34 to -0.69)	-0.97 ± 0.72 (-1.29 to -0.66)	-3.86	0.263 (0.05)	0.411 (0.04)	P vs T: 1.000 (0.39) P vs C: 1.000 (0.39)	P vs T: 1.000 (0.07) P vs C: 0.370 (0.07)
	C		-0.73 ± 0.97 (-1.04 to -0.41)	-0.75 ± 1.02 (-1.05 to -0.44)	2.74	0.555 (0.02)	0.687 (0.01)	T vs C: 1.000 (0.05)	T vs C: 1.000 (0.1)
10-year probability of a major osteoporotic fracture (%)	MT	0.11	0.12 ± 0.05 (0.11–0.14)	0.11 ± 0.03 (0.10–0.12)	-11.02	**0.003** (0.31)	**0.012** (0.18)	MT vs P: 0.274 (0.47) MT vs T: 0.098 (0.53)	MT vs P: 0.260 (0.28) MT vs T: 0.654 (0.2)
	P		0.11 ± 0.04 (0.10–0.13)	0.09 ± 0.02 (0.08–0.10)	-15.94	**0.000** (0.48)	**0.000** (0.44)	MT vs C: 1.000 (0.3)	MT vs C: 1.000 (0.13)
	T		0.10 ± 0.03 (0.09–0.12)	0.09 ± 0.02 (0.08–0.10)	-12.21	**0.007** (0.38)	**0.000** (0.43)	P vs T: 1.000 (0.12)	P vs T: 1.000 (0.07)
	C		0.10 ± 0.01 (0.08–0.11)	0.10 ± 0.01 (0.09–0.11)	0.71	0.873 (0.04)	0.211 (0.22)	P vs C: 1.000 (0.29) T vs C: 1.000 (0.39)	P vs C: **0.023** (0.62) T vs C: 0.074 (0.46)
10-year probability of a hip fracture (%)	MT	0.01	0.02 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.01–0.02)	-14.46	0.051 (0.36)	0.052 (0.22)	MT vs P: 1.000 (0.17) MT vs T: 0.126 (0.74)	MT vs P: 1.000 (0.1) MT vs T: 1.000 (0.27)
	P		0.02 ± 0.02 (0.0–0.02)	0.01 ± 0.01 (0.01–0.02)	-24.00	**0.002** (0.31)	**0.001** (0.17)	MT vs C: 1.000 (0.2)	MT vs C: 1.000 (0.12)
	T		0.01 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.01–0.01)	-16.48	0.119 (0.39)	**0.000** (0.6)	P vs T: 0.725 (0.4) P vs C: 1.000 (0.4)	P vs T: 1.000 (0.11) P vs C: 0.917 (0.11)
	C		0.01 ± 0.00 (0.01–0.02)	0.01 ± 0.00 (0.01–0.02)	-3.04	0.740 (0.06)	0.138 (0.11)	T vs C: 0.649 (0.01)	T vs C: 0.658 (0.19)

Note. Data are expressed as mean ± SD and 95% CIs. Sample size of each group: MT (n = 30), P (n = 28), T (n = 28), C (n = 30). MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; aBMD: areal bone mineral density; ES: effect size; Δ%: percentage of change; SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates are baseline values of dependent variables and age. Value of age as a covariate = 67.92.

Table D.3. *Intervention effects on bone biomarkers from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
OC (ng/mL)	MT	16.98	15.73 ± 5.07 (14.10–17.35)	19.25 ± 5.22 (17.51–20.98)	22.38	**0.000** (0.68)	**0.000** (0.66)	MT vs P: 0.177 (0.52)	MT vs P: 0.060 (0.36)
	P		16.61 ± 3.04 (14.93–18.29)	21.65 ± 3.82 (19.85–23.45)	30.35	**0.000** (1.46)	**0.000** (1.45)	MT vs C: 0.693 (0.29)	MT vs C: **0.000** (0.78)
	C		18.57 ± 4.92 (16.94–20.19)	17.76 ± 5.11 (16.02–19.49)	-4.36	0.096 (0.16)	0.179 (0.13)	P vs C: **0.008** (0.86)	P vs C: **0.000** (1.25)
β-CTx (ng/L)	MT	0.36	0.34 ± 0.15 (0.29–0.40)	0.30 ± 0.13 (0.26–0.35)	-11.87	**0.001** (0.28)	**0.000** (0.3)	MT vs P: 1.000 (0.04)	MT vs P: 1.000 (0.02)
	P		0.35 ± 0.11 (0.30–0.40)	0.31 ± 0.10 (0.26–0.36)	-11.87	**0.002** (0.38)	**0.000** (0.43)	MT vs C: **0.009** (0.74)	MT vs C: **0.001** (0.44)
	C		0.39 ± 0.14 (0.34–0.44)	0.40 ± 0.13 (0.36–0.45)	2.89	0.363 (0.08)	0.113 (0.12)	P vs C: **0.017** (0.77)	P vs C: **0.000** (0.51)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (n = 30), P (n = 28), C (n = 30). MT: multi-component training group; P: power strength training group; C: control group; OC: osteocalcin; β-CTx: beta C-terminal cross-linked telopeptide of type I collagen (β-CrossLaps); CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 68.39.

SUPPLEMENTARY MATERIAL E. PPA RESULTS ON BODY COMPOSITION OF PROJECT ONE

Table E. *Intervention effects on body composition from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total body mass (Kg)	M		67.38 ± 10.72 (63.46–71.31)	67.29 ± 10.50 (63.37–71.20)	-0.14	0.699 (0.01)	0.751 (0.01)	M vs HI: 0.570 (0.34)	M vs HI: 0.867 (0.04)
	HI	65.27	63.56 ± 9.80 (60.20–66.93)	63.86 ± 9.92 (60.50–67.22)	0.47	0.165 (0.03)	0.196(0.03)	M vs C: 1.000 (0.14)	M vs C: 0.737 (0.05)
	C		65.55 ± 8.61 (60.92–70.18)	65.93 ± 8.58 (61.31–70.54)	0.57	0.205 (0.04)	0.211 (0.04)	HI vs C: 1.000 (0.22)	HI vs C: 1.000 (0.01)
Total fat mass (Kg)	M		30.20 ± 7.16 (27.73–32.67)	28.55 ± 6.63 (26.18–30.93)	-5.45	**0.000** (0.24)	**0.000** (0.23)	M vs HI: 0.855 (0.28)	M vs HI: 0.057 (0.1)
	HI	28.68	27.81 ± 5.71 (25.69–29.93)	26.86 ± 5.50 (24.83–28.90)	-3.41	**0.000** (0.17)	**0.000** (0.17)	M vs C: 1.000 (0)	M vs C: **0.000** (0.3)
	C		28.23 ± 5.56 (25.32–31.14)	28.58 ± 5.77 (25.78–31.38)	1.24	0.124 (0.06)	0.142 (0.06)	HI vs C: 0.976 (0.31)	HI vs C: **0.000** (0.23)
Total fat-free massmass (Kg)	M		35.40± 4.40 (33.76–37.04)	36.68 ± 4.93 (34.96–38.40)	3.61	**0.000** (0.27)	**0.000** (0.29)	M vs HI: 1.000 (0.08)	M vs HI: **0.045** (0.14)
	HI	35.79	36.20 ± 4.19 (34.80–37.61)	37.02 ± 4.18 (35.55–38.50)	2.27	**0.000** (0.2)	**0.000** (0.17)	M vs C: 1.000 (0.29)	M vs C: **0.000** (0.33)
	C		35.54 ± 3.45 (33.61–37.47)	35.41 ± 3.52 (33.38–37.43)	-0.37	0.578 (0.04)	0.704 (0.02)	HI vs C: 0.604 (0.41)	HI vs C: **0.016** (0.2)
Total body fat percentage (%)	M		44.39 ± 4.45 (42.67–46.12)	42.92 ± 4.26 (41.16–44.68)	-3.32	**0.000** (0.34)	**0.000** (0.35)	M vs HI: 0.578 (0.33)	M vs HI: 0.226 (0.14)
	HI	43.11	42.35 ± 4.57 (40.87–43.83)	41.39 ± 4.81 (39.88–42.90)	-2.28	**0.000** (0.21)	**0.000** (0.19)	M vs C: 1.000 (0.01)	M vs C: **0.000** (0.42)
	C		42.75 ± 3.59 (40.72–44.78)	42.96 ± 3.78 (40.89–45.04)	0.49	0.495 (0.06)	0.580 (0.05)	HI vs C: 0.674 (0.35)	HI vs C: **0.020** (0.24)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 25), HI (*n* = 34), C (*n* = 18). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

SUPPLEMENTARY MATERIAL F. PPA RESULTS ON ANTHROPOMETRY AND BODY COMPOSITION OF PROJECT TWO

Table F.1. *Intervention effects on anthropometric measurements from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
WC (cm)	MT	98.81	98.50 ± 11.82 (94.60–102.40)	95.46 ± 10.99 (91.73–99.20)	-3.08	**0.000** (0.27)	**0.000** (0.27)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0)	MT vs P: 1.000 (0.03) MT vs T: 0.373 (0.13)
	P		97.71 ± 11.34 (93.67–101.75)	95.03 ± 10.60 (91.17–98.90)	-2.74	**0.000** (0.24)	**0.000** (0.25)	MT vs C: 0.080 (0.63)	MT vs C: **0.000** (0.41)
	T		97.07 ± 8.43 (93.03–101.10)	95.51 ± 9.38 (91.65–99.38)	-1.60	**0.005** (0.17)	**0.002** (0.19)	P vs T: 1.000 (0.05)	P vs T: 0.878 (0.11)
	C		100.93 ± 11.09 (97.03–104.83)	102.16 ± 10.19 (98.43–105.90)	1.22	**0.019** (0.12)	**0.006** (0.12)	P vs C: 0.059 (0.69) T vs C: 0.095 (0.68)	P vs C: **0.000** (0.11) T vs C: **0.000** (0.39)
HC (cm)	MT	105.87	106.50 ± 8.79 (103.53–109.46)	103.66 ± 8.22 (100.80–106.52)	-2.66	**0.000** (0.33)	**0.000** (0.33)	MT vs P: 1.000 (0.19) MT vs T: 1.000 (0.09)	MT vs P: 1.000 (0.03) MT vs T: 0.071 (0.19)
	P		104.71 ± 7.76 (101.64–107.78)	102.21 ± 7.11 (99.25–105.17)	-2.39	**0.000** (0.34)	**0.000** (0.35)	MT vs C: 0.536 (0.44)	MT vs C: **0.000** (0.47)
	T		105.57 ± 7.71 (102.50–108.63)	104.39 ± 8.36 (101.43–107.35)	-1.12	**0.010** (0.15)	**0.007** (0.15)	P vs T: 1.000 (0.28)	P vs T: 0.178 (0.18)
	C		106.20 ± 8.35 (103.23–109.16)	107.16 ± 7.84 (104.30–110.02)	0.91	**0.028** (0.12)	**0.011** (0.13)	P vs C: 0.113 (0.28) T vs C: 1.000 (0.66)	P vs C: **0.000** (0.48) T vs C: **0.002** (0.28)

Table F.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
WHR	MT	0.933	0.924 ± 0.07 (0.898–0.951)	0.920 ± 0.07 (0.894–0.947)	-0.43	0.416 (0.05)	0.803 (0.05)	MT vs P: 1.000 (0.12)	MT vs P: 1.000 (0.01)
	P		0.932 ± 0.08 (0.905–0.960)	0.929 ± 0.08 (0.903–0.957)	-0.31	0.566 (0.04)	0.867 (0.04)	MT vs T: 1.000 (0.06)	MT vs T: 1.000 (0.03)
	T		0.920 ± 0.06 (0.893–0.949)	0.916 ± 0.07 (0.889–0.943)	-0.52	0.345 (0.07)	0.740 (0.09)	MT vs C: 0.395 (0.52)	MT vs C: 1.000 (0.16)
	C		0.953 ± 0.06 (0.927–0.979)	0.955 ± 0.05 (0.929–0.981)	0.21	0.673 (0.03)	0.110 (0.19)	P vs T: 1.000 (0.18)	P vs T: 1.000 (0.04)
								P vs C: 1.000 (0.35)	P vs C: 1.000 (0.16)
								T vs C: 0.249 (0.6)	T vs C: 1.000 (0.14)
WHtR	MT	0.635	0.618 ± 0.06 (0.592–0.646)	0.599 ± 0.06 (0.574–0.626)	-3.07	**0.000** (0.29)	**0.000** (0.31)	MT vs P: 1.000 (0.36)	MT vs P: 1.000 (0.04)
	P		0.642 ± 0.08 (0.615–0.670)	0.625 ± 0.07 (0.598–0.652)	-2.75	**0.000** (0.22)	**0.000** (0.21)	MT vs T: 1.000 (0.34)	MT vs T: 0.235 (0.15)
	T		0.632 ± 0.06 (0.604–0.660)	0.621 ± 0.06 (0.595–0.649)	-1.60	**0.004** (0.16)	**0.003** (0.15)	MT vs C: **0.018** (0.79)	MT vs C: **0.000** (0.41)
	C		0.648 ± 0.08 (0.622–0.674)	0.655 ± 0.07 (0.630–0.681)	1.15	**0.023** (0.09)	**0.010** (0.11)	P vs T: 1.000 (0.04)	P vs T: 0.900 (0.1)
								P vs C: 0.625 (0.04)	P vs C: **0.000** (0.1)
								T vs C: 0.440 (0.39)	T vs C: **0.001** (0.34)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (n = 30), P (n = 28), T (n = 28), C (n = 30). MT: multi-component training group; P: power strength training group; T: traditional high-intensity resistance training group; C: control group; BMD: WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio. CIs: confidence intervals; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92

Table F.2. *Intervention effects on body composition from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Total body mass (Kg)	MT	68.86	71.16 ± 13.33 (67.26–75.07)	70.71 ± 13.30 (66.81–74.61)	-0.64	**0.025** (0.03)	**0.029** (0.03)	MT vs P: 0.464 (0.43)	MT vs P: 1.000 (0)
	P		66.12 ± 9.96 (62.08–70.16)	65.65 ± 10.02 (61.62–69.69)	-0.71	**0.027** (0.05)	**0.022** (0.05)	MT vs T: 1.000 (0.28)	MT vs T: 0.680 (0.04)
	T		67.32 ± 10.17 (63.27–71.36)	67.33 ± 10.18 (63.30–71.37)	0.03	0.930 (0)	0.914 (0)	MT vs C: 1.000 (0.02)	MT vs C: **0.038** (0.07)
	C		70.56 ± 9.15 (66.66–74.47)	70.90 ± 9.04 (67.00–74.80)	0.48	0.097 (0.04)	0.089 (0.04)	P vs T: 1.000 (0.17)	P vs T: 0.532 (0.05)
								P vs C: 0.400 (0.55)	P vs C: 0.032 (0.09)
								T vs C: 1.000 (0.37)	T vs C: 1.000 (0.03)
Total fat mass (Kg)	MT	30.07	31.39 ± 9.03 (28.74–34.04)	29.93 ± 8.94 (27.31–32.55)	-4.66	**0.000** (0.16)	**0.000** (4.53)	MT vs P: 1.000 (0.32)	MT vs P: 1.000 (0.06)
	P		28.38 ± 6.37 (25.63–31.12)	27.43 ± 6.43 (24.71–30.14)	-3.35	**0.000** (0.15)	**0.000** (6.39)	MT vs T: 1.000 (0.16)	MT vs T: 0.870 (0.06)
	T		29.53 ± 7.26 (26.79–32.28)	28.63 ± 7.08 (25.92–31.35)	-3.05	**0.000** (0.13)	**0.000** (5.81)	MT vs C: 1.000 (0.21)	MT vs C: **0.000** (0.28)
	C		30.83 ± 6.22 (28.18–33.48)	31.55 ± 6.14 (28.92–34.17)	2.31	**0.002** (0.12)	**0.000** (7.08)	P vs T: 1.000 (0.18)	P vs T: 1.000 (0.01)
								P vs C: 0.196 (0.18)	P vs C: **0.000** (0.01)
								T vs C: 0.773 (0.66)	T vs C: **0.000** (0.27)
Total fat-free massmass (Kg)	MT	36.98	37.912 ± 4.85 (36.37–39.45)	38.55 ± 5.06 (36.96–40.13)	1.69	**0.000** (0.13)	**0.001** (0.12)	MT vs P: 0.293 (0.5)	MT vs P: 1.000 (0.07)
	P		35.96 ± 3.96 (34.37–37.55)	36.25 ± 4.10 (34.61–37.89)	0.80	0.122 (0.07)	0.118 (0.07)	MT vs T: 0.574 (0.4)	MT vs T: 1.000 (0.03)
	T		35.96 ± 4.12 (34.37–37.56)	36.66 ± 4.39 (35.02–38.30)	1.93	**0.001** (0.16)	**0.000** (0.17)	MT vs C: 1.000 (0.26)	MT vs C: **0.000** (0.26)
	C		37.95 ± 3.97 (36.41–39.48)	37.39± 3.85 (35.80–38.97)	-1.47	**0.002** (0.14)	**0.001** (0.15)	P vs T: 1.000 (0.1)	P vs T: 0.459 (0.11)
								P vs C: 1.000 (0.29)	P vs C: **0.006** (0.21)
								T vs C: 1.000 (0.18)	T vs C: **0.000** (0.32)
Total body fat percentage (%)	MT	43.07	43.09 ± 4.45 (41.41–44.77)	40.90 ± 4.57 (39.20–42.59)	-5.09	**0.000** (0.49)	**0.000** (0.48)	MT vs P: 1.000 (0.08)	MT vs P: 1.000 (0.06)
	P		42.46 ± 4.15 (40.72–44.20)	40.55 ± 4.42 (38.80–42.31)	-4.49	**0.000** (0.44)	**0.000** (0.45)	MT vs T: 1.000 (0.23)	MT vs T: 0.082 (0.17)
	T		43.35 ± 5.59 (41.61–45.09)	42.05 ± 5.55 (40.29–43.80)	-3.00	**0.000** (0.23)	**0.000** (0.24)	MT vs C: **0.036** (0.78)	MT vs C: **0.000** (0.71)
	C		43.36 ± 4.27 (41.68–45.04)	44.28 ± 4.12 (42.59–45.98)	2.13	**0.000** (0.22)	**0.000** (0.22)	P vs T: 1.000 (0.3)	P vs T: 0.530 (0.12)
								P vs C: **0.018** (0.3)	P vs C: **0.000** (0.12)
								T vs C: 0.435 (0.87)	T vs C: **0.000** (0.67)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30).MT: multi-component training group; P: power strength training group; T: high-intensity traditional resistance training group; C: control group; CIs: confidence intervals; ES: effect size; Δ%: percentage of change; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

SUPPLEMENTARY MATERIAL G. PPA RESULTS ON MUSCLE STRENGTH OF PROJECT ONE

Table G.1. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Hip abd. 180°/s (N·m)	M	35.72	41.55 ± 28.69 (33.99–49.11)	48.88 ± 13.01 (43.92–53.83)	17.62	**0.041** (0.33)	**0.017** (0.38)	M vs HI: **0.026** (0.66)	M vs HI: 0.863 (0.22)
	HI		26.37 ± 10.86 (19.89–32.86)	40.06 ± 13.51 (35.82–44.31)	51.89	**0.000** (1.12)	**0.000** (0.95)	M vs C: **0.007** (1.05)	M vs C: **0.000** (1.15)
	C		39.26 ± 13.25 (30.35–48.17)	36.83 ± 8.85 (30.99–42.66)	-6.18	0.560 (0.22)	0.991 (0)	HI vs C: 1.000 (0.27)	HI vs C: **0.002** (0.85)
Hip add. 180°/s (N·m)	M	45.67	50.29 ± 20.75 (42.74–57.84)	55.47 ± 15.86 (47.95–62.99)	10.30	0.094 (0.28)	0.092 (0.28)	M vs HI: 1.000 (0.11)	M vs HI: 1.000 (0.04)
	HI		45.87 ± 13.85 (39.39–52.34)	53.37 ± 20.05 (46.92–59.83)	16.36	**0.005** (0.44)	**0.002** (0.48)	M vs C: **0.025** (0.89)	M vs C: **0.018** (0.65)
	C		40.87 ± 24.13 (31.97–49.77)	39.62 ± 20.37 (30.76–48.49)	-3.06	0.729 (0.06)	0.451 (0.12)	HI vs C: **0.044** (0.68)	HI vs C: **0.023** (0.54)
Hip abd. 60°/s (N·m)	M	49.30	55.89 ± 33.07 (45.85–65.94)	73.90 ± 25.21 (65.10–82.71)	32.22	**0.000** (0.61)	**0.000** (0.67)	M vs HI: **0.024** (0.68)	M vs HI: 1.000 (0.01)
	HI		37.24 ± 19.91 (28.63–45.85)	58.06 ± 21.99 (50.51–65.62)	55.91	**0.000** (0.99)	**0.000** (0.88)	M vs C: **0.003** (1.06)	M vs C: **0.000** (0.93)
	C		54.79 ± 21.22 (42.95–66.63)	50.41 ± 17.00 (40.03–60.79)	-7.99	0.261 (0.23)	0.484 (0.12)	HI vs C: 0.716 (0.37)	HI vs C: **0.000** (1.01)
Hip add. 60°/s (N·m)	M	41.53	41.54 ± 12.12 (35.80–47.27)	49.32 ± 10.68 (43.23–55.42)	18.75	**0.001** (0.68)	**0.002** (0.62)	M vs HI: 1.000 (0.13)	M vs HI: 0.613 (0.27)
	HI		40.91 ± 12.12 (35.99–45.83)	51.17 ± 16.10 (45.94–56.39)	25.07	**0.000** (0.72)	**0.000** (0.76)	M vs C: 0.104 (0.7)	M vs C: **0.007** (0.72)
	C		42.67 ± 20.19 (35.92–49.43)	39.16 ± 18.77 (31.98–46.34)	-8.23	0.195 (0.18)	0.174 (0.18)	HI vs C: **0.026** (0.7)	HI vs C: **0.000** (1.03)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 25), HI (*n* = 34), C (*n* = 18). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; abd: abduction; add: adduction; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table G.2. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Knee ext. 180°/s (N·m)	M	41.21	45.23 ± 11.89 (40.26–50.20)	57.72 ± 12.14 (52.24–63.21)	27.63	**0.000** (1.04)	**0.000** (1.08)	M vs HI: 1.000 (0.25) M vs C: 0.056 (0.73) HI vs C: 0.261 (0.48)	M vs HI: 0.144 (0.43) M vs C: **0.001** (0.8) HI vs C: **0.000** (1.22)
	HI		34.47 ± 11.76 (30.21–38.73)	54.46 ± 13.49 (49.76–59.17)	57.99	**0.000** (1.58)	**0.000** (1.47)		
	C		48.36 ± 14.43 (42.51–54.22)	47.50 ± 16.23 (41.03–53.97)	-1.78	0.725 (0.06)	0.682 (0.06)		
Knee flex. 180°/s (N·m)	M	35.84	35.53 ± 9.40 (31.78–39.28)	42.39 ± 11.12 (38.24–46.54)	19.29	**0.000** (0.67)	**0.000** (0.63)	M vs HI: 0.666 (0.33) M vs C: **0.011** (0.88) HI vs C: **0.000** (1.3)	M vs HI: 0.888 (0.24) M vs C:**0.014** (0.72) HI vs C: **0.001** (1.03)
	HI		37.70 ± 9.62 (34.48–40.91)	45.77 ± 9.75 (42.21–49.33)	21.42	**0.000** (0.83)	**0.000** (0.93)		
	C		32.78 ± 9.01 (28.36–37.20)	32.72 ± 10.64 (27.83–37.62)	-0.17	0.980 (0.01)	0.512 (0.14)		
Knee ext. 60°/s (N·m)	M	71.06	74.83 ± 16.95 (66.27–83.39)	87.84 ± 18.15 (79.02–96.65)	17.38	**0.000** (0.74)	**0.000** (0.76)	M vs HI: 1.000 (0.11) M vs C: 0.092 (0.68) HI vs C: 0.154 (0.54)	M vs HI: 0.262 (0.28) M vs C: **0.000** (0.7) HI vs C: **0.000** (0.89)
	HI		65.94 ± 22.16 (58.60–73.28)	85.55 ± 22.26 (77.99–93.10)	29.73	**0.000** (0.88)	**0.000** (0.86)		
	C		75.51 ± 25.45 (65.43–85.60)	72.77 ± 26.48 (62.39–83.16)	-3.63	0.354 (0.11)	0.459 (0.08)		
Knee flex. 60°/s (N·m)	M	40.75	41.04 ± 9.46 (36.93–45.16)	48.30 ± 11.41 (42.89–53.72)	17.69	**0.004** (0.69)	**0.003** (0.7)	M vs HI: 1.000 (0.13) M vs C: 0.058 (0.9) HI vs C: **0.011** (0.82)	M vs HI: 1.000 (0.11) M vs C: 0.059 (0.79) HI vs C: **0.014** (0.71)
	HI		41.41 ± 10.67 (37.88–44.94)	50.16 ± 16.13 (45.51–54.80)	21.12	**0.000** (0.64)	**0.000** (0.65)		
	C		39.11 ± 10.78 (34.26–43.96)	38.25 ± 10.71 (31.87–44.63)	-2.19	0.765 (0.08)	0.626 (0.13)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 25), HI (*n* = 34), C (*n* = 18). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ext: extension; flex: flexion; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

Table G.3. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Elbow ext. 180°/s (N·m)	M	27.91	30.00 ± 9.98 (27.06–32.93)	36.41 ± 6.99 (33.79–39.03)	21.37	**0.000** (0.74)	**0.000** (0.85)	M vs HI: 1.000 (0.01)	M vs HI: 1.000 (0.47)
	HI		24.08 ± 5.49 (21.56–26.59)	36.36 ± 6.41 (34.11–38.60)	50.99	**0.000** (2.06)	**0.000** (1.75)	M vs C: 0.061 (0.72)	M vs C: **0.005** (0.85)
	C		32.25 ± 6.06 (28.79–35.70)	31.60 ± 6.26 (28.51–34.68)	-2.02	0.686 (0.11)	0.244 (0.26)	HI vs C: **0.046** (0.75)	HI vs C: **0.000** (1.38)
Elbow flex. 180°/s (N·m)	M	15.44	14.57 ± 4.67 (12.40–16.74)	20.89 ± 6.93 (18.26–23.52)	43.36	**0.000** (1.07)	**0.000** (0.92)	M vs HI: 1.000 (0.13)	M vs HI: 1.000 (0.13)
	HI		16.22 ± 5.08 (14.35–18.08)	21.79 ± 6.79 (19.54–24.04)	34.36	**0.000** (0.93)	**0.000** (1.06)	M vs C: **0.004** (1.05)	M vs C: **0.001** (1.06)
	C		15.18 ± 6.96 (12.62–17.75)	14.12 ± 5.62 (11.02–17.21)	-7.02	0.495 (0.17)	0.334 (0.22)	HI vs C: **0.000** (1.19)	HI vs C: **0.000** (1.21)
Elbow ext. 60°/s (N·m)	M	30.96	33.31 ± 11.70 (29.83–36.79)	43.16 ± 8.87 (40.06–46.26)	29.57	**0.000** (0.95)	**0.000** (1.03)	M vs HI: 1.000 (0.17)	M vs HI: 0.961 (0.22)
	HI		28.00 ± 7.44 (25.01–30.98)	41.75 ± 7.48 (39.10–44.41)	49.11	**0.000** (1.84)	**0.000** (1.68)	M vs C: **0.000** (1.19)	M vs C: **0.000** (1.17)
	C		33.31 ± 5.58 (29.20–37.41)	33.61 ± 6.56 (29.96–37.26)	0.90	0.870 (0.05)	0.370 (0.23)	HI vs C: **0.002** (1.13)	HI vs C: **0.000** (1.55)
Elbow flex. 60°/s (N·m)	M	16.32	15.04 ± 4.42 (12.81–17.26)	21.52 ± 6.61 (19.22–23.81)	43.09	**0.000** (1.15)	**0.000** (0.97)	M vs HI: 1.000 (0.07)	M vs HI: 1.000 (0.05)
	HI		17.96 ± 5.98 (16.05–19.87)	21.89 ± 4.97 (19.92–23.86)	21.85	**0.001** (0.71)	**0.000** (0.94)	M vs C: **0.002** (1.01)	M vs C: **0.000** (1.03)
	C		15.22 ± 6.22 (12.60–17.85)	15.15 ± 5.87 (12.45–17.86)	-0.47	0.961 (0.01)	0.382 (0.17)	HI vs C: **0.000** (1.27)	HI vs C: **0.000** (1.18)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n* = 25), HI (*n* = 34), C (*n* = 18). M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; ext: extension; flex: flexion; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81.

SUPPLEMENTARY MATERIAL H. PPA RESULTS ON MUSCLE STRENGTH OF PROJECT TWO

Table H.1. *Intervention effects on isokinetic strength of hip abductor and adductor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Hip abd. 180°/s (N·m)	MT	12.70	12.53 ± 6.05 (10.02–15.03)	15.93 ± 5.98 (13.01–18.85)	27.13	**0.010** (0.56)	**0.005** (0.58)	MT vs P: **0.002** (0.88)	MT vs P: **0.001** (0.77)
	P		13.85 ± 8.12 (11.25–16.44)	23.81 ± 11.27 (20.79–26.84)	71.96	**0.000** (1.01)	**0.000** (1.06)	MT vs T: 1.000 (0.02)	MT vs T: 1.000 (0.02)
	T		11.84 ± 7.35 (9.25–14.43)	16.03 ± 7.44 (13.01–19.05)	35.40	**0.002** (0.57)	**0.005** (0.49)	MT vs C: 0.388 (0.61)	MT vs C: 0.113 (0.64)
	C		12.62 ± 6.04 (10.11–15.12)	12.04 ± 6.77 (9.12–14.96)	-4.57	0.655 (0.09)	0.632 (0.09)	P vs T: **0.003** (0.81)	P vs T: **0.002** (0.71)
								P vs C: **0.000** (1.28)	P vs C: **0.000** (1.19)
								T vs C: 0.375 (0.56)	T vs C: 0.106 (0.59)
Hip add. 180°/s (N·m)	MT	4.37	4.65 ± 3.43 (3.72–5.57)	6.52 ± 4.58 (5.09–7.94)	40.11	**0.006** (0.46)	**0.004** (0.48)	MT vs P: **0.021** (0.72)	MT vs P: **0.004** (0.76)
	P		4.41 ± 2.16 (3.45–5.37)	9.61 ± 3.93 (8.13–11.09)	117.88	**0.000** (1.64)	**0.000** (1.64)	MT vs T: 1.000 (0.03)	MT vs T: 1.000 (0.07)
	T		3.98 ± 2.53 (3.02–4.93)	6.37 ± 4.75 (4.89–7.85)	60.00	**0.001** (0.63)	**0.001** (0.6)	MT vs C: 0.079 (0.73)	MT vs C: 0.062 (0.69)
	C		4.44 ± 1.74 (3.51–5.36)	3.95 ± 1.93 (2.52–5.37)	-11.04	0.462 (0.27)	0.471 (0.26)	P vs T: **0.016** (0.74)	P vs T: **0.018** (0.67)
								P vs C: **0.000** (0.74)	P vs C: **0.000** (0.67)
								T vs C: 0.128 (1.85)	T vs C: **0.027** (1.85)

Table H.1. *Continued.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Hip abd. 60°/s (N·m)	MT	59.18	64.57 ± 22.09 (55.10–74.03)	71.14 ± 25.52 (61.51–80.76)	10.18	0.189 (0.28)	**0.027** (0.41)	MT vs P: 1.000 (0.01) MT vs T: 1.000 (0.17)	MT vs P: 1.000 (0.03) MT vs T: 1.000 (0.29)
	P		63.07 ± 28.47 (53.27–72.87)	71.48 ± 27.24 (61.52–81.45)	13.33	0.105 (0.3)	**0.020** (0.38)	MT vs C: **0.037** (0.82)	MT vs C: 0.141 (0.61)
	T		55.67 ± 25.40 (45.87–65.47)	76.17 ± 32.02 (66.21–86.14)	36.82	**0.000** (0.71)	**0.000** (0.63)	P vs T: 1.000 (0.16)	P vs T: 1.000 (0.25)
	C		53.43 ± 28.32 (43.96–62.90)	51.99 ± 20.87 (42.36–61.61)	-2.70	0.772 (0.06)	0.306 (0.18)	P vs C: **0.037** (0.81) T vs C: **0.005** (0.9)	P vs C: 0.108 (0.62) T vs C: **0.003** (0.84)
Hip add. 60°/s (N·m)	MT	41.42	39.98 ± 13.71 (34.03–45.93)	47.29 ± 14.70 (41.24–53.33)	18.27	**0.001** (0.51)	**0.001** (0.5)	MT vs P: 1.000 (0.02) MT vs T: 0.531 (0.50)	MT vs P: 1.000 (0.04) MT vs T: 1.000 (0.20)
	P		41.02 ± 19.74 (34.87–47.18)	47.59 ± 19.08 (41.34–53.85)	16.01	**0.005** (0.34)	**0.003** (0.34)	MT vs C: 0.139 (0.62)	MT vs C: **0.007** (0.61)
	T		45.45 ± 17.09 (39.29–51.60)	54.83 ± 15.69 (48.57–61.09)	20.65	**0.000** (0.57)	**0.000** (0.62)	P vs T: 0.647 (0.41)	P vs T: 1.000 (0.21)
	C		39.47 ± 14.88 (33.52–45.42)	37.35 ± 17.13 (31.30–43.39)	-5.38	0.338 (0.13)	0.210 (0.16)	P vs C: 0.129 (0.41) T vs C: **0.001** (0.57)	P vs C: **0.017** (0.21) T vs C: **0.000** (0.51)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30). MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; abd: abduction; add: adduction; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

Table H.2. *Intervention effects on isokinetic strength of knee flexor and extensor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Knee ext. 180°/s (N·m)	MT	50.86	53.14 ± 13.94 (48.16–58.11)	57.66 ± 13.40 (52.97–62.36)	8.52	**0.007** (0.33)	**0.001** (0.37)	MT vs P: 1.000 (0.23) MT vs T: 1.000 (0.07) MT vs C: 0.147 (0.51) P vs T: 1.000 (0.33) P vs C: **0.018** (0.33) T vs C: 0.295 (0.76)	MT vs P: 0.070 (0.47) MT vs T: 1.000 (0.01) MT vs C: 0.163 (0.33) P vs T: 0.093 (0.52) P vs C: **0.000** (0.52) T vs C: 0.149 (0.77)
	P		49.11 ± 12.36 (43.95–54.26)	60.35 ± 10.03 (55.49–65.21)	22.89	**0.000** (1)	**0.000** (0.96)		
	T		51.82 ± 11.20 (46.66–56.97)	56.80 ± 11.11 (51.94–61.66)	9.62	**0.004** (0.45)	**0.001** (0.47)		
	C		49.33 ± 16.66 (44.35–54.30)	50.02 ± 16.18 (45.32–54.71)	1.41	0.675 (0.04)	0.854 (0.02)		
Knee flex. 180°/s (N·m)	MT	27.19	29.36 ± 6.08 (26.60–32.12)	30.90 ± 7.18 (28.01–33.79)	5.24	**0.140** (0.23)	**0.045** (0.31)	MT vs P: 1.000 (0.23) MT vs T: 1.000 (0.21) MT vs C: **0.006** (0.88) P vs T: 1.000 (0.02) P vs C: **0.000** (1.04) T vs C: **0.000** (1.03)	MT vs P: 0.022 (0.57) MT vs T: 1.000 (0.23) MT vs C: 0.185 (0.4) P vs T: 0.497 (0.32) P vs C: **0.000** (0.89) T vs C: **0.007** (0.59)
	P		26.01 ± 8.19 (23.15–28.87)	32.66 ± 8.05 (29.66–35.65)	25.55	**0.000** (0.82)	**0.000** (0.79)		
	T		29.10 ± 7.23 (26.24–31.95)	32.47 ± 7.94 (29.48–35.47)	11.61	**0.002 (**0.44)	**0.000** (0.5)		
	C		24.36 ± 8.76 (21.60–27.12)	23.88 ± 8.71 (20.99–26.77)	-1.96	0.646 (0.05)	0.268 (0.13)		
Knee ext. 60°/s (N·m)	MT	87.78	90.94 ± 18.41 (83.38–98.50)	95.69 ± 22.21 (87.96–103.43)	5.22	**0.011** (0.23)	**0.006** (0.26)	MT vs P: 1.000 (0.2) MT vs T: 1.000 (0.29) MT vs C: 0.163 (0.53) P vs T: 0.471 (0.53) P vs C: 0.864 (0.53) T vs C: **0.008** (0.37)	MT vs P: 1.000 (0.06) MT vs T: 0.275 (0.26) MT vs C: 0.109 (0.27) P vs T: 0.768 (0.22) P vs C: **0.031** (0.22) T vs C: **0.000** (0.34)
	P		84.89 ± 16.95 (77.06–92.72)	91.60 ± 19.26 (83.60–99.61)	7.91	**0.001** (0.37)	**0.001** (0.36)		
	T		91.34 ± 21.70 (83.51–99.17)	101.75 ± 18.77 (93.74–109.75)	11.39	**0.000** (0.51)	**0.000** (0.52)		
	C		84.01 ± 25.34 (76.44–91.57)	83.34 ± 24.44 (75.61–91.07)	-0.79	0.719 (0.03)	0.569 (0.04)		
Knee flex. 60°/s (N·m)	MT	41.64	43.34 ± 8.64 (39.65–47.03)	46.35 ± 9.15 (42.79–49.90)	6.93	**0.004** (0.34)	**0.000** (0.4)	MT vs P: 1.000 (0.35) MT vs T: 1.000 (0.24) MT vs C: **0.003** (0.94) P vs T: 0.197 (0.57) P vs C: 0.175 (0.55) T vs C: **0.000** (1.17)	MT vs P: 0.892 (0.2) MT vs T: 1.000 (0.16) MT vs C: **0.002** (0.53) P vs T: 0.099 (0.34) P vs C: 0.144 (0.3) T vs C: **0.000** (0.68)
	P		41.38 ± 10.51 (37.57–45.20)	42.91 ± 10.64 (39.23–46.58)	3.68	0.153 (0.14)	0.126 (0.14)		
	T		43.82 ± 10.57 (40.01–47.64)	48.58 ± 9.17 (44.90–52.25)	10.85	**0.000** (0.48)	**0.000** (0.5)		
	C		38.15 ± 10.92 (34.46–41.84)	37.21 ± 10.21 (33.66–40.76)	-2.46	0.359 (0.09)	0.093 (0.15)		

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (n = 30), P (n = 28), T (n = 28), C (n = 30).MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; flex: flexion; ext: extension; ES: effect size; Δ%: percentage of change; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

Table H.3. *Intervention effects on isokinetic strength of elbow flexor and extensor muscles from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Elbow ext. 180°/s (N·m)	MT	26.26	26.35 ± 6.10 (23.68–29.02)	28.21 ± 5.72 (25.59–30.84)	7.07	**0.007** (0.32)	**0.006** (0.31)	MT vs P: 0.427 (0.49)	MT vs P: **0.000** (0.64)
	P		25.12 ± 8.33 (22.36–27.89)	31.68 ± 8.36 (28.97–34.40)	26.13	**0.000** (0.79)	**0.000** (0.77)	MT vs T: 1.000 (0.42)	MT vs T: 1.000 (0.2)
	T		27.91 ± 6.02 (25.14–30.68)	30.61 ± 5.77 (27.89–33.32)	9.66	**0.000** (0.46)	**0.000** (0.51)	MT vs C: 0.755 (0.39)	MT vs C: 0.090 (0.31)
	C		25.71 ± 8.65 (23.04–28.38)	25.32 ± 8.63 (22.70–27.95)	-1.50	0.572 (0.04)	0.477 (0.05)	P vs T: 1.000 (0.15)	P vs T: **0.004** (0.47)
								P vs C: **0.007** (0.15)	P vs C: **0.000** (0.47)
								T vs C: **0.039** (0.75)	T vs C**: 0.003** (0.81)
Elbow flex. 180°/s (N·m)	MT	3.13	2.94 ± 1.60 (2.26–3.61)	4.43 ± 2.26 (3.61–5.25)	50.68	**0.000** (0.76)	**0.000** (0.72)	MT vs P: **0.003** (0.97)	MT vs P: **0.000** (1.07)
	P		2.56 ± 1.59 (1.86–3.26)	6.58 ± 2.18 (5.73–7.43)	157.04	**0.000** (2.1)	**0.000** (1.99)	MT vs T: 1.000 (0.15)	MT vs T: 1.000 (0.01)
	T		3.54 ± 2.24 (2.84–4.24)	4.81 ± 2.75 (3.96–5.66)	35.79	**0.002** (0.5)	**0.000** (0.57)	MT vs C: 0.359 (0.54)	MT vs C: **0.034** (0.71)
	C		3.49 ± 1.96 (2.81–4.16)	3.31 ± 1.79 (2.49–4.13)	-4.97	0.650 (0.09)	0.918 (0.02)	P vs T: **0.025** (0.71)	P vs T: **0.000** (0.95)
								P vs C**: 0.000** (1.64)	P vs C: **0.000** (1.92)
								T vs C: 0.082 (0.65)	T vs C: **0.034** (0.64)
Elbow ext. 60°/s (N·m)	MT	35.50	36.16 ± 9.74 (32.72–39.59)	38.25 ± 5.59 (34.66–41.83)	5.78	0.148 (0.26)	0.075 (0.31)	MT vs P: 1.000 (0.17)	MT vs P: 0.585 (0.34)
	P		33.66 ± 10.16 (30.10–37.21)	39.88 ± 12.64 (36.17–43.59)	18.48	**0.000** (0.54)	**0.000** (0.5)	MT vs T: 0.374 (0.81)	MT vs T: 0.070 (0.83)
	T		35.48 ± 6.85 (31.92–39.03)	43.15 ± 6.48 (39.44–46.85)	21.61	**0.000** (1.15)	**0.000** (1.12)	MT vs C: 1.000 (0.34)	MT vs C: 0.323 (0.38)
	C		36.59 ± 10.66 (33.15–40.03)	34.95 ± 12.63 (31.37–38.53)	-4.48	0.256 (0.14)	0.344 (0.11)	P vs T: 1.000 (0.33)	P vs T: 1.000 (0.18)
								P vs C: 0.365 (0.33)	P vs C: **0.003** (0.18)
								T vs C: **0.013** (0.39)	T vs C: **0.000** (0.55)
Elbow flex. 60°/s (N·m)	MT	8.96	8.35 ± 2.60 (7.03–9.68)	11.62 ± 4.23 (10.04–13.20)	39.13	**0.000** (0.93)	**0.000** (0.89)	MT vs P: 1.000 (0.15)	MT vs P: 1.000 (0.06)
	P		7.85 ± 3.36 (6.48–9.22)	10.99 ± 4.40 (9.36–12.63)	39.95	**0.000** (0.8)	**0.000** (0.73)	MT vs T: **0.005** (1.09)	MT vs T: **0.004** (0.88)
	T		9.32 ± 3.61 (7.95–10.69)	15.54 ± 2.74 (13.90–17.17)	66.68	**0.000** (1.94)	**0.000** (1.96)	MT vs C: 1.000 (0.12)	MT vs C: 0.139 (0.42)
	C		10.28 ± 4.72 (8.95–11.60)	11.03 ± 5.52 (9.45–12.61)	7.33	0.238 (0.15)	0.091 (0.21)	P vs T: **0.001** (1.24)	P vs T: **0.002** (0.93)
								P vs C: 1.000 (0.01)	P vs C: 0.316 (0.36)
								T vs C: **0.001** (1.02)	T vs C: **0.000** (1.18)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30).T: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; flex: flexion; ext: extension; ES: effect size; Δ%: percentage of change; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

SUPPLEMENTARY MATERIAL I. PPA RESULTS ON PHYSICAL FUNCTION OF PROJECT ONE

Table I. *Intervention effects on physical function from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
30sec-CS (rep)	M		11.92 ± 2.64 (10.51–13.32)	23.28 ± 4.47 (21.38–25.17)	95.30	**0.000** (3.09)	**0.000** (3.41)	M vs HI: 1.000 (0.08)	M vs HI: 1.000 (0.12)
	HI	13.10	12.52 ± 2.64 (11.32–13.73)	22.94 ± 3.60 (21.31–24.56)	83.10	**0.000** (3.29)	**0.000** (3.31)	M vs C: **0.000** (1.63)	M vs C: **0.000** (2.18)
	C		15.83 ± 5.52 (14.18–17.48)	14.33 ± 6.67 (12.10–16.56)	-9.47	0.085 (0.24)	0.269 (0.17)	HI vs C: **0.000** (1.77)	HI vs C: **0.000** (2.36)
30sec-AC (rep)	M		16.56 ± 3.78 (14.84–18.27)	30.60 ± 4.39 (28.85–32.34)	84.78	**0.000** (3.42)	**0.000** (3.41)	M vs HI: 0.177 (0.53)	M vs HI: 0.422 (0.44)
	HI	16.46	15.08 ± 3.56 (13.61–16.55)	28.38 ± 3.99 (26.88–29.88)	88.11	**0.000** (3.51)	**0.000** (3.21)	M vs C: **0.000** (2.35)	M vs C: **0.000** (2.99)
	C		19.11 ± 5.96 (17.09–21.13)	19.61 ± 5.05 (17.55–21.67)	2.62	0.562 (0.09)	0.238 (0.24)	HI vs C: **0.000** (2)	HI vs C: **0.000** (2.77)
TUG (s)	M		7.05 ± 0.98 (6.63–7.46)	5.12 ± 0.55 (4.70–5.53)	-27.37	**0.000** (2.41)	**0.000** (2.06)	M vs HI: 1.000 (0.07)	M vs HI: 1.000 (0.19)
	HI	6.65	6.56 ± 0.91 (6.21–6.91)	5.16 ± 0.66 (4.80–5.51)	-21.38	**0.000** (1.75)	**0.000** (1.91)	M vs C: **0.001** (1.01)	M vs C: **0.000** (1.29)
	C		6.26 ± 1.28 (5.77–6.74)	6.39 ± 1.84 (5.90–6.87)	2.10	0.520 (0.08)	0.902 (0.01)	HI vs C: **0.000** (1.02)	HI vs C: **0.000** (1.25)
6MWT (m)	M		525.24 ± 60.80 (501.50–548.97)	573.56 ± 52.52 (548.57–598.54)	9.20	**0.000** (0.85)	**0.000** (0.96)	M vs HI: 0.368 (0.5)	M vs HI: 1.000 (0.04)
	HI	500.53	489.70 ± 47.42 (469.35–510.06)	547.76 ± 50.97 (526.34–569.18)	11.86	**0.000** (1.18)	**0.000** (1.15)	M vs C: **0.000** (1.65)	M vs C: **0.000** (1.08)
	C		486.66 ± 76.53 (458.69–514.64)	470.77 ± 90.39 (441.33–500.22)	-3.26	0.167 (0.19)	**0.048** (0.26)	HI vs C: **0.000** (1.15)	HI vs C: **0.000** (1.17)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: M (*n*=25), HI (*n*= 34), C (*n*=18).M: moderate-intensity group; HI: high-intensity group; C: control group; CIs: confidence intervals; 30sec-CS: 30 second sit-to-stand test; 30sec-AC: 30 second arm-curl test; TUG: timed up and go test; 6MWT: 6 minutes walking test; ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 69.81

SUPPLEMENTARY MATERIAL J. PPA RESULTS ON PHYSICAL FUNCTION OF PROJECT TWO

Table J. *Intervention effects on physical function from PPA.*

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
30sec-CS (rep)	MT	19.09	17.83 ± 4.81 (15.98–19.68)	21.60 ± 6.33 (19.48–23.71)	21.12	**0.000** (0.67)	**0.000** (0.66)	MT vs P: **0.045** (0.61) MT vs T: 0.549 (0.51) MT vs C: 0.119 (0.61) P vs T: 1.000 (0.27) P vs C: **0.000** (0.27) T vs C**: 0.001** (1.2)	MT vs P: 0.101 (0.32) MT vs T: 1.000 (0.06) MT vs C: **0.000** (0.73) P vs T: 0.256 (0.32) P vs C: **0.000** (0.32) T vs C: **0.000** (1)
	P		19.96 ± 6.27 (18.05–21.87)	25.78 ± 7.48 (23.59–27.97)	29.16	**0.000** (0.84)	**0.000** (0.86)		
	T		20.17 ± 3.77 (18.26–22.09)	24.21 ± 3.46 (22.02–26.40)	20.00	**0.000** (1.11)	**0.000** (1.11)		
	C		18.53 ± 5.28 (16.68–20.38)	18.03 ± 5.34 (15.91–20.14)	-2.70	0.425 (0.09)	0.388 (0.1)		
30sec-AC (rep)	MT	20.94	20.76 ± 4.56 (19.13–22.39)	24.90 ± 2.77 (23.43–26.36)	19.90	**0.000** (1.1)	**0.000** (1.1)	MT vs P: 1.000 (0.14) MT vs T: 1.000 (0.48) MT vs C: **0.042** (0.72) P vs T: 1.000 (0.22) P vs C: **0.011** (0.7) T vs C: **0.001** (1.03)	MT vs P: 1.000 (0.22) MT vs T: 0.904 (0.42) MT vs C: **0.000** (0.93) P vs T: 1.000 (0.1) P vs C: **0.000** (0.94) T vs C: **0.000** (1.19)
	P		19.92 ± 3.71 (18.23–21.61)	25.42 ± 4.81 (23.91–26.94)	27.60	**0.000** (1.28)	**0.000** (1.17)		
	T		20.60 ± 4.23 (18.91–22.29)	26.32 ± 3.17 (24.80–27.83)	27.73	**0.000** (1.53)	**0.000** (1.44)		
	C		22.36 ± 5.32 (20.73–23.99)	22.03 ± 4.93 (20.57–23.49)	-1.49	0.644 (0.06)	0.501 (0.08)		
5STS (s)	MT	8.58	8.54 ± 1.61 (7.91–9.17)	7.15 ± 1.77 (6.52–7.78)	-16.28	**0.000** (0.82)	**0.000** (0.85)	MT vs P: **0.043** (0.77) MT vs T: 1.000 (0.02) MT vs C: **0.010** (0.67) P vs T**: 0.043** (1.1) P vs C: **0.000** (1.32) T vs C**: 0.014** (0.77)	MT vs P: **0.000** (0.79) MT vs T: 1.000 (0.02) MT vs C: **0.000** (0.69) P vs T: **0.000** (1.14) P vs C: **0.000** (1.36) T vs C: **0.000** (0.79)
	P		8.61 ± 2.00 (7.96–9.26)	5.89 ± 1.47 (5.24–6.55)	-31.58	**0.000** (1.55)	**0.000** (1.55)		
	T		8.65 ± 1.16 (8.00–9.30)	7.17 ± 0.71 (6.52–7.82)	-17.11	**0.000** (1.53)	**0.000** (1.45)		
	C		8.52 ± 2.00 (7.89–9.15)	8.60 ± 2.46 (7.97–9.23)	0.89	0.737 (0.03)	0.793 (0.02)		

Table J. Continued.

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Timed stair-climbing (s)	MT	13.45	13.91 ± 2.16 (12.96–14.86)	12.25 ± 1.79 (11.38–13.11)	-11.94	**0.000** (0.84)	**0.000** (0.8)	MT vs P: 1.000 (0.45) MT vs T: 1.000 (0.31)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.16)
	P		13.04 ± 1.84 (12.05–14.02)	11.52 ± 1.42 (10.63–12.41)	-11.66	**0.000** (0.92)	**0.000** (0.98)	MT vs C: 0.148 (0.57)	MT vs C: **0.000** (0.77)
	T		13.51 ± 3.39 (12.52–14.49)	11.50 ± 2.94 (10.61–12.39)	-14.83	**0.000** (0.63)	**0.000** (0.62)	P vs T: 1.000 (0.01)	P vs T: 1.000 (0.16)
	C		13.31 ± 2.85 (12.36–14.26)	13.65 ± 2.96 (12.79–14.51)	2.52	0.137 (0.12)	0.137 (0.11)	P vs C: **0.006** (0.01) T vs C: **0.005** (0.91)	P vs C: **0.000** (0.82) T vs C: **0.000** (0.77)
SCS (steps/s)	MT	1.23	1.26 ± 0.19 (1.17–1.35)	1.11 ± 0.16 (1.03–1.19)	-11.94	**0.000** (0.84)	**0.000** (0.8)	MT vs P: 1.000 (0.45) MT vs T: 1.000 (0.31)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.16)
	P		1.18 ± 0.16 (1.09–1.27)	1.04 ± 0.12 (0.96–1.12)	-11.66	**0.000** (0.92)	**0.000** (0.98)	MT vs C: 0.148 (0.57)	MT vs C: **0.000** (0.77)
	T		1.22 ± 0.30 (1.13–1.31)	1.04 ± 0.26 (0.96–1.12)	-14.83	**0.000** (0.63)	**0.000** (0.62)	P vs T: 1.000 (0.01)	P vs T: 1.000 (0.15)
	C		1.21 ± 0.25 (1.12–1.29)	1.24 ± 0.26 (1.16–1.32)	2.52	0.137 (0.12)	0.137 (0.11)	P vs C: **0.006** (091) T vs C: **0.005** (0.73)	P vs C: **0.000** (0.82) T vs C: **0.000** (0.77)
SCP (W)	MT	202.61	201.57 ± 41.87 (187.25–215.90)	226.87 ± 46.05 (210.59–243.15)	12.55	**0.000** (0.57)	**0.000** (0.58)	MT vs P: 1.000 (0.08) MT vs T: 1.000 (0.31)	MT vs P: 1.000 (0.04) MT vs T: 0.529 (0.22)
	P		200.53 ± 42.00 (185.70–215.36)	224.07 ± 43.38 (207.22–240.93)	11.74	**0.000** (0.55)	**0.000** (0.55)	MT vs C: 1.000 (0.33)	MT vs C: **0.000** (0.66)
	T		199.59 ± 35.56 (184.76–214.42)	235.65 ± 49.15 (218.80–252.50)	18.06	**0.000** (0.84)	**0.000** (0.84)	P vs T: 0.580 (0.39)	P vs T: 0.288 (0.27)
	C		211.81 ± 38.52 (197.48–226.13)	208.31 ± 41.22 (192.03–224.59)	-1.65	0.401 (0.09)	0.401 (0.08)	P vs C: 1.000 (0.39) T vs C: 0.056 (0.25)	P vs C: **0.000** (0.27) T vs C: **0.000** (0.63)

Table J. Continued.

Variables	Group	Adjusted mean	Baseline	Post-test	Δ%	*P*-value (ES) ANOVA (time)	*P*-value (ES) ANCOVA[a] (time)	*P*-value (ES) ANOVA (group × time)	*P*-value (ES) ANCOVA (group × time)
Functional test (cm)	MT	25.34	26.76 ± 5.88 (24.66–28.86)	29.45 ± 5.00 (27.50–31.41)	10.08	**0.001** (0.49)	**0.000** (0.63)	MT vs P: 0.706 (0.46) MT vs T: 0.964 (0.38)	MT vs P: 1.000 (0.06) MT vs T: 1.000 (0.18)
	P		23.31 ± 6.01 (21.14–25.48)	27.21 ± 4.69 (25.19–29.24)	16.75	**0.000** (0.72)	**0.000** (0.58)	MT vs C: 0.142 (0.57)	MT vs C: **0.009** (0.59)
	T		24.36 ± 5.34 (22.19–26.53)	27.45 ± 5.57 (25.42–29.47)	12.66	**0.000** (0.56)	**0.001** (0.45)	P vs T: 1.000 (0.05)	P vs T: 1.000 (0.13)
	C		26.74 ± 5.92 (24.64–28.84)	26.25 ± 6.20 (24.30–28.21)	-1.83	0.553 (0.08)	0.882 (0.02)	P vs C: 1.000 (0.05) T vs C: 1.000 (0.17)	P vs C: **0.032** (0.54) T vs C: 0.165 (0.4)
TUG (s)	MT	5.95	5.89 ± 0.76 (5.56–6.22)	5.06 ± 0.59 (4.76–5.36)	-14.15	**0.000** (1.22)	**0.000** (1.31)	MT vs P: 1.000 (0.27) MT vs T: 1.000 (0.18)	MT vs P: 1.000 (0.15) MT vs T: 1.000 (0.21)
	P		6.10 ± 0.95 (5.75–6.44)	5.23 ± 0.67 (4.92–5.54)	-14.21	**0.000** (1.04)	**0.000** (0.97)	MT vs C: **0.001** (0.88)	MT vs C: **0.000** (0.95)
	T		6.02 ± 0.93 (5.68–6.37)	5.17 ± 0.62 (4.86–5.48)	-14.14	**0.000** (1.08)	**0.000** (0.97)	P vs T: 1.000 (0.09)	P vs T: 1.000 (0.05)
	C		5.80 ± 0.99 (5.47–6.13)	5.91 ± 1.23 (5.61–6.21)	1.88	0.432 (0.1)	0.813 (0.02)	P vs C: **0.014** (0.68) T vs C: **0.006** (0.75)	P vs C: **0.000** (0.05) T vs C: **0.000** (0.83)
6MWT (m)	MT	536.43	545.10 ± 53.53 (523.33–566.86)	564.73 ± 53.69 (543.36–586.10)	3.60	**0.009** (0.37)	**0.001** (0.45)	MT vs P: 1.000 (0.02) MT vs T: 1.000 (0.18)	MT vs P: 1.000 (0.05) MT vs T: 1.000 (0.19)
	P		537.42 ± 70.29 (514.90–559.95)	563.42 ± 59.60 (541.31–585.54)	4.84	**0.001** (0.4)	**0.000** (0.41)	MT vs C: **0.016** (0.84)	MT vs C: **0.002** (0.63)
	T		537.46 ± 52.09 (514.93–559.98)	575.10 ± 64.71 (552.98–597.22)	7.00	**0.000** (0.64)	**0.000** (0.6)	P vs T: 1.000 (0.19)	P vs T: 1.000 (0.14)
	C		525.86 ± 63.10 (504.10–547.62)	517.76 ± 58.18 (496.39–539.13)	-1.54	0.274 (0.13)	0.100 (0.19)	P vs C: **0.024** (0.78) T vs C: **0.002** (0.93)	P vs C: **0.001** (0.14) T vs C: **0.000** (0.65)

Note. Data are expressed as mean ± standard deviation and confidence interval (95% CIs). Sample size of each group: MT (*n* = 30), P (*n* = 28), T (*n* = 28), C (*n* = 30). MT: multi-component training group; P: power strength group; T: traditional high-intensity resistance training; C: control group; CIs: confidence intervals; 5STS: five times sit-to-stand test; 30sec-CS: 30 second sit-to-stand test; 30sec-AC: 30 second arm-curl test; SCS: stair-climbing speed; SCP: stair-climbing power; TUG: timed up and go test; 6MWT: 6 minutes walking test. ES: effect size; Δ%: percentage of change; ANOVA: analysis of variance; ANCOVA: analysis of covariance; a: covariates appearing in the model are evaluated by baseline values of dependent variables and age. Value of age as a covariate = 67.92.

CHAPTER XIII
Appendices

APPENDIX A. GRANTS CERTIFICATES

VNIVERSITAT DE VALÈNCIA

RESOLUCIÓ DEL RECTORAT DE LA UNIVERSITAT DE VALÈNCIA PER LA QUAL ES RESOL LA CONVOCATORIA D'UNA PLAÇA DE **INVESTIGADOR NO DOCTOR** DE LA UNIVERSITAT DE VALÈNCIA, AMB CONTRACTE LABORAL EVENTUAL (Projecte: "AYUDAS A LA INVESTIGACION IGNACIO HERNANDO LARRAMENDI 2014: EFECTO SOBRE PARAMETROS DE COMPOSICION CORPORAL, METABOLICOS, INMUNOLOGICOS, ESTRES OXIDATIVO, DE BIENESTAR Y FUNCIONALES AL ENTRENAR CON DIFERENTES DISPOSITIVOS DE RESISTENCIA A ALTAS INTENSIDADES EN ADULTOS MAYORES""), CONVOCADA PER RESOLUCIÓ D'AQUESTA UNIVERSITAT DE 23 DE JUNY DE 2015. (REF. CPI-15-206)

COGNOMS I NOM	PUNTUACIÓ
GARGALLO BAYO, PEDRO	**13,82 punts**

Contra aquesta resolució, que exhaureix la via administrativa, es pot interposar potestativament un recurs de reposició en el termini d'un mes a partir de l'endemà de la notificació o publicació davant del mateix òrgan que dicte la resolució o un recurs contenciós administratiu davant dels òrgans de la jurisdicció contenciosa administrativa de la Comunitat Valenciana en el termini de dos mesos comptats des de l'endemà de la notificació.

València,29 de juliol de 2015

Signat: Joan Oltra i Vidal
Gerent de la Universitat de València

MINISTERIO DE
EDUCACIÓN, CULTURA
Y DEPORTE

RESOLUCIÓN de 5 de agosto 2016, de la Secretaría de Estado de Educación, Formación Profesional y Universidades, por la que se conceden ayudas para contratos predoctorales para la Formación de Profesorado Universitario, de los subprogramas de Formación y Movilidad dentro del Programa Estatal de Promoción del Talento y su Empleabilidad.

GARGALLO BAYO, PEDRO	FPU15/05634	6	42

APPENDIX B. EXTRACTS OF PUBLICATIONS

Article

The Effect of Moderate- Versus High-Intensity Resistance Training on Systemic Redox State and DNA Damage in Healthy Older Women

Biological Research for Nursing
2018, Vol. 20(2) 205-217

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SAGE

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Abstract

This study investigated effects of a 16-week progressive resistance training program (RTP) with elastic bands at two different intensities on systemic redox state, DNA damage, and physical function in healthy older women. **Methods:** Participants were randomly assigned to the high-intensity group (HIGH; $n = 39$), moderate-intensity group (MOD; $n = 31$), or control group (CG; $n = 23$). The exercise groups performed an RTP twice a week with three to four sets of 6 (HIGH) or 15 (MOD) repetitions of six overall body exercises at a perceived exertion rate of 8–9 on the OMNI-Resistance Exercise Scale for use with elastic bands. Thiol redox state was determined by reduced glutathione (GSH), oxidized glutathione (GSSG), and GSSG/GSH in blood mononuclear cells. Degree of DNA damage was assessed by presence of the oxidized DNA base molecule 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-OHdG) in urine. Physical function monitoring was based on the arm curl, chair stand, up and go, and 6-min walk tests. **Results:** The HIGH group showed a significant increase in 8-OHdG (+71.07%, effect size [ES] = 1.12) and a significant decrease in GSH (−10.91, ES = −0.69), while the MOD group showed a significant decrease in 8-OHdG levels (−25.66%, ES = −0.69) with no changes in thiol redox state. GSH levels differed significantly between the HIGH and CG groups posttest. The exercise groups showed significant improvements in physical function with no differences between groups. **Conclusion:** RTP at a moderate rather than high intensity may be a better strategy to reduce DNA damage in healthy older women while also increasing independence.

Keywords

strength training, oxidative stress, urine 8-oxo-dG, GSSG/GSH, randomized controlled trial

Human aging is characterized by a progressive decline in the neuromuscular system, with marked decreases in skeletal muscle mass, muscle strength, and physical function beginning in the sixth decade in life (Delmonico et al., 2009; Manini & Clark, 2011). It has been hypothesized that one of the causes of these changes may be the deleterious and cumulative effects of reactive oxygen species (ROS) along with a decrease in endogenous antioxidants in older adults (Bouzid, Hammouda, Matran, Robin, & Fabre, 2014). These effects are especially marked in older women because they are exposed to particular risk due to the loss of the antioxidant effects of estrogen during menopause (Moreau & Hildreth, 2014) and the high levels of sarcopenia and dynapenia seen in women compared to men (Brady, Straight, & Evans, 2014).

Chronic oxidative stress (OS) has also been associated with the loss of skeletal muscle mass and muscle strength (Cesari et al., 2012; Howard et al., 2007). The production of excess ROS can cause chronic OS, affecting several different organic molecules, including nucleic acids, and provoking DNA damage. One of the most abundant and potentially mutagenic

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Proceeding

Supplementary Issue: Summer Conferences of Sports Science. Costa Blanca Sports Science Events, 25-26 September 2020. Alicante, Spain.

Effects of power resistance training program with elastic bands on body composition, muscle strength and physical function in older women

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ABSTRACT

The aim of this study was to investigate the effects of a power-strength resistance program with elastic bands on body composition, physical function, and muscle strength in older women. For such purpose, a randomized controlled trial with a pre-post-intervention design was conducted. Thus, 58 healthy, physically independent, sedentary women, aged 65-85 years, were randomly allocated to the intervention (n = 28) or control group (n = 30). Measurements of body composition (total mass, total fat mass, total skeletal-muscle mass, and body fat percentage), isokinetic muscle strength of knee flexors and extensors (at 60º/second and 180º/second), and physical performance (flexibility, agility/dynamic balance, and mobility) were taken pre-intervention and after 20 weeks of a power-strength protocol (light loads at maximum speed) with elastic bands consisting of 42 sessions (including familiarization) of between 80 and 90 minutes, with six exercises per session. The intensity was controlled with the OMNI-RES scale of perceived exertion. An analysis of variance (ANOVA) and covariance (ANCOVA) was carried out. All parameters of physical function, isokinetic strength, and body composition significantly improved ($p < .05$) in the intervention group, except the muscle mass and the knee flexion strength at 60º/sec, on which no statistical difference was observed ($p > .05$). All the variables got worsened or did not change in the control group. A resistance program with elastic bands using light loads and performing at maximum speed can reverse the deterioration in body composition, muscle strength, and physical function, and offer significant physical benefits in sedentary older women.

Keywords: Resistance training; Variable resistance; Functional capacity; Elder people; Female.

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(Fwd) [JHSE] Editor Decision

Para: "Juan Carlos Colado"
Asunto: [JHSE] Editor Decision
De: "Journal of Human Sport & Exercise" <jhse@ua.es>
Fecha: Wed, 20 Jan 2021 12:47:28 +0000

Juan Carlos Colado:

We have reached a decision regarding your submission to Journal of Human Sport and Exercise, "High-and moderate-intensity resistance training provokes different effects on body composition, functionality, and well-being in elderly".

Our decision is to:

ACCEPT SUBMISSION

We are pleased to inform you that your paper has been submitted to the review process and, according to reviewers, this article has been proposed for publication.

We appreciate your confidence in us.

Thank you very much.

Best Regards:

Journal of Human Sport & Exercise
University of Alicante
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J. Hum. Sport Exerc. ISSN 1988-5202. Faculty of Education. University of Alicante. C/ Aeroplano s/n - 03690 San Vicente del Raspeig - Alicante - Spain jhse@ua.es

Article

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Positive Effects of a Short-Term Intense Elastic Resistance Training Program on Body Composition and Physical Functioning in Overweight Older Women

Nicole B. Fritz, MSc[1,2], Álvaro Juesas, MSc[2], Pedro Gargallo, MSc[2], Joaquín Calatayud, PhD[3], Julio Fernández-Garrido, PhD[2,4], Michael E. Rogers, PhD[5], and Juan C. Colado, PhD[2,3]

Abstract

The aim of this study was to investigate the effects of a resistance training program (RTP) in older overweight women (OOW) using two different types of elastic devices. **Methods:** This study was a randomized controlled trial with pre- and postintervention measures. Participants included OOW, aged 60–85 years, with no medical history of disease that would preclude them from engaging in physical exercise. Participants were randomly divided into the following groups: elastic tubes with handles group (ETG; $n = 22$), traditional elastic bands group ($n = 21$), and control group (CG; $n = 20$). Exercise groups (EGs) performed the following supervised RTP: 8 weeks, twice weekly, six overall body exercises, and 3–4 sets of 10 repetitions at a rate of perceived exertion (RPE) of 7–9 on the OMNI-Resistance Exercise Scale of perceived exertion. The controls did not change their usual lifestyle. Outcome measures included body composition (BC; total and regional percentage of fat mass [FM] and fat-free mass [FFM]) and physical performance (PP; dynamic and isometric strength, flexibility, agility/dynamic balance, and endurance). **Results:** Both EGs exhibited significantly reduced FM in the upper limbs (ULs) and trunk and increased FFM in the UL, while the ETG exhibited a significantly increased trunk FFM. Both EGs improved in PP, and there were no intergroup differences. Trunk FM and FFM and meters walked differed significantly between the ETG and CG. The CG did not exhibit any significant changes. **Conclusion:** Training with elastic devices at a moderate–high RPE produces short-term improvements in BC and PP in OOW.

Keywords

fat and fat-free mass, strength, perceived effort, elastic bands and tubes

Body composition (BC) changes are a hallmark of the physiological aging process, including an increase in fat mass (FM), particularly in central and visceral depots, and a decrease in fat-free mass (FFM). These changes are associated with an increased risk of metabolic and cardiovascular disease (Chodzko-Zajko et al., 2009; Rossi et al., 2017). Due to aging, inactivity, and poor nutrition, the prevalence of overweight and obesity in the general U.S. population has doubled over the past 10 years (Fakhouri, Ogden, Carroll, Kit, & Flegal, 2007), with recent rates of obesity in non-Hispanic White women and Hispanic women over 60 years of age estimated at 32.8% and 44.4%, respectively (Fitzpatrick et al., 2008). Overweight and obesity are more common in older women than in older men, and changes in BC occur more frequently in women in the later decades of life due to menopause (Pucci et al., 2017). The combination of aging and obesity accelerates the loss of muscle strength and physical functioning, which leads to a decrease in the performance of instrumental daily activities, independence, and quality of life and, consequently, an increase in the risk of falls, morbidity, and mortality in older adults (OAs; Delmonico et al., 2007; Mally, Trentmann, Heller, & Dittmar, 2011).

Among the different types of physical exercise, resistance training (RT) has well-established positive effects on weight loss because, unlike aerobic training, RT leads to a decrease in FM and attenuates the loss of FFM. Modification of some

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Effects of strength training with variable elastic resistance across the lifespan: a systematic review

Efectos del entrenamiento de la fuerza con resistencia variable elástica a lo largo de la vida: una revisión sistemática

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Abstract

The benefits of strength training programs with isotonic free weights or machines have been well-documented in all age groups. However, exercise and healthcare professionals sometime question whether it is possible to obtain the same results with devices of variable resistance, such as elastic bands. To answer this question, the purpose of this systematic review was to identify and summarize the positive effects of elastic resistance exercises used across the lifespan on health outcomes including body composition, functional and performance capacity, and biochemical variables. A secondary aim was to identify common dosage parameters of strength training programs using elastic resistance.

Key words: elastic bands; functional capacity, body composition; health biomarkers.

Resumen

Los beneficios de los programas de entrenamiento de la fuerza con peso libre y máquinas isocinéticas del tipo isotónico han sido bien documentados en todas las franjas de edad. Sin embargo, los profesionales del ejercicio y la salud algunas veces se preguntan si es posible obtener los mismos resultados con dispositivos de resistencia variable, como por ejemplo las bandas elásticas. Para responder a esta pregunta, el objetivo de esta revisión sistemática fue identificar y resumir los efectos positivos de los ejercicios de fuerza con elásticos empleados a lo largo de las diferentes etapas de la vida sobre resultados relacionados con la salud, incluyendo la composición corporal, capacidad funcional, rendimiento físico y algunas variables bioquímicas. Un objetivo secundario fue identificar los parámetros de dosificación comunes de los programas de entrenamiento de la fuerza usando resistencia elástica.

Palabras clave: bandas elásticas; capacidad funcional; composición corporal; biomarcadores de salud.

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Concurrent validation of the OMNI-Resistance Exercise Scale of perceived exertion with elastic bands in the elderly

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Keywords:
RPE
Heart rate
Applied force
Resistance training

ABSTRACT

Purpose: To examine the concurrent validity of the OMNI-Resistance Exercise Scale of perceived exertion using elastic bands in elder population.
Methods: Twenty-six participants performed three separate sets of 15 repetitions (low- medium- and high-intensity) for 4 different exercises (2 for the upper-limb and 2 for the lower limb), over two different testing sessions. The criterion variables were heart rate and applied force (average and maximum). In addition to these dependent variables, the active muscle and overall body OMNI-RES for elastic bands scores were collected at the end of each repetition.
Results: Significant differences in heart rate, applied force and OMNI-RES scores between the low- and high-intensity sets were observed. For all the four exercises, high intensity sets elicited higher heart rate, applied force, and RPE compared to the medium and the low overloads. Intraclass correlation coefficient was 0.79 in heart rate and ranged 0.69–0.80 in OMNI-RES Scale and 0.76–0.86 for the applied force.
Conclusion: A strong positive and linear relationship was observed between the rating of perceived exertion and both heart rate and applied force. The OMNI-RES scale with elastic bands demonstrated to be a valid method for assessing the perceived exertion during resistance exercises and consequently represent a useful tool for prescribing exercise intensity to the elderly.

1. Introduction

Aging is characterized by a loss of muscle strength and physical functioning (Rossi et al., 2017), which leads to a decrease in the performance of instrumental daily activities, independence and quality of life and, consequently, an increase in the risk of falls, morbidity and mortality in older adults (OA) (Delmonico et al., 2007; Mally et al., 2011). Resistance training (RT) has well-established positive effects to decreasing fat mass and attenuating progressive loss of fat-free mass in elderly (Chodzko-Zajko et al., 2009). Even though, the use of free weights and machines is currently very popular among coaches and clinicians these devices are not always feasible for OA, who may need specific and strong personalized support. Indeed, it has been demonstrated that the attrition rate during the first year of training using free weight is approximately 50% in OA (Colado and Triplett, 2008). Conversely, elastic resistances represent alternative very easy to use, transport and maintain devices that in addition have showed a reduced risk of injury in "healthy" and "not healthy" elderly (Martins et al., 2013). Several recent publications have highlighted the advantages of using elastic material for increasing strength and performance in OA. José and Dal Corso (2016) indicate that using elastic materials in healthcare settings is an effective method, easier to transport and store (in settings that often have very limited space) and are significantly less expensive. Furthermore, elastic resistances have elicited higher intrinsic motivation in healthcare practitioners to advocate for strength exercises that can be even performed at home (Polyte et al., 2015).

The control of exercise intensity is an important factor to ensure the safety and efficacy of physical activity in any context of application,

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Metabolic and Functional Profile of Premenopausal Women With Metabolic Syndrome After Training With Elastics as Compared to Free Weights

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Abstract

The aim of this study was to compare the effects of a strength training program (STP) using free weights (FW) versus elastic tubing (ET) in 62 premenopausal, sedentary women diagnosed with metabolic syndrome (MS). Participants were randomly assigned to the FW or ET experimental group (EG) or a control group whose members remained sedentary. Members of each EG followed their assigned STP for 12 weeks, and biomarkers (BMs) related to MS and motor function (MF) parameters were evaluated. Both EGs showed a significant reduction in C-reactive protein level and a positive trend in the other BMs. Almost all MF parameters increased significantly in both EGs. No positive changes were found in the CG. These results indicate that the implementation of an STP, with either FW or ET, improves both metabolic health and MF and should be considered part of the basic approach to health care in women.

Keywords

strength, elastic tubing, free weights, cardiovascular risk

Women between 45 and 55 years old are close to the end of their reproductive lives. The hormonal changes associated with menopause contribute to the development of metabolic risk factors such as dyslipidemia, insulin resistance, and increased abdominal fat (Orsatti, Nahas, Maesta, Nahas-Neto, & Burini, 2008), which are all possible triggers for various cardiovascular risk factors (Huebschmann et al., 2015). Conclusive scientific evidence demonstrates a relationship between physical inactivity and the presence of risk factors associated with metabolic syndrome (MS) and obesity (J. W. Kim & Kim, 2012). Moreover, regular exercise may reduce the loss of strength that is common among women in this age-group (Lauretani et al., 2003), in turn enhancing their physical performance (Clark & Manini, 2008) and metabolic health (Gudmundsdottir, Flanders, & Augestad, 2013).

Several studies have shown the effectiveness of resistance training in reducing cardiovascular risk and dynapenia in women of different ages, including the menopausal age-group (Colado, Garcia-Masso, Rogers, et al., 2012; Colado & Triplett, 2008; Martins et al., 2015). However, we could not find any previous experimental intervention programs comparing the effects of traditional devices (such as free weights [FWs] or machines) with novel devices (e.g., multifunctional training with elastic tubes) during muscular strength training. Therefore, the possible metabolic and functional adaptive effects of these novel types of strength training programs (STPs) in sedentary women aged 40–50 years with MS remain unknown.

Recent studies have confirmed that STPs using elastic tubes can create the same levels of muscle activation in both the trunk and the extremities as machines or FWs (Aboodarda, Hamid, Muhamed, Ibrahim, & Thompson, 2013; Jakobsen, Sundstrup, Andersen, Aagaard, & Andersen, 2013). In addition, STPs using elastic tubes may provoke higher intrinsic motivation among health practitioners advocating strength exercises

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Physiological and psychological effects of a new racket sport in children with and without overweight at primary school

Efectos fisiológicos y psicológicos de un nuevo deporte de raqueta en niños con y sin sobrepeso en la escuela primaria

Pedro Gargallo[1,2], Álvaro Juesas[1,3], Alejandro Bruño[4], José F. Guzmán[1,3], Juan F. Lisón[5], Rosa M. Baños[1,6], Jorge Flández[7], Michael E. Rogers[8], Juan C. Colado[1,3]

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Abstract

Literature have shown the positive effects of participation in classical sports on children health. However, innovative ideas are necessary to increase their participation according to motivations and individual needs. The purpose of the present study was to know if a new racket sport of reduced play space provokes similar physiological and psychological effects to traditional sports [basketball (BASKET) and indoor football (FUTSAL)] in children with and without overweight at primary school. A cross-sectional study was developed with 54 children (10.4±0.1 years old; 44.4% with overweight) who participated in one session of 25 minutes of each sport. Physiological [total physical activity (TPA), mean (MHR) and maximum heart rate (MXHR), activity energy expenditure (AEE)] and psychological [rate of perceive exertion (RPE), affect, Results showed that the new racket sport is indicated for overweight children because its physiological and psychological effects are similar to other traditional team sports.

Key words: Spiribol; basketball; futsal; health.

Resumen

La literatura ha demostrado los efectos positivos de la participación en los deportes clásicos sobre la salud de los niños. Sin embargo, se necesitan ideas innovadoras para aumentar su participación de acuerdo con las motivaciones y las necesidades individuales. El propósito del presente estudio fue saber si un nuevo deporte de raqueta de espacio de juego reducido provoca efectos fisiológicos y psicológicos similares a los deportes tradicionales (baloncesto y fútbol sala) en niños con y sin sobrepeso en la escuela primaria. Se desarrolló un estudio transversal con 54 niños (10.4 ± 0.1 años; 44.4% con sobrepeso) que participaron en una sesión de 25 minutos de cada deporte. Se evaluaron los parámetros fisiológicos (actividad física total, frecuencia cardíaca media y máxima, gasto energético de actividad) y psicológicos (tasa de esfuerzo percibido, afecto, disfrute). Los resultados mostraron que el nuevo deporte de raqueta está indicado para niños con sobrepeso porque sus efectos fisiológicos y psicológicos son similares a otros deportes de equipo tradicionales.

Palabras clave: Spiribol; baloncesto: fútbol sala; salud.

Proceeding

Supplementary Issue: Summer Conferences of Sports Science. Costa Blanca Sports Science Events, 25-26 September 2020. Alicante, Spain.

A systematic review on the muscular activation on the lower limbs with five different variations of the squat exercise

JAVIER GENE-MORALES[1,2], JORGE FLANDEZ[3], ALVARO JUESAS[2], PEDRO GARGALLO[2], IVÁN MIÑANA[2], JUAN C. COLADO[2]

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ABSTRACT

The squat is one of the most commonly used resistance exercises for performance and health due to its biomechanical and neuromuscular similarities to a wide range of athletic and everyday activities. There is a large number of squat variations (based on the descent depth, width of the stance, bar placement) with significant biomechanical and neuromuscular differences between them. The aim of this study was to systematically review the scientific literature to gather data on the muscular activation of the lower limb during different variants of the squat exercise. High-bar squat (full range of motion, to parallel and partial range of motion), low-bar squat, front squat, overhead squat and guided squat on Smith machine were included in the analysis. 30 articles met the inclusion criteria and were reviewed. Quality of the included studies was analysed with the PEDro scale. Main findings were that in the squat exercise activation of the knee-extensors is predominant. However, different activation patterns were observed with different distances between the feet, different depths, hips rotation or flexion, intensities. For instance, low-bar squat involves a greater hip hinge and thus, provokes major activation on the hip-extensors than other squat variations. It is worth highlighting that similar activation patterns were observed between the front squat and the high-bar squat. The variation with least activation was the guided squat. The evidence presented in this study may help the strength and conditioning professionals and practitioners with the exercise selection depending on the muscular targets and the individual characteristics of the athlete.

Keywords: Electromyographic activity; Resistance exercise; Quadriceps; Gluteus; Hamstrings; Calves.

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Influencia de los distintos tipos y parámetros del ejercicio físico sobre la calidad seminal: una revisión sistemática de la literatura

Influence of the different types and parameters of the physical exercise on seminal quality: a systematic review of the literature

Víctor Muñoz[1], Pedro Gargallo[1], Álvaro Juesas[1], Jorge Flández[2], Joaquín Calatayud[3], Juan C. Colado[1,3]

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Resumen

Es de sobra conocida la importancia positiva de la actividad física correctamente prescrita en términos de intensidad y volumen sobre diferentes alteraciones metabólicas, osteomusculares, cognitivas, etc. La infertilidad es una patología cuya epidemiología está al alza por los cambios en los hábitos de nuestra vida cotidiana, como la dieta inadecuada o la radiación de las nuevas generaciones de aparatos eléctricos. No existen demasiadas evidencias divulgativas sobre sus causas y efectos, así como tampoco del papel del ejercicio en la reversión de sus síntomas. Con la finalidad de obtener y sintetizar la información más relevante sobre la influencia de los diferentes tipos y parámetros del ejercicio físico en los criterios de calidad seminal se decidió realizar una revisión bibliográfica sistemática en las bases de datos WOS, PubMed y Google Scholar hasta marzo de 2016. Los resultados arrojaron que mientras que el entrenamiento de alta intensidad y volumen prolongado produce un descenso de las concentraciones hormonales gonadales y los niveles antioxidantes y, por lo tanto, en la calidad del esperma, el ejercicio moderado revierte estos efectos aumentando los mismos y podría llegar a influir en una posible optimización de los procesos generadores del espermatozoide.

Palabras clave: Entrenamiento, infertilidad masculina, hormonas gonadales, estrés oxidativo seminal, calidad seminal.

Abstract

The positive importance of physical activity properly prescribed in terms of intensity and volume on a variety of metabolic, musculoskeletal, cognitive and other disorders is widely known. The increasing epidemiology of infertility is due to the changes in lifestyle habits, such as inappropriate diets or the radiations from new-generation electrical devices. There are not many informative evidences regarding either infertility causes and effects, or the exercise role in reversing its symptoms. In order to obtain and summarize the most relevant information about the influence of the different training types and parameters in the semen quality criteria, a descriptive literature review without temporal restriction of WOS, PubMed and Scholar data bases has been conducted. The study produced the following results; whilst a high intensity and prolonged volume training produce a drop in the gonadal hormone concentrations and the antioxidant levels and, therefore, in the sperm quality, moderate exercise reverts these effects and could potentially influence a possible optimization of the sperm generating processes.

Key words: Training, male infertility, gonadal hormones, seminal oxidative stress, sperm quality.

CCD 40 I AÑO 15 I VOLUMEN 14 I MURCIA 2019 I PÁG. 25 A 42 I ISSN: 1696-5043

Original Clinical Science—Liver

Clinical Relevance of a Balance Training Program on Liver Transplant Patients. A Randomized Controlled Trial

Diego Moya-Nájera,[1] Ángel Moya-Herraiz, PhD,[2] Pedro Gargallo,[3] Joaquin Calatayud, PhD,[1] Javier Escrig-Sos, PhD,[4] and Juan C. Colado, PhD[1,3]

Background. Although some studies have reported significant improvements in physical function and strength after training programs on liver transplant (LT) recipients, there is a lack of knowledge on how it affects in static and dynamic balance, being an important part of these participants' tasks development. The aim of the study was to determine the effects of a 6-month multicomponent circuit training program on static and dynamic balance in LT participants. **Methods.** Fifty-four participants were randomized at 6 months after LT into 2 groups: exercise (EXER) group and control (CONTROL) group, with repeat testing at 6 (baseline) and 12 months after LT. The intervention consisted of a multicomponent training, including balance, strength, endurance, and flexibility training, with exercises arranged in a circuit setup and a moderate intensity with high perceived exertion. Training sessions were performed in the hospital facilities with qualified trainers. To determine differences over time between EXER and CONTROL, mixed-regression linear models with subject variable as random factor and variables of treatment duration, type, and interaction as predictors were used. **Results.** The EXER group showed significant differences ($P < 0.05$) compared with CONTROL in all variables of static and dynamic balance, hip strength (49% versus 13%), agility (−16% versus −1%), and flexibility (78% versus −26%). Adherence to the intervention was 94%, and 80% of the participants continued voluntarily training after the 6 months. **Conclusions.** This study demonstrated that a multicomponent circuit training program at a moderate intensity with high perceived exertion could reduce the probability of injuries because it improves balance on LT recipients.

(*Transplantation* 2019;103: 965–972

Approximately 10 000 patients undergo a liver transplant (LT) every year, Spain being the country with the highest deceased-donor transplant rate by population, with 23 to 25 LT per million population and >1 000 transplants performed yearly.[1-3] There is a large volume of transplants, together with the increase in the 1-, 3-, 5-year patient survival rates of 82%, 79%, and 73%.[4] Although survival remains the main goal, a simple focus on mortality and morbidity after transplantation can no longer provide an appropriate view of the effects of medical care and interventions after LT. Thus, more ambitious purpose is needed to fully reinstate the patient's daily life.

Disorders, such as sarcopenia, loss of muscle strength and function, weight gain, reduced exercise tolerance, and decreased physical capacity are prevalent in end-stage liver disease because of long bedding time and medication intake.[5,6,7] These factors, in combination with a sedentary lifestyle, cause a drastic reduction in quality of life and sociability,[7] adversely impacting the activities of daily living, with a physical status similar to that of an older adult without, or even with, frailty.

Falls and fall-related injuries occur commonly, especially with the elderly and chronically patients, strongly related to the deterioration of balance, agility, and hip muscle strength.[8] The short- and long-term effects of serious fall-associated injuries are a significant source of morbidity and mortality[9] and represent an important public health problem (US $31 billion in 2015 in the United States).[10]

Exercise is usually used for rehabilitation programs, following the idea that exercise programs can improve physical performance and quality of life in LT patients.[11,12]

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D.M.-N. contributed to design and study preparation, participants' recruitment, training instruction, data acquisition (or data collection) of physical tests, data interpretation, and drafting the article. Á.M.-H. contributed to the design and study preparation, participants' recruitment, data interpretation, and revising the article. P.G. contributed to training instruction and data acquisition of physical tests and helped to draft and revise the article. J.C. contributed to design study, data acquisition of physical tests, and revising the article. J.E. performed the statistical analysis and data interpretation. J.C.C. contributed to design study, supervision of the project, data interpretation, and revising the article.

All authors read and approved the final article.

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Original article

Trunk muscle activity during different variations of the supine plank exercise

Joaquin Calatayud [a, d], Jose Casaña [b], Fernando Martín [a], Markus D. Jakobsen [c, d], Juan C. Colado [a, *], Pedro Gargallo [a], Álvaro Juesas [a], Víctor Muñoz [a], Lars L. Andersen [d, e]

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ABSTRACT

Background: Exercises providing neuromuscular challenges of the spinal muscles are desired for core stability, which is important for workers with heavy manual labour as well as people recovering from back pain.
Purpose: This study evaluated whether using a suspended modality increases trunk muscle activity during unilateral or bilateral isometric supine planks.
Design: Cross-sectional.
Methods: Twenty university students participated in this cross-sectional study. Each subject performed four different conditions: bilateral stable supine plank, unilateral stable supine plank, bilateral suspended supine plank and unilateral suspended supine plank. Surface electromyography (EMG) signals were recorded for the upper rectus abdominis (UP ABS), lower rectus abdominis (LOW ABS), external oblique (OBLIQ) and lumbar erector spinae (LUMB). Peak EMG of the filtered signals were normalized to the maximum voluntary isometric contraction (MVIC).
Results: No differences between exercises were found for UP ABS, LOW ABS and OBLIQ muscle activity. The unilateral suspended supine plank provided the highest LUMB activity (20% of MVIC) whiles the bilateral stable supine plank provided the lowest activity (11% of MVIC).
Conclusions: The combination of unilateral variations with a suspended support provides the greatest LUMB muscle activity, while using these variations separately only provides advantages when compared with regular planks.

1. Introduction

Non-specific low back pain is a major public health problem worldwide with a lifetime prevalence of 84% (Balagué et al., 2012). Among working age adults, approximately one third suffer from moderate to severe low back pain (Andersen et al., 2011). Low back pain is associated with decreased work ability and consequently increased risk of long-term sickness absence (Andersen et al., 2012).

Physical exercise in general seems to be beneficial to reduce low back pain incidence and sick leave related with low back pain, at least in short-term (Steffens et al., 2016). However, a recent meta-analysis found that trunk stability exercise resulted in greater short-term physical function and pain reductions than general exercise in patients with chronic low back pain (Wang et al., 2012). Exercises providing greater neuromuscular challenges are desired for low back rehabilitation, since greater muscle activation (i.e., greater intensity of muscle contraction) results in enhanced joint stiffness and spine stability (McGill, 2001). As explained by Lee and McGill (2015), trunk stiffness improves load bearing ability and limb strength, providing resilience against external torques. Interestingly, greater time under tension with higher muscle activity is

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IJSPT

ORIGINAL RESEARCH

THE VALIDITY AND RELIABILITY OF A NEW INSTRUMENTED DEVICE FOR MEASURING ANKLE DORSIFLEXION RANGE OF MOTION

Joaquin Calatayud, MsC, CSCS[1]
Fernando Martin, PhD[1]
Pedro Gargallo, MsC[1]
Jessica Garcia-Redondo, MsC[2]
Juan Carlos Colado, PhD[1]
Pedro J. Marin, PhD, PT[3]

ABSTRACT

Purpose/Background: A restriction in ankle dorsiflexion range of motion (ROM) has been linked to several clinical manifestations such as metatarsalgia, heel pain, nerve entrapment, ankle joint equinus, patellar and ankle injuries. The purpose of the present study was to examine the validity and reliability of the Leg Motion system for measuring ankle dorsiflexion ROM.

Study Design: Descriptive repeated-measures study.

Methods: Twenty-six healthy male university students were recruited to test the reliability of the Leg Motion system, which is a portable tool used for assessment of ankle dorsiflexion during the weight-bearing lunge test. The participants were tested two times separated by two weeks and measurements were performed at the same time of the day by the same single rater. To test the validity of the Leg Motion system, other maximal ankle dorsiflexion ROM assessments (goniometer, inclinometer and measuring tape) were measured in a single session (i.e., the first test session) during the weight-bearing lunge position using a standard goniometer, a digital inclinometer and a measuring tape measure with the ability to measure to the nearest 0.1 cm.

Results: Paired t-tests showed the absence of significant differences between right and left limb measurements of dorsiflexion in all tests. Mean values ± standard deviations were as follows: Leg Motion test (left 11.6cm ± 3.9; right 11.9cm ± 4.0), tape measure (left 11.6cm ± 4.0; right 11.8cm ± 4.2), goniometer (left 40.6° ± 5.2; right 40.6° ± 5.2), and digital inclinometer (left 40.0° ± 5.8; right 39.9° ± 5.6). The Leg Motion composite values (i.e., average of the two legs) showed a significant ($p < 0.05$) positive correlation with the tape measure ($r = 0.99$), with the goniometer ($r = 0.66$), and with the digital inclinometer ($r = 0.72$).

Conclusions: The results of the present study provide evidence to support the use of the Leg Motion system as a valid, portable, and easy to use alternative to the weight-bearing lunge test to assess ankle dorsiflexion ROM in healthy participants.

Level of evidence: 2b.

Key words: Ankle dorsiflexion, goniometer, inclinometer, weight-bearing lunge

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Conflict of interest
The last author declared potential conflicts of interest. He has patent pending for Leg Motion system.

Funding
None declared.

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APPENDIX C. CERTIFICATIONS OF INTERNATIONAL ORAL COMMUNICATIONS

25TH ANNIVERSARY CONGRESS

OCTOBER 28-30, 2020

EUROPEAN COLLEGE OF SPORT SCIENCE

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register of associations: VR12508

Cologne, 04.11.2020 - 09:11:43

Confirmation of Presentation

This is to certify that the following title has been presented at the 25th Annual Congress of the European College of Sport Science between 28 - 30 October 2020.

Pedro Gargallo Bayo

University of Valencia
Camino Viejo de Alboraya 28, B, esc1 n13
46020 Valencia, Spain

Abstr.-ID: 2448, Presentation format: Oral , Session name: OP-PN07 - Molecular biology and biochemistry
Title: Effects of Power and Multi-component training with elastic resistance on oxidative stress, physical function and strength
Authors: Gargallo, P.1,2, Fernández-Garrido, J.1, Flández, J.3, Saez, G.1,2,4, Colado, J.C.1
Institution: 1Prevention and Health in Exercise and Sport Research Group , Department of Physical Education and Sport, University of Valencia, Valencia, Spain. 2Oxidative Pathology Unit, Department of Bioche
Presentation date: 29.10.2020, 08:00, Lecture room: Virtual 24h, No: 16

European College of Sport Science

This document has been created digitally and is valid without a signature

Summer Event - September 25-26, 2020. Alicante (Spain)

Costa Blanca Sports Science
Certificate of Communication

Effects of a power strength training with elastic bands on body composition, physical function and muscle strength in older women

To: Jorge Flandez; Pedro Gargallo; Javier Gene-Morales; Nicole Modena; Fernando Martin; Juan C. Colado

Prof. Dr. José Pérez Turpin

Alicante, October 5, 2020

Gmail - Fwd: 2020 NSCA Abstract Notification

Dear Fernando Martin,

Thank you for submitting your abstract for presentation at the 2020 NSCA National Conference in Las Vegas, NV. A panel of your professional colleagues conducted a blind review of the abstract. Each abstract was reviewed for formatting, scientific content, appropriate methodology, correct statistical analysis, proper interpretation of results, and contribution to the field of strength and conditioning.

Congratulations, the following abstract(s) that you are listed as an author on has/have been accepted for presentation. The format, award consideration, location, date, time, presentation number, and your role are listed below. You are scheduled to present any abstracts where your role is listed as Primary Presenter.

EFFECT OF MODERATE VERSUS HIGH-INTENSITY RESISTANCE TRAINING ON OXIDATIVE STRESS MARKERS AND ANTIOXIDANT CAPACITY IN OLDER WOMEN
Primary Presenter: Fernando Martin
Author: Pedro Gargallo
Author: Guillermo Saez
Author: Celia Bañuls
Author: Jorge Flandez
Author: Alvaro Juesas
Author: Juan C Colado

Format: Thursday Poster Session B
Date: Thursday July 9, 2020
Time: 2:00 PM - 3:30 PM
Room: Exhibit Hall
Your Role: Primary Presenter
Presentation Number or Poster Number: 31


V CONGRESO INTERNACIONAL
OPTIMIZACIÓN DEL ENTRENAMIENTO
Y READAPTACIÓN FÍSICO-DEPORTIVA
Certificado de Comunicaciones
- Autor 1: Pedro Gargallo Bayo
- Autor 2: Guillermo Sáez Tormo
- Autor 3: Julio Fernández Garrido
- Autor 4: Álvaro Juesas Torres
- Autor 5: Juan Carlos Colado Sánchez
Han expuesto su comunicación "Differential effects of Multi-component, Power and Traditional resistance training on balance and gait speed in older men" en el " V Congreso Internacional en Optimización del Entrenamiento y Readaptación Físico-Deportiva", celebrado los días 29 y 30 de mayo de 2020 por el Grupo Dogesport y la Fundación San Pablo Andalucía CEU.
Por lo que se expide el presente certificado a fecha de 8 de junio de 2020
Francisco Javier Muñoz Cintado
Fdo. Presidente del Comité Organizador
Grupo Dogesport
María Luisa Ríos Camacho
Fdo. Directora del Instituto de Posgrado
Fundación San Pablo Andalucía CEU
DOGESPORT
CEU
Fundación San Pablo Andalucía


V CONGRESO INTERNACIONAL
OPTIMIZACIÓN DEL ENTRENAMIENTO
Y READAPTACIÓN FÍSICO-DEPORTIVA
Certificado de Comunicaciones
- Autor 1: Pedro Gargallo Bayo
- Autor 2: Guillermo Sáez Tormo
- Autor 3: Álvaro Juesas Torres
- Autor 4: Jorge Flández Valderrama
- Autor 5: Juan Carlos Colado Sánchez
Han expuesto su comunicación "Comparison effects of Multi-component, Power and Traditional resistance training with elastic bands on strength in older men" en el " V Congreso Internacional en Optimización del Entrenamiento y Readaptación Físico-Deportiva", celebrado los días 29 y 30 de mayo de 2020 por el Grupo Dogesport y la Fundación San Pablo Andalucía CEU.
Por lo que se expide el presente certificado a fecha de 8 de junio de 2020
Francisco Javier Muñoz Cintado
Fdo. Presidente del Comité Organizador
Grupo Dogesport
María Luisa Ríos Camacho
Fdo. Directora del Instituto de Posgrado
Fundación San Pablo Andalucía CEU
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SMD

Gargallo P, Juesas A, Sáez G, Guzmán JF, Flández J, Colado JC.

HAN PRESENTADO LA COMUNICACIÓN ORAL TITULADA

Effects of multi-component, power and traditional resistance training on cardiovascular risk in older men

EN EL II CONGRESO INTERNACIONAL SOBRE PRESCRIPCIÓN Y PROGRAMACIÓN
DE DEPORTE Y DE EJERCICIO EN LA ENFERMEDAD CRÓNICA

CON UNA DURACIÓN DE 1,5 CRÉDITOS ECTS

Realizado en Murcia el 05 y 06 de marzo de 2020

Por la Cátedra Internacional de Medicina del Deporte de la Universidad Católica San Antonio de Murcia

Dr. D. Pedro Manonelles Marqueta
Presidente del Comité Organizador

José Alarcón Teruel
Secretario general de la UCAM


CONGRESO INTERNACIONAL
24, 25 y 26 Enero 2020
Jornadas teórico prácticas de alto nivel
Alto Rendimiento, Salud y Ejercicio Físico
READAPTACIÓN Y PREVENCIÓN de LESIONES en la actividad física y el deporte
VALENCIA 2020
6º
4º
SALUD Y EJERCICIO FISICO
CERTIFICADO DE COMUNICACIÓN
VALENCIA 27 DE ENERO, 2020
Pedro Gargallo Bayo
Ha presentado el Trabajo de Investigación con el Título:
MULTI-COMPONENT VS POWER TRAINING USING VARIABLE RESISTANCE: EFFECTS ON BONE HEALTH IN OLDER WOMEN.
En Coaturía Con: Jorge Flández, Joaquín Calatayud, Julio Fernámdez-Garrido, Guillermo Saez, Juan C. Colado.
en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020.
Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.
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CONGRESO INTERNACIONAL

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VALENCIA 27 DE ENERO, 2020

Pedro Gargallo Bayo

Ha presentado el Trabajo de Investigación con el Título:

EFFECTS OF POWER AND MULTI-COMPONENT TRAINING WITH ELASTIC RESISTANCE ON METABOLIC, LIPIDIC AND INFLAMMATORY PROFILE IN OLDER WOMEN

En Coautría Con: *Eva Tamayo, José F. Guzmán, Joaquín Calatayud, Julio Fernández-Garrido, Guillermo Saez, Juan C. Colado.*

en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020. Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.

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VALENCIA 27 DE ENERO, 2020

Pedro Gargallo Bayo

Ha presentado el Trabajo de Investigación con el Título:

WHICH TRAINING MODALITIES ARE MOST EFFECTIVE FOR IMPROVING GAIT SPEED AND BALANCE IN OLDER WOMEN. A 5-MONTH RANDOMIZED CONTROLLED TRIAL.

En Coaturía Con : *Álvaro Juesas, Jorge Flández, José Casaña, Guillermo Saez, Juan C. Colado.*

en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020. Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.

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CERTIFICADO DE COMUNICACIÓN

VALENCIA 27 DE ENERO, 2020

Pedro Gargallo Bayo

Ha presentado el Trabajo de Investigación con el Título:

IMPROVEMENT OF MUSCLE QUALITY IN OLDER WOMEN WITH DIFFERENT EXERCISE INTERVENTIONS

En Coaturía Con: *Alvaro Juesas, Jorge Flández Jose Casaña, Guillermo Saez, Juan C. Colado.*

en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020. Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.

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VALENCIA 27 DE ENERO, 2020

Pedro Gargallo Bayo

Ha presentado el Trabajo de Investigación con el Título:

COMPARISON EFFECTS OF MULTI-COMPONENT, POWER AND TRADITIONAL RESISTANCE TRAINING WITH ELASTIC BANDS ON BODY COMPOSITION AND CARDIOVASCULAR RISK IN OLDER WOMEN.

En Coaturía Con: *Javier Gené, Joaquín Calatayud, Jorge Flández, Guillermo Saez, Juan C. Colado.*

en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020. Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.

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Pedro Gargallo Bayo

Ha presentado el Trabajo de Investigación con el Título:

DIFFERENTIAL EFFECTS OF MULTI-COMPONENT, POWER AND TRADITIONAL RESISTANCE TRAINING ON HEALTH-RELATED QUALITY OF LIFE, ANXIETY AND DEPRESSIVE SYMPTOMS IN OLDER RISK IN OLDER WOMEN.

En Coaturía Con: *Javier Gené, Jessica Navarro, Rosa María Baños, José Casaña, Guillermo Saez, Juan C. Colado.*

en el 6º Congreso Internacional de Readaptación y Prevención de Lesiones en la Actividad Física y el Deporte y 4º Congreso Internacional de Salud y Ejercicio Físico, con 18h de duración, celebrado en Valencia durante los días 24, 25 y 26 de Enero de 2020. Para que conste a los efectos oportunos y a petición de la persona interesada, firmo el presente certificado.

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Otorga la presente

CONSTANCIA

A: PEDRO GARGALLO BAYO

Por impartir la ponencia

"EFECTO OSTEOGÉNICO DEL EJERCICIO FÍSICO EN LA EDAD ADULTA Y LA VEJEZ"

en el **4to. Congreso Internacional de Fisioterapia Momentum**
realizado en la **Ciudad de México, Octubre de 2017.**

GUY SIMONEAU PHD., PT.
Presidente Honorario
Congreso Internacional de Fisioterapia Momentum

FRANCISCO TAVERA BAUTISTA
Rector Sistema IPETH

momentum
cuerpo, salud & movimiento

IPETH

IPETH, INSTITUTO PROFESIONAL EN TERAPIAS Y HUMANIDADES

Otorga la presente

CONSTANCIA

A: PEDRO GARGALLO BAYO

Por impartir la ponencia

"TEJIDO ÓSEO, MUSCULAR Y GRASO: INTERCONEXIÓN E INFLUENCIA SOBRE LA FUNCIONALIDAD DEL ADULTO Y ADULTO MAYOR"

en el **4to. Congreso Internacional de Fisioterapia Momentum**
realizado en la **Ciudad de México, Octubre de 2017.**

GUY SIMONEAU PHD., PT.
Presidente Honorario
Congreso Internacional de Fisioterapia Momentum

FRANCISCO TAVERA BAUTISTA
Rector Sistema IPETH

Summer Event - September 25-26, 2020. Alicante (Spain)

Costa Blanca Sports Science
Certificate of Communication

Muscular activation on the lower limbs with five different variations of the squat exercise

To: Jorge Flandez; Javier Gene-Morales; Alvaro Juesas; Pedro Gargallo; Ivan Miñana; Juan C. Colado

Prof. Dr. José Pérez Turpin

Alicante, October 5, 2020

1º CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO

VALENCIA 30 DE ENERO, 2017

CERTIFICADO DE COMUNICACIÓN

PEDRO GARGALLO BAYO

HA PRESENTADO EL TRABAJO DE INVESTIGACIÓN TITULADO

INCREMENTO AGUDO DE LA FUERZA EXPLOSIVA DESPUÉS DE VARIOS PROTOCOLOS DE UNA INTERVENCIÓN MEDIANTE PAP.

EN EL 3ER CONGRESO INTERNACIONAL DE READAPTACIÓN Y PREVENCIÓN DE LESIONES EN LA ACTIVIDAD FÍSICA Y EL DEPORTE Y 1ER CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO, CELEBRADO EN VALENCIA DURANTE LOS DÍAS 27, 28 Y 29 DE ENERO DE 2017. PARA QUE CONSTE A LOS EFECTOS OPORTUNOS Y A PETICIÓN DE LA PERSONA INTERESADA, SE FIRMA EL PRESENTE CERTIFICADO

JUAN ÁNGEL MAÑAS MARTÍNEZ
PRESIDENTE DEL CONGRESO

JOSÉ CASAÑA GRANELL
SECRETARÍA TÉCNICA

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1ª CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO

VALENCIA 30 DE ENERO, 2017

CERTIFICADO DE COMUNICACIÓN

PEDRO GARGALLO BAYO

HA PRESENTADO EL TRABAJO DE INVESTIGACIÓN TITULADO

MEJORAS EN DIFERENTES VARIABLES FISIOLÓGICAS EN PERSONAS SEDENTARIAS TRAS UNA INTERVENCIÓN MEDIANTE HIIT.

EN EL 3ER CONGRESO INTERNACIONAL DE READAPTACIÓN Y PREVENCIÓN DE LESIONES EN LA ACTIVIDAD FÍSICA Y EL DEPORTE Y 1ER CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO, CELEBRADO EN VALENCIA DURANTE LOS DÍAS 27, 28 Y 29 DE ENERO DE 2017. PARA QUE CONSTE A LOS EFECTOS OPORTUNOS Y A PETICIÓN DE LA PERSONA INTERESADA, SE FIRMA EL PRESENTE CERTIFICADO

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1º CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO

VALENCIA 30 DE ENERO, 2017

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PEDRO GARGALLO BAYO

HA PRESENTADO EL TRABAJO DE INVESTIGACIÓN TITULADO

MIND-MUSCLE CONNECTION TRAINING PRINCIPLE: INFLUENCE OF MUSCLE STRENGTH AND TRAINING EXPERIENCE

EN EL 3ER CONGRESO INTERNACIONAL DE READAPTACIÓN Y PREVENCIÓN DE LESIONES EN LA ACTIVIDAD FÍSICA Y EL DEPORTE Y 1ER CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO, CELEBRADO EN VALENCIA DURANTE LOS DÍAS 27, 28 Y 29 DE ENERO DE 2017. PARA QUE CONSTE A LOS EFECTOS OPORTUNOS Y A PETICIÓN DE LA PERSONA INTERESADA, SE FIRMA EL PRESENTE CERTIFICADO

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1ª CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO

VALENCIA 30 DE ENERO, 2017

CERTIFICADO DE COMUNICACIÓN

PEDRO GARGALLO BAYO

HA PRESENTADO EL TRABAJO DE INVESTIGACIÓN TITULADO

EFECTOS EN GANANCIAS DE ALTURA EN SALTO VERTICAL Y FUERZA DINÁMICA MÁXIMA CON EL USO DEL FOAM ROLLING CONJUNTAMENTE A UN PROGRAMA DE ENTRENAMIENTO DE LA FUERZA

EN EL 3ER CONGRESO INTERNACIONAL DE READAPTACIÓN Y PREVENCIÓN DE LESIONES EN LA ACTIVIDAD FÍSICA Y EL DEPORTE Y 1ER CONGRESO INTERNACIONAL DE SALUD Y EJERCICIO FÍSICO, CELEBRADO EN VALENCIA DURANTE LOS DÍAS 27, 28 Y 29 DE ENERO DE 2017. PARA QUE CONSTE A LOS EFECTOS OPORTUNOS Y A PETICIÓN DE LA PERSONA INTERESADA, SE FIRMA EL PRESENTE CERTIFICADO

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APPENDIX D. CERTIFICATIONS OF INTERNATIONAL AND NATIONAL POSTERS

857 Board #91 May 29 3:30 PM - 5:00 PM

Multicomponent, Power, And Resistance Training With Elastic Resistance: Effects On Physical Function In Older Women

Michael E. Rogers, FACSM[1], Pedro Gargallo[2], Álvaro Juesas[2], Eva Tamayo[2], Sara Torkamanech[2], J.F. Guzmán[2], J. Fernández-Garrido[2], Guillermo Saez[2], Nicole L. Rogers[1], Juan C. Colado[2]. [1]*Wichita State University, Wichita, KS.* [2]*University of Valencia, Valencia, Spain.*
Email: michael.rogers@wichita.edu
(No relationships reported)

For older adults, the maintenance of muscle power and balance is a key factor in everyday task performance. Understanding the effects of emerging training modalities such as power training (PT) and multicomponent training (MT) compared to traditional resistance training (TRT) is of benefit to this age group.
PURPOSE: To investigate the effects of 20-weeks of PT, MT, and TRT using variable resistance (elastic bands with loops) on physical function in older women (OW).
METHODS: 136 sedentary OW (68.09 ± 4.78 yr) were randomized into PT (n=34), MT (n=34), TRT (n=34), and control groups (CG) (n=34). All exercise groups trained twice weekly for 20 weeks. PT performed 6 exercises, 3-4 sets of 10-12 repetitions, at a 4 rate of perceived exertion (RPE) in the first repetition and no more than 6 in the last. MT performed balance, muscular endurance (2 exercises, 3-4 sets of 15 repetitions at 7-9 RPE), aerobic, flexibility, and coordination exercises. The TRT performed 6 exercises, 3-4 sets of 6 repetitions at 7-9 RPE. Variables analyzed were static balance (Romberg), agility (Up & Go), gait speed (4m), muscle strength (30-s chair stand), and aerobic capacity (6-minute walk test). Trial (2) by group (4) repeated measures ANOVA was used to determine differences regarding time and groups.
RESULTS: MT showed significant improvements ($p<0.05$; +56.8%) in static balance with significant differences between TRT and CG. PT showed significant improvements in all variables except static balance, with significant differences between MT and CG in muscle strength (PT: +29.20%; MT: +21.14%; CG: -2.69%), being the group with greatest improvements in 3 of 5 variables (agility: -14.26%; gait speed: -13.83%; muscle strength: +29.20%). PT, MT, and TRT showed significant improvements over time and between CG in agility, gait speed and aerobic capacity. No significant changes were observed for the CG.
CONCLUSIONS: The three interventions are effective in improving physical function in OW, although the PT program induces greater adaptations in lower limb muscle strength, gait speed, and agility, while MT had a larger influence on balance. The use of elastic bands with loops (CLX bands) can facilitate the application of these types of programs.

856 Board #90 May 29 3:30 PM - 5:00 PM

Effects Of Resistance, Power, And Multicomponent Training With Elastic Resistance On Strength In Older Women

Nicole L. Rogers[1], Pedro Gargallo[2], Álvaro Juesas[2], Eva Tamayo[2], Sara Torkamanech[2], J.F. Guzmán[2], J. Fernández-Garrido[2], Guillermo Saez[2], Michael E. Rogers, FACSM[1], Juan C. Colado[2]. [1]*Wichita State University, Wichita, KS.* [2]*University of Valencia, Valencia, Spain.* (Sponsor: Michael E. Rogers, FACSM)

Email: nicole.rogers@wichita.edu

(No relationships reported)

The associations between strength losses in lower limbs and functional limitations are high for older adults. It is necessary to know the effects of modalities such as power training (PT) and multicomponent training (MT) on muscle strength compared to traditional resistance training (TRT) in this population.

PURPOSE: To investigate the effects of 20-weeks of PT, MT, and TRT using variable resistance (elastic bands with loops) on isokinetic strength in older women (OW).

METHODS: 136 sedentary OW (68.09 ± 4.78 yr) were randomized into PT (n=34), MT (n=34), TRT (n=34), and control groups (CG) (n=34). All exercise groups trained twice weekly for 20 weeks. PT performed 6 exercises, 3-4 sets of 10-12 repetitions, at a 4 rate of perceived exertion (RPE) in the first repetition and no more than 6 in the last. MT performed balance, muscular endurance (2 exercises, 3-4 sets of 15 repetitions at 7-9 RPE), aerobic, flexibility, and coordination exercises. The TRT performed 6 exercises, 3-4 sets of 6 repetitions at 7-9 RPE. Maximum strength of knee extensors (KE) and hip abductors (HA) was measured at 60°/s and 180°/s in the dominant side with an isokinetic dynamometer. Trial (2) by group (4) repeated measures ANOVA was used to determine differences regarding time and groups.

RESULTS: PT group showed a significant increase in HA (+89.61%) and KE (+22.75%) muscle strength at 180°/s with significant differences ($p<0.05$) between MT, TRT, and CG groups for HA, and between CG for KE. TRT group showed a significant improvement in HA (+76.74) and KE (+11.29) at 60°/s with significant differences between CG in both. MT showed a significant increase in HA at 60°/s (+13-5%) and 180°/s (+29.85%), and also in KE at 60°/s (+4.62%) with significant differences between CG in HA at 180°/s and KE at 60°/s. No significant changes were observed for the CG.

CONCLUSIONS: PT is the most effective training modality for increasing muscle strength output at high velocity, while TRT is more effective for improving maximal strength at low velocity, for HA and KE. MT can be an effective alternative as it induces adaptation at high velocity on HA and at low velocity on KE. The use of elastic bands with loops (CLX bands) can facilitate the application of these types of programs.

J Perform Health Res. 2018. 2(2)

Effects of multicomponent and power training programs using elastic devices on motor function, body composition, and metabolic, bone and inflammatory profile in older adults

J.C. Colado,[1,2] P. Gargallo,[1] A. Juesas,[1] S. Torkamaneh,[2] E. Tamayo,[2] J.F. Guzmán,[1] J. Fernández-Garrido,[1] and G.T. Sáez[1,3]

[1]*Research Group in Prevention and Health in Exercise and Sport, University of Valencia, Spain*
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[3]*Service of Clinical Analysis, Hospital Universitario Doctor Peset-FISABIO, University of Valencia, Valencia, Spain*

Background: It is needed to understand what type of training strategy can be the most effective for contributing to a healthier, active, and more independent elderly population. Nowadays, there are novel types of training interventions and devices, but only little is known regarding whether these can provoke positive benefits in this target population. Concretely, no evidence has examined the effectiveness of high-speed resistance training and multicomponent training in older adults in respect of not only physical function but also bone, immunity, and metabolic status. Developing an understanding these novel training strategies can ultimately provide a viable alternative to traditional modes of exercise training for a broader range of participants.

Purpose: The purpose of this paper was to investigate the effects of a high-speed resistance training and multicomponent training program with variable resistance on molecular, body composition, and physical functions in older adults.

Design: This study used a randomized clinical trial with the following 3 parallel arms: (1) high-speed/power elastic band CLX resistance training group (P) (6 exercises at 10–12 repetitions (R) at 4–6 rate of perceived exertion (RPE), 3–4 sets, 60-s rest); (2) multicomponent training group (MC) (balance, aerobic [65% at 85% maximum heart rate), flexibility, muscular endurance (2 exercises with CLX elastic bands, 3–4 sets, 15 R at 8–9 RPE, 60-s rest and ratio 2/2]) and coordination); and (3) control group (CG). Subjects developed a 20-week training program with 2 sessions each week: each session lasted 75 min for P (325 kcal/session) and 60 min for MC (317 kcal/session). Variables analyzed were bone metabolism; metabolic, inflammatory, and immune profile; functional performance; and fat mass. Statistical analysis was developed with SPSS (Version 24.0, SPSS Inc., Chicago, IL). All data were reported as mean and standard deviation. The assumption of normality and homogeneity of the dependent variables was verified with the Kolmogorov–Smirnov and Levene tests, respectively. An analysis of repeated measures was used to determine the effects of the group and moment on the variables analyzed. When significant differences were found, Bonferroni post hoc test was applied. A 95% confidence level was accepted (significance of $P < 0.05$). Cohen coefficients (value *d*) were used as indicators of effect size in intragroup evolution (trivial, <0.02, 0.2–0.49; moderate, 0.5–0.8; large, >0.8). The percentage increase/decrease of each variable was calculated with the following formula: % = [(posttest value – pretest value/pretest value] × 100.

Results: There were no significant changes for CG in assessment of hip perimeter, glycosylated hemoglobin, C-reactive protein, osteocalcin; up and go, Romberg, functional, 5-repetition sit-to-stand, 30-s chair stand, 30-s elbow flexion, and manual dynamometry; 4-Meter Gait Speed and 6-min walk tests. CG got significantly worse in percent body fat, waist perimeter, glycemia, cholesterol, LDC-c, triglycerides, type 1 cross-linked C-telopeptide, and climbing stairs and 10-meter gait speed's tests. P and MC had positive significant changes in all these variables without differences between them and with significant changes regarding CG. MC had positive changes in C-reactive protein level for P and CG, and the P group showed significant and positive differences in osteocalcin level, 5-repetition sit-to-stand and 30-s chair stand, and manual dynamometry tests for MC and CG. MC was the only group with significant changes in lymphocytes, although without intergroup differences.

Conclusions: Although both groups had similar caloric consumption in each session, the most important findings of this study were that a P program with high volume can improve metabolic risk parameters like an MC program, in which endurance activities are predominant. Moreover P training provoked larger positive adaptations in bone profile and strength. Meanwhile MC training had a larger influence on inflammatory and immune profiles. Positive improvements were equal in both groups regarding body composition, balance, and mobility. Trainers, physicians, and physiotherapists must take into account the different adaptions for prescribing more efficient training programs in this type of population. CLX bands could provoke very significant health improvements in older people.

ADAPTATIONS IN MUSCLE MASS AND MOTOR FUNCTION DURING RESISTANCE TRAINING WITH ELASTIC BANDS AT DIFFERENT INTENSITIES IN OLDER ADULTS

GARGALLO, P.1, MUNOZ, V.1, JUESAS, A.1, SAEZ, G.1,2, HERNANDO, A.2, IRADI, A.3, COLADO, J.C.1

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1: University of Valencia (Valencia, Spain), 2: Clinical Analysis, Universitary Hospital Dr. Peset, (Valencia, Spain), 3: Physiology Department, University of Valencia (Valencia, Spain). Introduction Resistance training (RT) is an intervention frequently used to improve muscle strength and body composition in older adults (OA) (Chodzko-Zajko et al., 2009). Despite this, there is a lack of knowledge on how elastic resistance training (ERT) affects the muscle mass (MM) and motor function (MF) in this population. The purpose of this study was to determine the effects of ERT at different intensities on MM and MF in OA. Methods 121 OA (70.07 ± 5.12 years) were randomized into three groups: Control Group (CG) (n=45); High Intensity Group (HIG) (n=39); and Moderate Intensity Group (MIG) (n=37). A 16 weeks (WK) elastic resistance training (ERT) (TheraBand) program twice a WK was applied with 6 exercises. HIG were performed with 6 repetitions (REP) while MIG with 15 REP and both at intensity of 6-7 on the OMNI-RES perceived exertion for the first 4 WK and 8-9 the next 12. Total, upper, lower limbs MM and isometric strength (IS) were measured. Nonparametric tests were performed. Results The results showed significant improved in HIG and MIG respectively, comparing pre and post-training in total MM (+1.73 and +1.55%), upper limbs MM (+6.35 and +4.75%) and lower limbs MM (+2.99 and 2.64%). Regarding IS, HIG and MIG had significant improvements in vertical rowing (+38.71 and +46.19%, respectively) and horizontal leg press (+52.82 and 73.07%, respectively). Analysis between groups showed no significant effects. Discussion Our results could indicate that variables of prescription applied are not enough stimuli to provoke significant effects between intensities in OA and agree with previous studies (Borde R, Hortobágyi T, Granacher U, 2015; Martins et al., 2015). ERT are an effective method for improving MM and MF in OA but more research is necessary to identify the effect of different intensities in middle and long programs. References Borde R, Hortobágyi T, Granacher U. (2015). Dose-Response Relationships of Resistance Training in Healthy Old Adults: A Systematic Review and Meta-Analysis, Sport Med, 45(12), 1693-1720. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, Salem GJ, Skinner JS. (2009). American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc, 41(7),1510–1530. Martins WR, Safons MP, Bottaro M, Blasczyk JC, Diniz LR, Fonseca RM, Bonini-Rocha AC, Oliveira RJ. (2015). Effects of short term elastic resistance training on muscle mass and strength in untrained older adults: a randomized clinical trial. BMC Geriatrics, 12, 15-99. Contact: pedro11gb@gmail.com

THE RELATIONSHIP BETWEEN AMOUNT OF PHYSICAL ACTIVITY AND SLEEP HABITS IN UNIVERSITY STUDENTS

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Introduction It has been reported that people having some sleep problems is about 13% in Japan (Ministry of Health, Labour and Welfare, Japan, 2011). In addition, people who feel daytime sleepiness were 37.7% in male and 43.0% in female (Ministry of Health, Labour and Welfare, Japan, 2013). However, it has been reported that increased amount of physical activity improved sleep quality (King et al., 1997). On the other hand, it has also been reported that Japanese students had shorter sleep hours than the other countries (Steptoe A et al., 2006). The purpose of this study is to examine the relationship between amount of physical activity and sleep habits in university students. Methods Subjects in this study were 1,741 university students with a mean age of 19.9±1.4 (±SD). We carried out a questionnaire from November to December 2011 and 2012. The questionnaire was composed of personal profiles, life-style, including physical activity and sleep habits. In this study, it was classified people performing habitual physical activity into three levels by physical activity minutes per week; under 120 minutes (under 120), under 600 minutes (under 600) and over 600 minutes (over 600). Sleep quality was assessed by Japanese version of Pittsburgh Sleep Quality Index (PSQI-J). Lower sleep quality was assessed by using a cutoff total score point of >5.5. Daytime sleepiness also was assessed by Japanese version of Epworth Sleepiness Scale (JESS). Statistical analysis used SPSS ver.21.0. Statistical analysis used by analysis of variance, χ2test, Mann-Whitney U-test and correlative analysis and multiple. Results The amount of physical activity divided into four categories, those were non-habitual, under 120, under 600 and over 600 minutes per week. We compared with those four categories for male and female respectively. Compared with four categories, ratio of non-habitual students increased according to grade year rises in male and female. In male, there were significant differences in weight, BMI and points of JESS. The under 120 was lower than the other categories in the points of JESS. The under 120 group had a tendency to later the time of getting up than the other categories. In female, the over 600 was significantly shorter than the other categories in hours to fall asleep. Discussion It became clear that there were differences of male and female in the relationship between amount of physical activity and sleep habits. In female, increased amount of physical activity improved sleep latency, but not improved in male. In male, increased amount of physical activity increased daytime sleepiness because of earlier getting up time in the morning. It was suggested that the amount of physical activity was not necessarily related to sleep quality in university students. Acknowledgment This study was supported by grant from Grants-in Aid for Scientific Research (C), (JSPS KAKENHI Grant Number 23601021), 2011-2013. Contact Please contact to SASAKI Hiroko (hiros22@hokusho-u.ac.jp)

EFFECTS OF GROUP EXERCISE CLASS FOR REGIONAL ELDER PEOPLE HELD AT THE UNIVERSITY ON FUNCTIONAL FITNESS AND HEALTH-RELATED QUALITY OF LIFE

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Purpose The purpose of this study was to investigate the effect of regional elder people on functional fitness and health-related quality of life (HRQOL) in group exercise classes held at the university. Methods Twenty-nine healthy people (age; 69.0±3.4years, men; n=13, age; 70.2±2.6, female; n=16, age; 68.0±3.6 years) volunteered to participate in this study. Subjects participated in 8-week group exercise class (90min./d, 2times/week, total 16 sessions). This exercise program consisted of 15 min. of warm-up and stretching, 20 min. of resistance exercise, 10 min. of step exercise, 20 min. of endurance-type exercise (walking), 20 min. of ball exercise (recreation), and 5 min. of cooling down. All exercise session was led by trained fitness instructors and supervised by the researchers. After the every exercise session, subjects were recorded Borg scale. Before (pre-) and after (post-) the group exercise classes, the following physical performances were measured; hand grip strength (HG), chair stand (CS), arm curl (AC), sit-up (SU), timed up & go (TUG), sit & reach (SR), back scratch (BS), functional reach (FR), 10-m walking (10-mWK), 10-m obstacle walking (10-mOWK) and 6-min walking (6-MW). In addition, blood pressure, brachial-ankle pulse wave velocity (baPWV), body composition, blood property, and 36-Item Short Form Survey (SF-36) were measured before and after the course. Results Participation rate of the group exercise class was 88.3±8.9%. Borg scale in the exercise class was

PHYSICAL FITNESS OF LITHUANIAN PRIMARY SCHOOL CHILDREN. PILOT STUDY

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Lithuanian Sports University

Introduction At present, studies have shown that despite the physical activity recommendations and greater investment in the promotion of children's physical activity, there is still not enough attention paid to testing children's physical fitness. In particular, there is a lack of analysis of younger school-age children's physical fitness and its influencing factors. It is well known that underdeveloped physical abilities of children have a negative impact on their health and well-being in childhood and adulthood (Corbin et al., 2014). Therefore, such studies are very important aiming at improving children's health indicators. Methods Data from 242 primary school students aged 7 – 11 years were gathered, 52.7% of them were boys. The 9 items test battery, developed by Fjørtoft et al. (2011), included the following tests: standing broad jump, jumping a distance of 7 m on 2 feet, jumping a distance of 7 m on one foot, throwing a tennis ball with one hand, pushing a medicine ball with 2 hands, climbing wall bars, performing a 10 x 5 m shuttle run, running 20 m as fast as possible, and performing a reduced Cooper test (6 minutes). Results Boys performed better than girls ($p < .05$) on total fitness and most separate tests, except for performing a 10 x 5 m shuttle run, jumping a distance of 7 m on 2 and 1 feet. Comparison of physical abilities of differently aged boys has shown that strength and strength endurance indicators improve with age. Agility, coordination, aerobic endurance did not statistically significantly differ comparing the indicators for 7-, 8-, 9-, and 10- year-old boys. Comparing physical fitness indicators for differently aged girls we did not find statistically significant differences. Height, weight, BMI and body fat mass were not related to the total physical fitness. Pushing a medicine ball with 2 hands was associated with a higher score on height, weight and BMI (r= .332, .343, .260, respectively). Discussion Results obtained from the girls do not reflect the distribution of the overall children's physical fitness indicators in the aspect of age groups. While the improvement of these indicators is observed with age, it is not statistically significant ($p > .05$). These findings may be influenced by the small sample size which is characteristic of the pilot study. We did not observe significant differences comparing physical fitness indicators for children in Lithuania and other countries. Boys' physical fitness indicators improved with age and were statistically significantly ($p < .05$) different from those of girls. References Corbin, C. B., Welk, G. J., Richardson, C., Vowell, C., Lambdin, D., & Wikgren, S. (2014). Recreation & Dance, 85(2), 24-31. Fjørtoft, I., Pedersen, A. V., Sigmundsson, H., & Vereijken, B. (2011). Physical Therapy, 91(7), 1087-1095.

EFFECTS OF RESISTANCE TRAINING WITH ELASTIC BANDS AT DIFFERENT LEVELS OF INTENSITY ON THE IMMUNE SYSTEM OF OLDER ADULTS

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University of Valencia

1: University of Valencia (Valencia, Spain), 2: Clinical Analysis Service, Universitary Hospital Dr. Peset, (Valencia, Spain). Introduction Resistance training has proven to be an efficient method for the improvement of the immune system (IS) in older adults (OA) but there are no evidences that the use of elastic bands is efficient for these purposes. The main objective of this study was to analyse the chronic effects of a strength training program with elastic bands at different intensities, on the IS parameters and the inflammatory profile of OA. Methods 86 OA (69.47 ± 5.16), were randomized in 3 groups: Control group (CG) (n=37), Moderate Intensity Training Group (MITG) (n=26) and High Intensity Training Group (HITG) (n=23). 16 weeks (WK) of elastic bands (TheraBand) resistance training program was conducted, twice a WK, with 6 exercises. The training groups exercised at moderate and high intensity, performing 15 and 6 repetitions respectively, with a perceived exertion of 6-7 OMNI-RES for the first 4 WK and 8-9 the next 12 WK. Leukocytes (LK), neutrophils (NT), lymphocytes (LP), monocytes (MN), eosinophils (EN), basophils (BS), C-reactive protein (CRP) and interleukin 6 (IL) were measured. Non parametric tests were performed. Results Main results showed significant differences between HITG and MITG in LP and MN ($p<0.05$) and a tendency in LK post measurement ($p <0.09$) was detected. Differences in between the HITG and CG were found in LK and MN ($p<0.05$). Significant differences occurred in the intragroup results of HITG in the LK (-7.27%) and monocyte variable (-20%). In the intragroup analysis, in MITG and HITG CRP diminished (-22,1% and -18,58% respectively), whereas CG increased IL-6 (+15,78%). Discussion Training protocol performed improved the immune response of both groups, even though high intensity is linked to a worsening of it. So, although it is claimed that there are no chronic changes in the IS in studies of less than 6 months of duration (Walsh et al., 2011), it has been proven that, after 4 months, signs of improvement of this system can be detected. References Walsh NP, Gleeson M, Shephard RJ, Gleeson M, Woods JA, Bishop, NC, Fleshner M, Green C, Pedersen BK, Hoffman-Goetz L, Rogers CJ, Northoff H, Abbasi A, Simon P. (2011). Position statement part one: immune function and exercise. Exerc Immunol Rev, 17, 64-103. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. (2011). The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol, 11(9), 607-615. Contact: Victor.m.cutillas@gmail.com

THE RELATIONSHIP BETWEEN PHYSICAL ACTIVITY, INACTIVITY AND PHYSICAL FITNESS AMONG LITHUANIAN PRIMARY SCHOOL CHILDREN

EMELIANOVAS, A., MIEZIENE, B., CESNAITIENE, V., PETERYTE, I., DAUGININKAS, D.

Lithuanian sports university

Introduction Recently it is emphasized that physical education should focus on physical fitness rather than physical activity (Corbin et al., 2014). Health related physical fitness acts as a preventive factor to various chronic diseases. The aim of this study is to examine the relationship of physical fitness and physical activity as well as inactivity in Lithuanian primary school students. Methods Data from 242 primary school students from grade 1 to grade 4 were gathered, 52.7% were boys. The 9-item test battery was applied tomeasure physical fitness. The test baterry was developed by Fjørtoft et al. (2011) and included tests: standing broad jump, jumping a distance of 7 m on 2 feet, jumping a distance of 7 m on one foot, throwing a tennis ball with one hand, pushing a medicine ball with 2 hands, climbing wall bars, performing a 10 x 5 m shuttle run, running 20 m as fast as possible, and performing a reduced Cooper test (6 minutes). Data about leisure time physical activity and sitting time were also gathered. Results Regression analysis revealed that physical activity was related to total physical fitness ($\beta = .228$, $t=-2.590$, $p=.011$) and added 5% to total physical fitness variance until the inactivity was added to the equation. Then it became insignificant ($p> .05$). The results were obtained controlling for gender and age. Meanwhile, physical inactivity predicted lower total physical fitness ($\beta=-.278$, $t=-3.057$, $p=.003$) and added 6% to the explanation of physical fitness variance. Physical activity had positive predictive value on reduced Cooper test ($\beta = .200$, $t=1.955$, $p=.05$). Physical inactivity predicted lower scores on throwing a tennis ball, running 20 m, performing a 10 x 5 m shuttle run ($\beta=-.225$, $t=-2,593$, $p=.011$); $\beta=.205$, $t=2,003$, $p=.048$; $\beta=-.275$, $t=-2,623$, $p=.010$, respectively). Discussion Results of this study support the premise that poor physical fitness related to low physical activity,

CERTIFICADO

La Escuela de Kinesiología de la Universidad Finis Terrae certifica que

Fritz, N., Colado JC., Juesas, A., Gargallo, P., Muñoz, V.

Participaron en calidad de asistentes y presentaron como Poster la siguiente investigación: "**Short-term effects of strength training with elastic bands at different levels of intensity on body composition, motor function and wellness in older adults"** en el **VI Congreso Internacional de Ciencias del Deporte**, organizado por la Escuela de Kinesiología de la Universidad Finis Terrae en colaboración con Copenhagen Centre of Team Sports and Health de la University of Copenhagen realizado el 18 y 19 de diciembre de 2015 en Santiago, Chile.

Dr. Hermann Zbinden, PhD.
Presidente Congreso
Universidad Finis Terrae

Santiago, diciembre de 2015

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Effects of a resistance training program on functional performance, oxidative stress and cardiovascular risk factors in healthy older adults

Ronda Serrat, Mar[1]; Colado Sánchez, Juan Carlos[2]; Hernandez Espinilla, Amaya[3]; Gargalló Bayo, Pedro[2]; Iradi Casal, Antonio[4]; Muñoz Cutillas, Victor[2]; Estany Capell, Nuria[3]; Juesas Torres, Álvaro[2]; Tormo Muñoz, M.Carmen[1]; Monzó Beltrán, Lidia[1]; Rivera Ballesteros, Sergio[1]; and Sáez Tormo, Guillermo[5].
[1]Faculty of Medicine-INCLIVA (University of Valencia), Department of Biochemistry and Molecular Biology, Valencia, Spain; [2]Research Group in Sport and Health (University of Valencia), Valencia (Spain); [3]University of Valencia - INCLIVA (Universitary Hospital Doctor Pesset), Valencia (Spain); and [4]Faculty of Medicine-INCLIVA (University of Valencia), Department of Physiology, Valencia, Spain; [5]Oxidative Stress Commission-SEQC, Faculty of Medicine-INCLIVA (University of Valencia), Department of Biochemistry and Molecular Biology, University Hospital Dr. Peset, Valencia, Spain.

Introduction

Aging is known to develop parallel to different cardiovascular and metabolic complications. Vast amount of literature supports the theory of the Free Radicals as the explanation for the aging process. Hypothesis of how physical activity can improve this aging progression are made. However, contradiction is obvious based on the concept that physical exercise increases oxidative stress.

Incongruity can come from the fact that there are different types of physical exercise, each one producing a distinct action on many body macromolecules. We therefore try to establish an exercising protocol on older adults for being trained and to assess its effects on their clinical and oxidative stress status.

Material and methods

96 healthy adults (60 – 88 years old) were randomly distributed in the control group or the exercise groups with different resistance intensities (15RS or 6RS) twice a week during a regular 4-months exercise. Functional performance was recorded and representative markers of lipid metabolism, oxidative stress and related cardiovascular risk factors were analyzed in blood and urine of all participants following standard laboratory methods.

Results and conclusions

We observed an on-going and significant decrease of the oxidative footprints on lipids (LDLox and 8-isoprostanes) together with an improvement of the lipid metabolic profile in the older adult group after exercise. Functional performance and cardiovascular risk was improved without significant differences between exercises groups.

The obtained results may emphasize the important role of a controlled exercise program for the prevention of oxidative stress and cardiovascular related alterations in the older adult subjects.

Supported by PI13/01848, Plan Estatal de I D I 2013-2016; ISCIII-Subdirección General de Evaluación y el Fondo Europeo de Desarrollo Regional (FEDER). Department of Social Welfare of the City of Valencia (Spain). Fundación Mapfre.

AMERICAN COLLEGE of SPORTS MEDICINE®
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3441 Board #202 May 30, 9:30 AM - 11:00 AM

Effects Of Resistance Training With Elastic Bands At Different Levels Of Intensity In Older Adults

Nicole Fritz[1], Juan C. Colado[2], Pedro Gargallo[2], Joaquín Madera[2], Joaquín Calatayud[2], Michael E. Rogers, FACSM[3]. [1]*Universidad Austral, Valdivia, Chile.* [2]*University of Valencia, Valencia, Spain.* [3]*Wichita State University, Wichita, KS.* (Sponsor: Michael E. Rogers, FACSM)

(No relationships reported)

Resistance training using weights is a good method for increasing the functional fitness of older adults, but less is known about the efficiency of non-traditional devices in this population.
PURPOSE: To analyze the effects on performance of a short-term resistance training program with elastic bands (EB) at different intensities in older adults.
METHODS: 105 older adults (69.90 ± 5.47 yr) took part in two familiarization sessions where they were instructed on the technique of EB exercises and use of the OMNI-RES for EB to evaluate perceived exertion. A total of 15 (15group (G), n=26), 10 (10G, n= 28) or 6 (6G, n= 28) repetitions were performed for each set at an intensity of 6-7 on the OMNI-RES for the first 3 wk and 8-9 the next 5 wk. Recovery times between sets were: 60, 90 and 120 sec for the 15G, 10G, and 6G, respectively. Two sec were allowed for each phase of the movements. The following exercises were performed for 2 sessions per wk: vertical and inclined rowing, elbow flexion, squat with wide and narrow base of support, and lunge. A control group (CG, n=23) continued normal activities without performing any new physical training. Dependent variables measured pre/post were: isometric maximum strength (IMS) for vertical rowing, squat and back extension; and functional fitness with the Senior Fitness Test (SFT).
RESULTS: After averaging the results for all SFT assessments, the exercise groups improved significantly ($p<0.05$) compared to the CG, but there were not differences between the exercise groups (+25.66% 15G, +29.18% 10G, and +28.07% 6RG). The CG had a significant ($p<0.05$) decrease of 6.75% for the SFT. Increases ($p<0.05$) in IMS were also similar between exercise groups (15G +32.99%, 10G +30.91%, 6G +32.91%) while the CG decreased 5.04%.
CONCLUSION: EB are an effective tool for improving performance and adaptations are similar between exercise intensities in short-term programs. Further research is needed to evaluate the effects of longer programs of different intensities.

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CERTIFICADO DE PARTICIPACIÓN

La Presidenta del Comité Científico del
XII Congreso Nacional del Laboratorio Clínico

CERTIFICA QUE:

A. Hernando Espinilla, P. Gargallo Bayo, J.C. Colado Sanchez, L. Monzó Beltrán, M. Santaolaria Ayora, A. Carbonell Moncho, G. Sáez Tormo

han presentado el póster con título:

Efecto del entrenamiento de fuerza sobre el estado redox y lesión del material genético en mujeres adultas mayores.

en el **XII Congreso Nacional del Laboratorio Clínico,**
celebrado en Bilbao del 24 al 26 de octubre de 2018

Y para que conste se expide el presente certificado en Bilbao,
a 26 de octubre de 2018.

DOCUMENTO FIRMADO DIGITALMENTE

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Presidenta del Comité Científico

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266 Board #107 May 30 9:30 AM - 11:00 AM

Squatting With Elastic Bands Facilitates More Weight Used And Time Under Muscle Tension

Nicole L. Rogers[1], Javier Gene[2], Alvaro Juesas[2], Pedro Gargallo[2], Andres Gene[2], Rosario Salvador[2], Juan C. Colado[2], Michael E. Rogers, FACSM[1].
[1]*Wichita State University, Wichita, KS.* [2]*University of Valencia, Valencia, Spain.* (Sponsor: Michael E. Rogers, FACSM)
(No relevant relationships reported)

In has been shown that the variable resistance associated with elastic band training improves strength and several other outcomes. However, the efficacy of combining elastic bands (EB) with traditional resistance exercises is not well understood.
PURPOSE: To evaluate performance (kg used and number of repetitions) during the squat exercise using free weights (FW) versus FW with EB applied with tension at the sticking point (50 degrees of knee flexion).
METHODS: Twenty healthy, physically active men (25.5±4.7 yr) with resistance training experience performed four squat conditions on a Smith Machine in random order: (A) 10 maximum repetitions (RM) with FW; (B) 10RM with CLX EB added at the stand-up position (SUP) with the weight of 10RMFW; (C) number of repetitions with CLX EB added at the SUP using the weight of 10RMFW; (D) number of repetitions with CLX EB added at 50 degrees of knee flexion prior to the SUP using the weight of 10RMFW. Goniometer, tactile markers, and metronome were used to standardized range of motion and pace of movement. The eccentric phase was performed at a pace of 2 sec with a 1 sec pause before the concentric phase performed with maximum velocity. A validated bascule was used to measure kg. Friedman test identified differences between conditions and Wilcoxon signed-rank tests examined where differences occurred.
RESULTS: Condition D employed more ($p<0.05$) weight than the other conditions (+24.70%). Conditions C and D performed more RM than the other conditions (8.4 and 3.45, respectively) with significant differences between conditions 3 and 4.
CONCLUSIONS: Performing resistance exercises with EB increased the kg employed and time under muscle tension. This could be because EB provide an additional element of variable tension that changes through the range of motion. Combining EB with traditional weight training exercises may enhance the training effect.

extremity maximal and rapid strength and reaction time in career firefighters. **Methods:** Thirty-two firefighters (29 males, 3 females; age: 33.7 ± 9.2 years [20–50]; stature: 177.2 ± 7.6 cm [153.0–190.5]; mass: 94.5 ± 20.8 kg [64.0–152.0]; BMI: 30.0 ± 5.5 [22.0–44.4]) volunteered for this repeated measures investigation. Participants performed leg extension isometric maximal voluntary contractions (MVC) on a custom-built calibrated isometric load-cell dynamometer. Maximal strength, or isometric peak force (PF), was calculated as the highest 100 ms value during the MVC plateau. Absolute and normalized (%MVC) force variables were calculated from the force-time curve at 50, 100, 150, and 200 ms from onset (F_{50}, F_{100}, F_{150}, and F_{200}). Reaction time (RT) was measured concurrently with the strength assessments. By using a randomly delayed light stimulus which signaled the participants to initiate the isometric MVC, RT was determined as the time period between the light stimulus presentation and the onset of force production. Following 2–3 submaximal warm-up contractions, participants performed 3–4 MVCs with a 2 minute recovery period in between each muscle contraction. Local firefighters work three 24-hourshifts on-off over one rotation followed by 4 days of rest. Testing occurred on 3 separate occasions at local fire stations. During the first testing session, participants were familiarized with the testing procedure after finishing a rotation. Four days following the familiarization session, in coordination with the start of the participants' respective shift rotation, pre-testing (PRE) was performed. All participants were instructed to avoid strenuous exercise 24 hours preceding testing. At the conclusion of the participants' respective shift rotation, 5 days after PRE, post testing (POST) was completed. Independent *t*-tests were performed on all variables to examine differences between PRE and POST rotation. An alpha level was set a priori at $p \leq 0.05$ for all analyses. **Results:** There were no significant differences in PF ($p = 0.594$), absolute and normalized F_{50} ($p = 0.072$; $p = 0.072$), F_{100} ($p = 0.484$; $p = 0.445$), F_{150} ($p = 0.740$; $p = 0.614$), F_{200} ($p = 0.980$; $p = 0.761$), respectively, and RT ($p = 0.349$) between PRE and POST. **Conclusions:** These findings indicate that the repeated bouts of shiftwork (i.e., three 24-hourshifts) do not significantly influence maximal and rapid strength, or reaction time in career firefighters. **Practical Applications:** The results of the current study indicate that a work schedule that includes a 24-hour, 3 day on-off schedule may not influence lower extremity neuromuscular function in career firefighters. However, work volume and sleep may be important factors that should be considered in future research as shift workload may vary considerably across fire stations. **Acknowledgments:** This project was sponsored in part by a grant from the National Institute of Occupational Safety and Health (T42OH008673).

Potentiation Post-Activation Effects on a Squat Jump Using Elastic Resistance or Free Weights

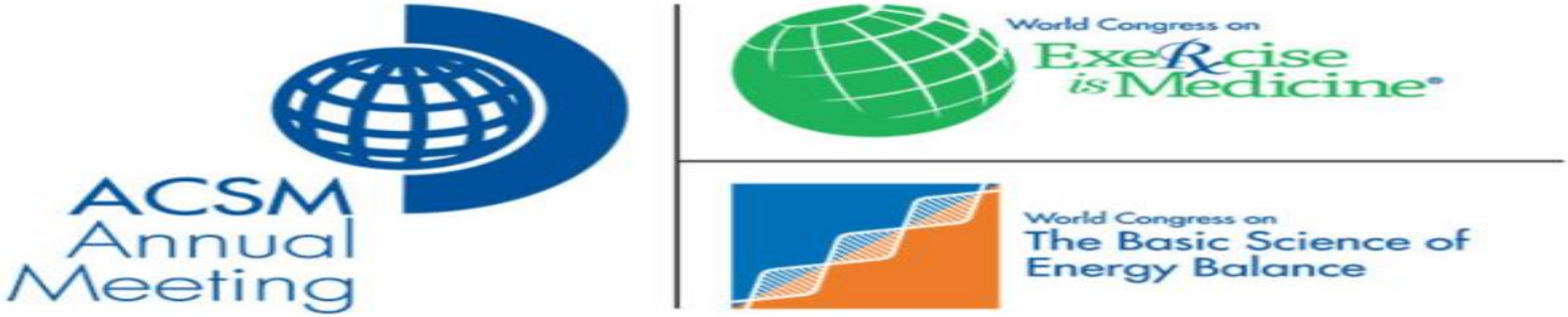
F. Martin, J. Calatayud, J. Casaña, J. Hernández, P. Gargallo, A. Juesas, and J. Colado

University of Valencia

Purpose: the study aimed to evaluate the post-activation potentiation (PAP) effects of using elastic resistance or free-weights on squat jump performance. **Methods:** Twenty-five subjects with less than 6 months of resistance training experience (age: 20.71 ± 1.42 years; weight: 73.98 ± 7.78 kg; height: 173.38 ± 6.87 cm; body fat: 14.01 ± 4.46%) were randomly assigned to 2 experimental groups: Elastic Resistance or Free Weight. The subjects participated in 2 different sessions. During the first session, the anthropometric variables were taken and the subjects were randomly assigned to one of the groups: elastic resistance or free-weights. Afterwards, a 6 repetition-maximum (RM) test was determined during a Squat exercise performed either with elastic resistance or free-weights (according with the respective group). In the second session, a squat jump (measured with a force plate) was assessed prior to performing the PAP protocol. After the test, the subjects performed a set of 6RM Squats with their assigned resistance mode. Once this activity was completed, the subjects remained seated during a 10-minute rest period and then the Squat jump was evaluated again. **Results:** The results did not show a statistical positive PAP effect in any of the 2 experimental groups without between-group difference. The Elastic Resistance group values were as follows: pre-PAP: 37.63 ± 6.99 cm; post-PAP: 37.65 ± 6.65 cm. The Free Weights group values were as follows: pre-PAP: 35.16 ± 5.07 cm; post-PAP: 34.99 ± 5.70 cm. **Conclusions:** No positive PAP effects were found and thus the use of a 6RM Squat set cannot be recommended to improve squat jump performance in subjects with less than 6 months of resistance training experience. In addition, elastic or free-weights resistance seem to provide comparable results. **Practical Applications:** Strength coaches and specialists must be aware that not all PAP protocols will result in a positive effect on jumping.

Influence of Body Build and Training Modality on Strength Gain Following Resistance Training in College Women

J. Mayhew,[1] W. Brechue,[2] B. Mann,[3] and J. Arabas[1]



2136 Board #288 June 2, 3:30 PM - 5:00 PM

Effects Of Drinking Seawater During A Resistance Training Program On Kidney, Performance And Cardiovascular Health

Nicole L. Rogers[1], Alvaro Juesas[2], Nicole Fritz[3], Pedro Gargallo[2], Victor Munoz[2], Guillermo Saez[4], Amaya Hernando[4], Juan C. Colado[2], Michael E. Rogers, FACSM[1]. [1]*Wichita State University, Wichita, KS.* [2]*University of Valencia, Valencia, Spain.* [3]*Universidad Austral, Valdivia, Chile.* [4]*Universitary Hospital Dr. Peset, Valencia, Spain.* (Sponsor: Michael E. Rogers, FACSM)

(No relationships reported)

The oceans contain a vast amount of potential resources for pharmaceuticals and nutritional supplements. Recently, the most widely available component of the oceans, seawater (SW), has been incorporated into supplements designed to improve physical performance and overall health but the efficacy of this is currently unknown.
PURPOSE: To analyze the effects of consuming a SW-based electrolyte drink during a resistance-training (RT) program on kidney health, physical performance, and cardiovascular risk in older adults.
METHODS: 56 sedentary older adults (71.3±6.2 yr) were divided into three groups: control group (CG) (n=18) that continued normal activities without additional physical training or nutritional supplementation; placebo group (PG) (n=19) that drank a 20 ml sample of mineral water before and after each training session; and a SW group (SWG) (n=19) that consumed a 20 ml sample of electrolyte drink (Totum Sport) before and after each training session. A 12 wk RT program using elastic bands was performed on 2 d/wk with 6 exercises and 4 sets of 6 repetitions. Isometric strength for the upper (vertical row (VR)) and lower (horizontal leg press (HLP)) extremities, levels of creatinine and urea (kidney health indicators), and atherogenic index (AI) (cardiovascular health indicator) were assessed pre and post training.
RESULTS: SWG significantly ($p<0.05$) improved VR (+44.6%) and HLP (+52.8%), significantly reduced urea levels (-6.6%) and AI (-4.9%), and showed a trend towards reducing creatinine levels (-5.4%). PG significantly improved VR (+29.3%) and HLP (+52.5%), and significantly reduced AI (-4.50%) with no changes in urea and creatinine values. There were no significant differences between the exercise groups. VR (+9.5%), urea (+5.4%), and creatinine (+1.3%) did not change in CG but there were significant changes in AI (+14.1%) and HLP (-24.7%). There was not an interaction between groups for VR, HLP, and AI, but there was for urea and creatinine levels with CG showing significant differences compared to the exercise groups.
CONCLUSIONS: Drinking SW while involved with a RT program may improve kidney health, cardiovascular health, and IS in older adults.

2726 Board #249 June 3, 9:30 AM - 11:00 AM

Effects Of Using Elastic Bands On Strength And Muscle Mass In Well-trained Young Men

Phil Page, FACSM[1], Nicole L. Rogers[2], Jose Casana[3], Josep Benitez[3], Pedro Gargallo[3], Yasmin Ezzatvar[3], Victor Tella[3], David Delfa[3], Javier Jorda[3], Juan C. Colado[3], Michael E. Rogers, FACSM[2]. [1]*Louisiana State University, Baton Rouge, LA.* [2]*Wichita State University, Wichita, KS.* [3]*University of Valencia, Valencia, Spain.*

(No relationships reported)

There is a lack of information regarding the efficacy of using elastic bands (EB) to increase strength and fat free mass (FFM) in the upper extremities of young well-trained men.

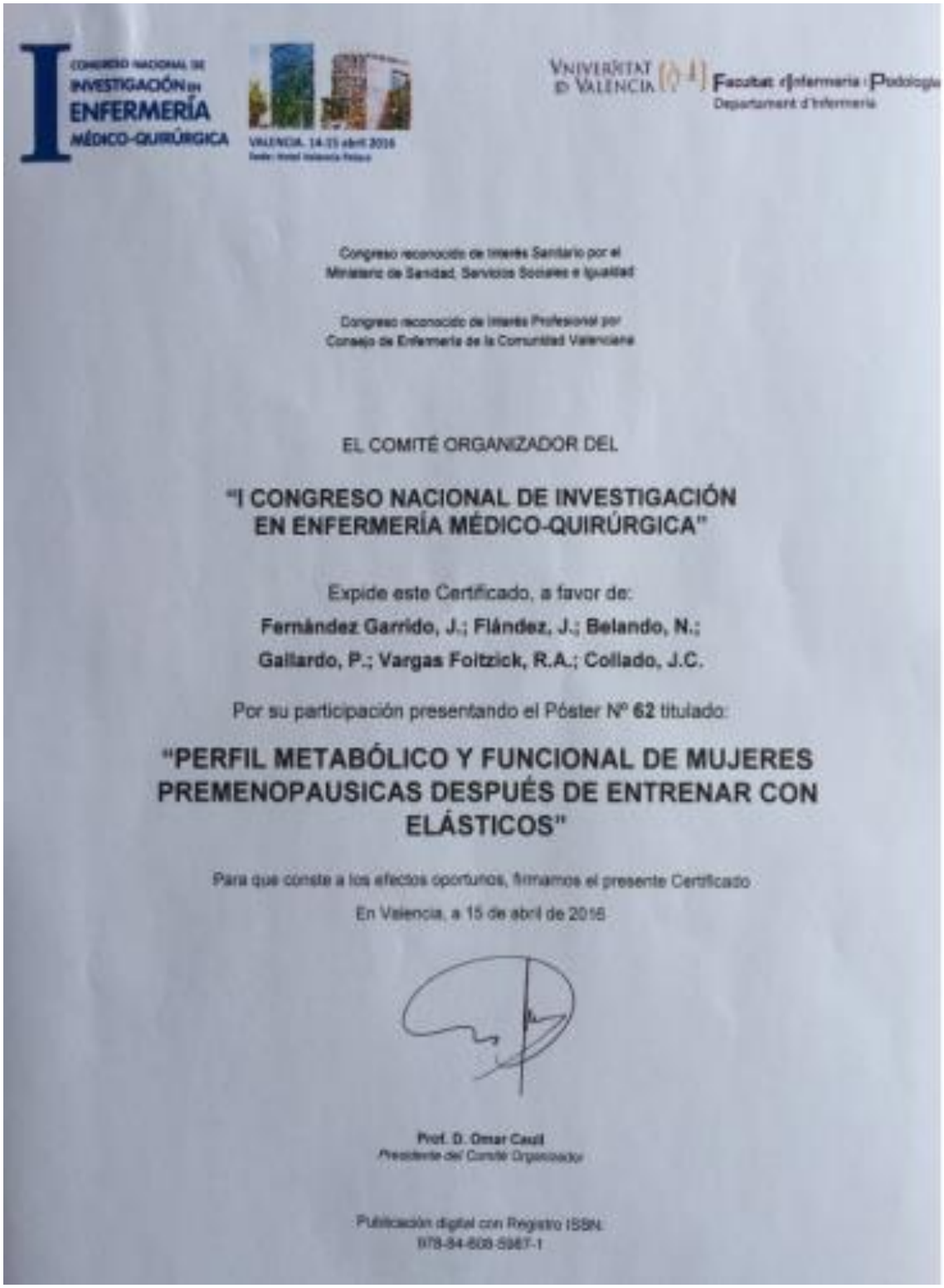
PURPOSE: To assess strength and muscle adaptations in the upper extremities of young well-trained men after a short-term resistance program using EB versus traditional weight devices.

METHODS: 14 well-trained men were randomly divided into two groups: 1) EB group (EBG), 22.1 ±3.5yr, 12.8 ± 4.6% fat mass; and 2) weight Machine and Free Weight Group (MFWG), 21.2 ± 2.6yr, 12.7 ± 7.1% fat mass. An 11 week resistance-training program of 2-sessions-wk was performed. During the first 5 weeks, 6 exercises of 5 sets with 10 maximum repetitions (RM) and 60-90 sec of recovery time between exercises were performed. During weeks 6-11, 12 exercises of 5 sets with 8RM were performed in supersets with 90 sec of rest time between superssets. Subjects did not modify their usual diet habits. Pre-post training measurements were performed for arm FFM with a dual-energy X-ray absorptiometer and for elbow flexion peak power (PP) using an isokinetic device. Three nonparametric tests were performed assuming a p-value less than 0.05 (Wilcoxon test for paired samples, Kruskal-Wallis test and Mann-Whitney U test for 2 samples using the Bonferroni correction coefficient when there were differences between groups).

RESULTS: EBG increased ($p<0.05$) FFM by 3.6% and PP by 6.46%. MFWG increased ($p<0.05$) FFM by 3.2% and PP by 2.9%. There were no differences between groups.

CONCLUSIONS: It is possible to improve PP and FFM in well-trained recreational men using EB alone during a short-term resistance program. Furthermore, improvements from EB training are similar to those of traditional weight devices. More studies are needed regarding the effects of EB on maximal voluntary strength in this population.

764



I CONGRESO NACIONAL DE INVESTIGACIÓN EN ENFERMERÍA MÉDICO-QUIRÚRGICA

VALENCIA, 14-15 abril 2016

VNIVERSITAT DE VALÈNCIA — Facultat d'Infermeria i Podologia
Departament d'Infermeria

Congreso reconocido de Interés Sanitario por el Ministerio de Sanidad, Servicios Sociales e Igualdad

Congreso reconocido de Interés Profesional por Consejo de Enfermería de la Comunidad Valenciana

EL COMITÉ ORGANIZADOR DEL

"I CONGRESO NACIONAL DE INVESTIGACIÓN EN ENFERMERÍA MÉDICO-QUIRÚRGICA"

Expide este Certificado, a favor de:

Fernández Garrido, J.; Flández, J.; Belando, N.; Gallardo, P.; Vargas Foitzick, R.A.; Collado, J.C.

Por su participación presentando el Póster Nº **62** titulado:

"PERFIL METABÓLICO Y FUNCIONAL DE MUJERES PREMENOPAUSICAS DESPUÉS DE ENTRENAR CON ELÁSTICOS"

Para que conste a los efectos oportunos, firmamos el presente Certificado

En Valencia, a 15 de abril de 2016

Prof. D. Omar Cauli
Presidente del Comité Organizador

Publicación digital con Registro ISBN:
978-84-608-5987-1

4 months of training was significantly greater in all tests [SJ ($p \leq 0.011$) y CMJ ($p \leq 0.001$)]. **Discussion:** TMG results shown that adaptations to training are achieved differently on every muscle assessed. Moreover, those results reinforce the role of TMG as an equipment enough sensitive to detect changes produced by training in professional volleyball players. Gains in jump height support these results as they were detected after applying the training program.

Decreasement on Metabolic Risk Biomarkers With a Resistance Training Program Using Elastic Tubing

Colado, JC,[1] Flandez, J,[2] Gargallo, P,[1] Calatayud, J,[1] Benavent, J,[1] and Tella, V[1]

[1]Research Group in Sport and Health, University of Valencia, Valencia, Spain; and [2]Universidad Austral, Valdivia, Chile

Introduction: Physiologic alterations during pre and post-menopausal ages decrease life quality. Resistance training programs demonstrated their effectiveness to improve cardiovascular parameters. However, the effectiveness of alternative and portable devices as elastic tubing during exercise interventions still remains poorly investigated in comparison with the use of traditional resistance training. **Methods:** The aim was to evaluate the effects on the cardiovascular risk caused by strength training with different types of devices in women 40 to 50 years with low metabolic risk. Sixty-two women took part in a randomized design. Subjects were divided in 3 groups: Group 1 (G1 = 22), elastic tubing on the Thera-Band exercise station; Group 2 (G2 = 20), free weights; Group 3 (G3 = 20), control. C-reactive protein (CRP), glycosylated hemoglobin (HbA1c), low-density lipoprotein (LDL) and total cholesterol (TC) were used to assess cardiovascular health. The program consisted of 10 exercises organized in a circuit. During the first and second month, 3 laps with 15 repetitions (OMNI-RES 7-8) per exercise were performed, 4 laps with 10 repetitions (OMNI-RES 9) per exercise were performed in the third month. Recovery from exercise was 30 seconds and 60 seconds between sets. All parameters were analyzed pre and post intervention with the respective statistical treatment later. **Results:** In a positive way, G1 significantly improved ($p \leq 0.05$) their baseline CRP (−33.96%), HbA1c (−6.74%) and LDL (−9.9%) values and also tended to improve their TC levels. In addition, G1 showed greater CRP values than the control group. Control group worsened significantly the HbA1 c (+3.49%). G2 improved their HbA1 c (−3.03%) values. However, there were no differences between both intervention groups. **Discussion:** A 12-week elastic tubing-based program showed their effectiveness to achieve similar improvements as the traditional free weights intervention in sedentary pre and post-menopausal women. Our results are in accordance with previous studies that showed comparable improvements during elastic and free weight exercises or weight machines. Thus, elastic tubing may be used as an alternative to traditional resistance training in order to improve cardiometabolic health. **Mail to:** juan.colado@uv.es.

Normalized Response Speed and Jumping-Related Techniques After Training in Female Volleyball Players

Diez-Vega, I,[1] Molina, JJ,[1] Fernández-del-Valle, M,[2] Rodríguez-Matoso, D,[3] and Rodríguez-Ruiz, D[3]

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Introduction: The true effectiveness in volleyball is related to the ability to perform quick displacements and jumping-related techniques. The monitoring of the muscular response has been related to functional capacity of the knee flexor and extensor muscles in other population. It is of utmost importance to the study the muscular structures that enhance volleyball performance. The aim of this study was to analyze the responses of the normalized response speed and jumping-related techniques in a group of professional female volleyball players. **Methods:** A total of 16 professional female volleyball players were assessed (age: 20.32 ± 1.68; body weight: 67.75 ± 9.13; height: 178.26 ± 7.12; BMI: 21.41 ± 1.75) from 2 Spanish Super league teams. Normalized response speed (Vm) was measured using the Tensiomyography (TMG) on Vastus Medialis (VM), Rectus Femoris (RF), Vastus Lateralis (VL), Biceps Femoris (BF) y Semitendinous (ST) previous to the season and after 4 months of training and physical conditioning. Abalakov jump test including volleyball specific arm movement (BLQ) and 3 steps approach-attack jump (ATT) were also assessed using a contact platform. **Results:** The Vm resulted improved for all the muscles except VM in both limbs were Vm was maintained, but only Vm results shown significant improvements on VL ($p \leq 0.001$). Height reached after training was significantly greater in both jump test BLQ ($p \leq 0.05$) y ATT ($p \leq 0.001$). **Discussion:** Height gains support that the training and physical conditioning (adaptation, hypertrophy, maximal strength and transfer) results in an improved jumping-related techniques. TMG-related results also

Relationship Between Lumbatex and Pressure Biofeedback Unit in Segmental Motion in the Lumbopelvic Spine

Cortell-Tormo, JM,[1] Hernández-Sánchez, S,[2] Fuster-Lloret, V,[3] Pérez-Soriano, P,[3] Carreres-Ponsoda, F,[1] Tortosa-Martínez, J,[1] and Chulvi-Medrano, I[4]

[1]University of Alicante; [2]University Miguel Hernandez; [3]University of Valencia; and [4]Benestar Wellness Center

Introduction: The pressure biofeedback unit (PBU) is a tool developed by physiotherapists to aid the retraining of stabilizing muscles using specific exercises, and detects movement of the lumbar spine in relation to an air-filled reservoir. However, most of the exercises performed to train stabilizing muscles of the spine as well as daily activities are performed in other positions that do not have the support needed to use the Stabilizer™. Lumabatex® is a new device that allows evaluating the posture and segmental changes in the lumbar spine without support tests or exercises that are not available support surfaces. The information provided by Lumbatex® may be considered as a protective aid when aiming to control the segmental changes of the lumbar spine in different exercises. **Mail to:** jm.cortell@ua.es.

Validity of a New Device for Assessing Ankle Dorsiflexion Range of Motion

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[1]Research Group in Sport and Health, University of Valencia, Valencia, Spain; [2]University Institute of Science in Physical Activity and Sports, Catholic University of Valencia, Valencia, Spain; [3]Centro de Ciências Biológicas e da Saúde, Universidade Federal de Sergipe, Brasil; and [4]Laboratory of Physiology, European University Miguel de Cervantes, Valladolid, Spain

Introduction: Ankle dorsiflexion range of motion is associated with patellar and ankle injuries, also having an important implication in the performance of strengthening exercises. Despite the weight-bearing lunge test, the goniometer and

the digital inclinometer are usually used to assess ankle dorsiflexion range of motion (ROM), there is no universal agreement regarding which measurement device is most preferred. An alternative option could be the leg motion test, which is a portable device designed to assess ankle dorsiflexion ROM, miming the weight-bearing lunge test condition while allows a greater standardization. However, no study has been conducted to evaluate the association of this novel device with other typical ankle dorsiflexion range of motion measures. **Methods:** Fifteen healthy male subjects (age = 23 ± 3 years) took part in this study. The leg motion dorsiflexion ROM was assessed according to procedures for the performance of the weight-bearing lunge test and both tests were performed in a counterbalanced order. In addition, other ankle dorsiflexion ROM measures were obtained during the weight-bearing lunge position using a standard goniometer and a digital inclinometer. **Results:** Paired t-test showed the absence of significant differences between right and left limb in all the tests. Mean values ± standard deviations were as follows: leg motion (left 12.49 cm ± 3.51; right 12.70 cm ± 3.0), weight-bearing lunge test (left 11.52 cm ± 3.71; right 11.71 cm ± 3.56), goniometer (left 43.20° ± 5.46; right 42.56° ± 5.64), and digital inclinometer (left 42.18° ± 6.65; right 41.42° ± 5.91).The leg motion composite values (i.e., average of the 2 legs) showed a significant ($p \leq 0.05$) positive correlation with the weight-bearing lunge test ($r = 0.99$), with the goniometer ($r = 0.85$) and with the digital 42.56° ± 5.64), and digital inclinometer (left 42.18° ± 6.65; right 41.42° ± 5.91).The leg motion composite values (i.e., average of the 2 legs) showed a significant ($p \leq 0.05$) positive correlation with the weight-bearing lunge test ($r = 0.99$), with the goniometer ($r = 0.85$) and with the digital inclinometer ($r = 0.86$). **Discussion:** This is the first study that aims to validate the leg motion. The high correlation values during the leg motion test show their validity as an alternative to the weight-bearing lunge test, goniometer, and digital inclinometer for the measurement of the ankle dorsiflexion ROM. **Mail to:** pedro11gb@gmail.com.

Time Motion Analysis in U-14s and U-16s During Competitive 11-A-Side Football Matches

Etxeazarra, I,[1] Castellano, J,[1] Usabiaga, O,[1] and Casamichana, D[2]

[1]University of the Basque Country (UPV/EHU), Spain; and [2]University School associated with the University of Cantabria (EU Gimbernat-Cantabria), Spain

Introduction: Competition is considered as a key element in the development in the youth football player formative process. To that end, the competitive formats needs to be adapted to the characteristics of those involved, and this does not always happen. By understanding the physical demands generated by the competition in the players, through different age periods, appropriate training strategies will be identified to optimize the competition model. **Methods:** Time-motion match analysis data was collected on 44 young football players (24 U-14; 20 U-16) on 18 official 11-a-side football matches (9 for each age group). Portable global positioning system (GPS) devices were used to record the following variables: total distance covered (DC) and distance covered in different speed zones, work-rest ratio (W:R), maximum velocity (MV), player-load (PL) and distance and frequencies of sprints. **Results:** U-14 football players presented significantly lower values during the second half on DC, PL, W:R and distance covered in medium speed zone (8–13 km·h^{-1}). However, no significant differences between halves were found for U-16 players. **Discussion:** A decrease on fitness performance was observed in U-14s during the second half, similar to other studies. On the other hand, we underline that there were no physical activity variation along the match in U-16, so that, no sign of fatigue was found in this age group. The study concludes that the 11 vs. 11 format seems to be adequate to U-16s, since it allows them to maintain the same pace of game during the second half. However, physical demands for U-14s seem to be excessive to their characteristics to keep the physical activity constant during the game. In this line, other studies to isolate variables like pitch dimensions, number of players or duration of each part, could be implement to adequate competition formats to the possibilities of each age group.
to keep the physical activity constant during the game. In this line, other studies to isolate variables like pitch dimensions, number of players or duration of each part, could be implement to adequate competition formats to the possibilities of each age group.

Changes in Plantar Pressure Distribution During Nordic Walking are Constant Between Diagonal and Alfa Technique

Encarnación, E,[1] Gea, G,[1] Orquín, J,[1] Marcos, P,[1] and Manzanares, A[1]

[1]Catholic University San Antonio, Murcia, Spain

Introduction: During the practice of Nordic walking (NW) ground reaction forces are higher than during walking (W). This increase is associated with the technique employed during NW. Previous studies demonstrated that the practice of NW reduced plantar pressures by 50% in the central metatarsal (CM). The objective was to analyze the differences in plantar pressures distribution during NW with alpha technique (AT) against diagonal technique (DT) and these in turn with walking. **Methods:** Twenty physically active students were randomized into a group of alpha technique (n = 15) and a group of diagonal technique (n = 12). Nordic walking and walking were performed at the subject's preferred speed, controlled by 2 photocells (Velleman

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Elastic Tubing and Free Weights Achieved Comparable Improvements in Pre And Post-Menopausal Women

Gargallo, P,[1] Flandez, J,[2] Colado, JC,[1] Calatayud, J,[1] Madera, J,[1] and Moya, D[1]

[1]Research Group in Sport and Health, University of Valencia, Valencia, Spain; and [2]Universidad Austral de Chile, Valdivia, Chile

Introduction: Menopause is associated with a loss of muscle strength and physical fitness. The implementation of exercise programs that prioritize strength training may reverse or reduce these declinations, improving the quality of life (1). However, the effectiveness of alternative, portable and accessible devices as elastic tubing resistancestill remains poorly investigated in comparison with the use of traditional resistance training, especially in this population. **Methods:** A randomized control trial design with a sample of 62 adult women was employed. Subjects took part in a 12-week program and were divided in 3 groups: Group 1 (G1 = 22), elastic tubing on the Thera-Band Exercise Station; Group 2 (G2 = 20), free weights; Group 3 (G3 = 20), control. Timed Up and Go (TUG) test, Prone Bridge Test (PBT), 6-minute walking test (6MWT), and Upright Row (UR) were analyzed pre and post intervention to evaluate training effects. The program consisted of 10 exercises. First and second month 3 laps with 15 repetitions (OMNI-RES 7-8) were performed and 4 laps with 10 repetitions (OMNI-RES 9) in the third month. All parameters were analyzed with the respective statistical treatment. **Results:** G1 showed a significant intragroup improvement ($p \leq 0.05$) in TUG (−9.26%), PBT (+74.47%), 6MWT (+7.77%), UR (+38.96%). G2 showed a significant intragroup improvement ($p \leq 0.05$) in 6 MWT (+6.59%), UR (+31.42%) and PBT (+120.64%). No significant differences were found between G1 and G2 and both showed improvements than G3. However, G3 showed no significant intragroup improvements ($p > 0.05$). **Discussion:** The performance of an elastic tubing-based exercise program showed their effectiveness to achieve similar short-term improvements on the physical performance as traditional free weights in sedentary and adult women, according to previous elastic-resisted programs with healthy, physically active subjects and sedentary middle-aged women. Present data provides additional scientific evidence supporting the use of elastic-resisted exercise programs as an alternative to traditional free weights in pre and post-menopausal women. **Mail to:** pedro11gb@gmail.com.

Effect of a Sport Education Season on Some Psychological Variables in Youth Swimming

Meroño, L, and y Calderón, A

UCAM Catholic University of Murcia, Spain

Introduction: In the school setting, the effectiveness of the teaching and learning process is being a research "hot-topic." However in the sport context actually is not a research interest, not a lot of studies have the purpose to analyze the effect of teaching models on performance. A large number of investigations reflect the relationship between psychological state and performance, the model may be applied a flattering teaching tool for this situation. Sport Education (SE) is a pedagogical model applied more on team sports (more tactical). However there are not studies that focus on the individual sports (more technical). Therefore, the purpose was to analyze the effect of SE season on psychological variables in youth swimming. **Methods:** A quasi-experimental design was performed with pre-post measures, applied in youth swimmers ($n = 24$) of different categories, with a training program of 16 sessions. The questionnaires used were: Perceived Autonomy Support, Sport Commitment, and Enjoyment and Perceived Competence. Were statistically analyzed using Wilcoxon Ranks and Spearman Rho. **Results:** The intervention program based on the SE caused statistically significant improvements from pre to post ($p = 0.00^*$) on the variables and their indicators: (A) Perceived autonomy (autonomous behaviour and athlete review); (B) Sport commitment (present and future commitment); and (C) Level of Experience and Perceived Competence. Furthermore, appreciated that the variables are positively correlated with each other (A&B: $r = 0.40^*$; A&C: $r = 0.37^*$; B&C: $r = 0.22^*$). **Discussion and Conclusion:** The results of this study corroborated the positive effect of the Sport Education on the psychological variables also in the sport context. Sport Education could be an alternative to other teaching models to develop the excellence, in sports that focus on technical execution (such as swimming). So it should be applied in different sports clubs to improve the learning experience engagement of youth swimmers in the sport context.

and biceps femoris (BF). Maximal radial deformation (Dm), delay time (Td), and contraction time (Tc) were analyzed. **Results:** Data obtained in both lower limbs show a greater rigidity (Dm) on BF ($p \leq 0.001$) in males, and lower rigidity in the extensor muscles [RF, VM y VL ($p \leq 0.05$)]in males compared to females. Delay time (Td) was lower in males on BF ($p \leq 0.001$), RF ($p \leq 0.001$) and VL ($p \leq 0.05$), and only for VM (right leg $p \leq 0.05$) in females. Contraction time (Tc) on BF ($p \leq 0.001$) and VL were lower for males, while it was similar for both genders on RF, and lower for females on VM (right leg $p \leq 0.05$). **Discussion:** Our findings are consistent with previous results reported by Diez et al and with the differences found on BF reported by Rodriguez-Ruiz et al. Moreover, the results obtained on VM in females reinforce the stabilization role of the knee joint musculature compared to males. However, further research is needed in order to determine other biomechanical aspects of the knee musculature in professional male and female volleyball players.

Between-Session Star Excursion Balance Test Reliability in School Primary Students

Colado, JC,[1] Calatayud, J,[1] Borreani, S,[1] Moscardó, L,[1] Gargallo, P,[1] and Martín, F[1]

[1]Research group in Sport and Health, University of Valencia, Valencia, Spain

Introduction: Dynamic balance is required in daily and sport activities. Star Excursion Balance Test (SEBT) is a cost-effective test that has demonstrated the ability to assess dynamic postural control and to predict injuries in the lower extremity. Despite SEBT has showed moderate and high reliability in young and adults, no study has proved the reliability in children. **Methods:** Eight healthy participants (10.1 ± 0.3 years) were tested in 2 different times with 2 weeks of separation and measurements were performed at the same time of the day by the same researchers. Before performing the test, subjects were informed about the aim of this study and the test procedure by using verbal and visual demonstration. The SEBT was performed in 3 directions (anterior, posteromedial and posterolateral). Participants undertook the testing barefoot with the stance foot aligned at the most distal aspect of the toes for anterior direction and the most posterior aspect of the heel for the backward directions. During trials, hands were placed on hips and minimal stance foot movement was allowed. Four practice trials were performed in each direction before recording 3 additional measured trials. Leg length was measured with participants lying supine and was used to normalize excursion distances. A trial was discarded and repeated if participants used the reaching leg for a substantial amount of support at any time, removed the foot from the center of the grid, or were unable to maintain balance. **Results:** Intraclass correlation coefficient values for raw and normalized scores showed fair to good reliability (0.65 to 0.88) and standard error of measurement values for raw and normalized scores ranged from 1.84 to 5.90. **Discussion:** SEBT is a reliable measure in school primary students. Similar results have been reported previously in young and adults. Therefore, SEBT may be used as a reliable test in school primary students in order to assess dynamic postural control. **Mail to:** juan.colado@uv.es.

Characterization of Health Fitness as Motor Dysfunctions Indicator: Pilot Study in Adolescents of Valdivia City (Chile)

Colado, JC,[1] Fritz, N,[2] Monrroy, M,[2] Sotomayor, C,[2] Calatayud, J,[1] and Madera, J[1]

[1]Research group in Sport and Health. Universidad de Valencia, Valencia, España; and [2]Universidad Austral de Chile, Valdivia, Chile

Introduction: The balance of components of health fitness it's associated with a lower risk of developing a functional disease and/ or disability that keep away people from motor dysfunction defined by Lopez et al as "phenomenon expressed by a limitation in the capacity of movement of a person at systemic or global level, resulting in a decrease performance or restriction in the execution of motor functions or actions considered normal." Often it's considered a healthy individual when he or she is in a condition free of disease, under the biomedical model. Where a physical assessment by characterizing the motor function contribute to research movement disorders present at early age in children without diagnosed illness, safeguarding the healthy lifestyles that during childhood plays a decisive role in the future health and risk of develop of chronic diseases. **Methods:** A descriptive, cross-sectional study. A sample of 105 adolescents participated. The test that characterized health fitness as movement translator was strength (dynamometer hand grip, horizontal jump test), endurance muscular (push-up), flexibility (sit and reach test), aerobic fitness (6MWT) and body composition (BMI, waist-circumference and waist-to-height ratio). For the descriptive analysis were used abstract parameters as the average and were described percentiles of performance with which graduated individual performance in the Dysfunction Motor Kinesic Index (DMKI) created from the overall performance to confront individual

APPENDIX E. CERTIFICATE OF THE THREE-MONTH RESEARCH STAY AT WICHITA STATE UNIVERSITY

PROGRAMA ESTATAL DE PROMOCIÓN DEL TALENTO Y SU EMPLEABILIDAD

CERTIFICADO DEL CENTRO RECEPTOR TRAS LA ESTANCIA BREVE O TRASLADO TEMPORAL
CERTIFICATE OF STAY IN A FOREING INSTITUTION

1. Beneficiario/ *Applicant:*
Nombre y apellidos/ *Name:Pedro Gargallo Bayo*
D.N.I./ *National identity Card:53255721-A*
Centro de adscripción de la beca/ *Home Institución:* Universidad de Valencia (Estudio General). Facultad de Medicina y Odontología.
2. Centro en el que se ha realizado la estancia/ *Host institution:*
Nombre/ *Name:* Wichita State University (Department of Human Performance Studies). Center of Physical Activity and Aging.
Dirección/ *Adress:* 106G Heskett Center. Wichita State University Wichita, Kansas 67260-0016
Localidad/ *Country:* Kansas, USA
3. Investigador responsable en el centro de la estancia/ *Responsable person in the Host*
Institución/ *Institution:* Wichita State University
Nombre/ *Name: Michael Rogers*
Cargo/ *Post:* Chair, Professor, Research Director Center for Physical Activity and Aging.
CERTIFICO: que el becario arriba mencionado ha realizado una estancia en este centro en las siguientes fechas: desde 17 / 09 / 2018 hasta 15 / 12/ 2018 ***THIS IS TO CERTIFY:*** *that the above mentioned person has performed a stay in this Institution in the following dates: From: 17 / 09 / 2018 To: 15 / 12 / 2018* Lugar y fecha: Kansas, Wichita State University, 14/12/2018 ***City and date:*** Kansas, Wichita State University, 14/12/2018
Firma y Sello/ *Signature & Stamp*  WICHITA STATE UNIVERSITY COLLEGE OF EDUCATION *Department of Human Performance Studies*

MECD/SGU. Programa nacional de ayudas de FPU. Certificado del centro receptor tras el traslado temporal o la estancia breve.

APPENDIX F. CERTIFICATE OF THE SIX-MONTH RESEARCH STAY AT APPALACHIAN STATE UNIVERSITY

MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES

PROGRAMA ESTATAL DE
PROMOCIÓN DEL TALENTO Y SU EMPLEABILIDAD
Subprograma Estatal de Movilidad

ESTANCIAS BREVES Y TRASLADOS TEMPORALES
CERTIFICADO DEL CENTRO RECEPTOR
MOBILITY CERTIFICATE FROM THE RECEIVING INSTITUTION

1. IDENTIFICACIÓN DEL BENEFICIARIO/A DE LA AYUDA FPU / *FPU PROGRAMME BENEFICIARY*

Referencia de la ayuda FPU / *FPU programme identification number*:
FPU15/05634

Apellidos y nombre / *Last and First Name*:
Gargallo Bayo, Pedro

2. CENTRO DE REALIZACIÓN DE LA ESTANCIA BREVE O TRASLADO TEMPORAL / *RECEIVING CENTRE DURING THE MOBILITY*

Nombre del Organismo receptor / *Name of the receiving institution*:
Appalachian State University.

Nombre del centro / *Name of the centre*:
Leon Levine Hall, Department of Health & Exercise Science.

Ciudad y País / *City and Country*:
Boone, North Carolina (USA)

Investigador/a responsable de la Estancia Breve o Traslado Temporal / *Researcher in charge during the mobility*:
Travis Triplett

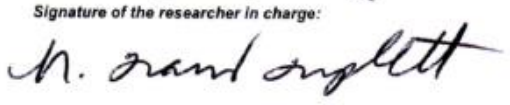
Cargo o Categoría del o de la responsable / *Position of the researcher in charge*:
Professor, PhD, Physiology of Exercise, Exercise Science Undergraduate Program Director, Graduate Faculty

3. DURACIÓN DE LA ESTANCIA BREVE O TRASLADO TEMPORAL / *DURATION OF THE MOBILITY*

Fecha inicio / *Start date*: June/30/2019

Fecha fin / *End date*: December/30/2019

Firma del Investigador/a responsable:
Signature of the researcher in charge:



APPENDIX G. ETHICS COMMITTEE APPROVAL

VNIVERSITAT
DE VALÈNCIA
Vicerectorat d'Investigació i Política Científica

D. Fernando A. Verdú Pascual, Profesor Titular de Medicina Legal y Forense, y Secretario del Comité Ético de Investigación en Humanos de la Comisión de Ética en Investigación Experimental de la Universitat de València,

CERTIFICA:

Que el Comité Ético de Investigación en Humanos, en la reunión celebrada el día 14 de mayo de 2014, una vez estudiado el proyecto de investigación titulado:
"Efecto sobre parámetros musculoesqueléticos, metabólicos, inmunológicos, de bienestar y funcionales al entrenar con diferentes dispositivos de resistencia a altas intensidades y un programa de Ai-chi en adultos mayores de las CMAPM Valencia", número de procedimiento H1395923230221 ,
cuyo investigador responsable es D. Juan Carlos Colado Sánchez, ha acordado informar favorablemente el mismo dado que se respetan los principios fundamentales establecidos en la Declaración de Helsinki, en el Convenio del Consejo de Europa relativo a los derechos humanos y cumple los requisitos establecidos en la legislación española en el ámbito de la investigación biomédica, la protección de datos de carácter personal y la bioética.

Y para que conste, se firma el presente certificado en Valencia, a quince de mayo de dos mil catorce.

FERNANDO ALEJO|VERDU| PASCUAL
2014.05.15
11:22:19 +02'00'

APPENDIX H. PROJECT AUTHORIZATION BY THE VALENCIA CITY COUNCIL

AJUNTAMENT DE VALENCIA
REGISTRE D'ENTRADA
15.04.14 013898

Data / *Fecha*	10 de Abril de 2014
Ref.	Expte.: 02201/2014/3575
Servici / *Servicio*	BIENESTAR SOCIAL E INTEGRACIÓN.
Secció / *Sección*	PERSONAS MAYORES
ASSUMPTE / *ASUNTO*	Notif. Informe.

AJUNTAMENT DE VALENCIA de Gavia, 11

Destinatari(ària) / *Destinatario(a)*

D. JUAN CARLOS COLADO SÁNCHEZ
Aulario V. Universidad de Valencia
C/ Gascó Oliag, 3
4601[illegible] – VALENCIA

2645

Vista la solicitud presentada por D. Juan Carlos Colado Sánchez, dese traslado del informe técnico de fecha 9 de abril de 2014, que literalmente dice:

"Visto el escrito presentado por D. Juan Carlos Colado Sánchez, miembro de la Unidad de Investigación en Deporte y Salud, del Departamento de Educación Física y Deportiva de la Universidad de Valencia, desde la Sección de las Personas Mayores se informa de lo siguiente:

En relación a su petición de realizar un programa de actividad física con el fin de mejorar los parámetros músculo-esqueléticos, inmunológicos, metabólicos, de bienestar y funcionales de los usuarios de los Centros Municipales de Actividades para Personas Mayores, se valora favorablemente su petición siempre y cuando se comprometa a hacer frente con un seguro de responsabilidad civil en caso de surgir cualquier tipo de incidencia en el devenir de la actividad a realizar, y se respete la legislación existente en el área de la Protección de Datos."

Lo que le comunico a Vd. para su conocimiento y efectos.

EL SECRETARIO, P.D.
La Jefa de Sección
(Por Delegación de 5 de Febrero 2010)

Amparo Montaner

APPENDIX I. INFORMED CONSENT

FORMULARIO DE CONSENTIMIENTO CON CONOCIMIENTO DE CAUSA

Este documento certifica su aceptación en la participación del estudio denominado "EFECTO SOBRE PARÁMETROS MUSCULOESQUELÉTICOS, FUNCIONALES Y DE BIENESTAR AL ENTRENAR CON DIFERENTES DISPOSITIVOS DE RESISTENCIA A ALTAS INTENSIDADES EN ADULTOS MAYORES DE LOS CIMAPM VALENCIA". También queda informado de que puede retirarse del estudio en cualquier momento y que no recibirá compensación económica alguna por su participación en el mismo. El estudio está dirigido por el Dr. Juan Carlos Colado Sánchez y Dr. Víctor Tella Muñoz del Departamento de Educación Física y Deportiva de la Universidad de Valencia.

Con su firma de este Consentimiento Informado, usted manifiesta explícitamente que ha entendido la descripción del tipo de ejercicio a realizar y sus posibles complicaciones, así como de las evaluaciones pertinentes. Además, usted indica que cualquier duda que haya podido surgir sobre el proceso de evaluación y sus posibles riesgos ha sido respondida con claridad, quedando satisfecho con las explicaciones aportadas.

Las pruebas, tests y cuestionarios realizados para evaluar su aptitud física y cognitiva permitirán obtener información sobre su estado general de salud.

Las prueba específicas de cineantropométia, en las que se recopilen los datos correspondientes a su composición corporal se realizarán siguiendo los procedimientos característicos de la ISAK (International Society of Advancement in Kineantropometry). En estas exploraciones puede ser conectado a un aparato eléctrico: analizador de impedancia bioeléctrica. Las molestias pueden provenir de la necesidad de desnudar alguna zona del cuerpo para la toma de medidas.

Las pruebas de aptitud funcional darán una información sobre sus cualidades físicas condicionales y coordinativas, siguiendo los protocolos científicos habituales al respecto. Las valoraciones psicosociales se harán mediante cuestionarios científicamente validados. Durante las valoraciones y tras las mismas, podrá experimentar fatiga.

La información obtenida como consecuencia de dicho ejercicio será confidencial y su uso será meramente informativo y científico, salvaguardando su identidad. Para ello será necesario su expreso consentimiento mediante autorización por escrito, valiendo como tal el presente escrito.

Al firmar el presente documento usted acepta la completa responsabilidad de su propia salud, y reconoce que ha sido informado y ha entendido que esta responsabilidad no es asumida por los responsables de su programa de ejercicio físico ni de la investigación. Del mismo modo, admite la creación, utilización y difusión del material fotográfico y de vídeo, que con fines científicos pueda generarse con su participación en el estudio.

De igual forma manifiesta que se le ha informado del compromiso por parte de los responsables del estudio acerca de la confidencialidad de aquellos datos personales que respecto de su persona pueden recabar los mismos durante la realización de la investigación.

En Valencia a _____de_____de 2014.
D. Dña._____
DNI_____

Firma_____

APPENDIX J. INFORMED CONSENT OF THE UNIVERSITY HOSPITAL DR. PESET

HOSPITAL UNIVERSITARI DOCTOR PESET

Consentimiento Informado para Pruebas Genéticas

Título del proyecto: ´´***Efecto sobre parámetros musculoesqueléticos, metabólicos, inmunológicos, de bienestar y funcionales al entrenar con diferentes dispositivos de resistencia a altas intensidades en adultos mayores***.

Por el presente documento se solicita su participación en un trabajo de investigación cuyo título arriba señalado tiene como objetivo valorar el efecto del ejercicio físico controlado, utilizando distintos dispositivos de resistencia sobre su estado de salud a través de la determinación de diferentes parámetros clínicos y genéticos. En este estudio un aspecto de gran interés es la valoración y seguimiento de la capacidad funcional y el grado de envejecimiento biológico de las personas que es posible monitorizar en base a los obtenidos en los análisis de sangre y orina. Los distintos parámetros bioquímicos y moleculares disponibles en la actualidad permiten conocer la capacidad metabólica así como la estructura y función del material genético de los individuos que se someten a este tipo de examen clínico-experimental.

La manipulación de las muestras, su conservación y el tratamiento de los datos personales y resultados obtenidos se llevará a cabo siguiendo las normas de confidencialidad y éticas que se describen más abajo.

Usted puede requerir información y aclarar los aspectos que no entienda como suficientemente explícitos consultando con el investigador principal de este proyecto Profesor Juan Carlos Colado Sánchez (Facultad de Ciencias de la Actividad Física y el Deporte) y/o el médico responsable de los análisis clínico-moleculares Profesor Guillermo Sáez Tormo (Facultad de Medicina y Odontologia. Servicio de Análisis Clínicos, Hospital Universitario Dr. Peset de Valencia).

Yo, (nombre y apellidos) .....

Autorizo la extracción de una muestra sanguínea estudio y análisis genético de alteraciones y polimorfismos genéticos relacionados con el de investigación del que he sido informado.

La información obtenida será protegida por la ley 15/1999 de Protección de Datos de Carácter Personal, que se complementa con la ley 41/2002 de 14 de Noviembre, que regula la autonomía del paciente y de los derechos y obligaciones en materia de información y documentación clínica. (http://www.uv.es/uvetica/normativa.html). A los datos registrados por los investigadores de campo se les asignará de una código en clave alfa-numérica, para proteger la información de los pacientes que solo podrá ser gestionada por personal investigador autorizado.

Soy consciente de que al concluir la investigación objeto del estudio, las muestras biológicas restantes serán destruidas a menos que autorice su conservación para la realización de futuros estudios genéticos. En caso de conservación estas muestras no podrán ser identificadas ni custodiarse por un periodo superior a 5 años.

Autorizo la conservación de las muestras tras el estudio (señale la casilla siguiente)

☐

Firmo mi conformidad de participación voluntaria en el estudio

Fecha y lugar:

Firma del participante

APPENDIX K. RECOMMENDATIONS FOR BLOOD SAMPLES EXTRACTIONS

1. The day before the exam:

    - Eat regular meals
    - Do not take unnecessary medications
    - Do not ingest alcoholic beverages

2. The night before the exam.

    - Consume the last meal between 7-8:00 p.m.
    - If possible do not smoke
    - Avoid strenuous physical activity
    - Take only the medications prescribed by your doctor

3. The day of the exam:

    - Fasting between 10-12 hours
    - Avoid strenuous physical activity
    - No Smoking

APPENDIX L. MMSE TEST

MINI MENTAL STATE EXAMINATION (MMSE)

Basado en Folstein et al. (1975), Lobo et al. (1979)

Nombre: Varón [ ] Mujer [ ]
Fecha: F. nacimiento: Edad:
Estudios/Profesión: Nº Hª:
Observaciones:

¿En qué año estamos? 0-1 **¿En qué estación? 0-1** **¿En qué día (fecha)? 0-1** **¿En qué mes? 0-1** **¿En qué día de la semana? 0-1**	**ORIENTACIÓN TEMPORAL (Máx.5)**	
¿En qué hospital (o lugar) estamos? 0-1 **¿En qué piso (o planta, sala, servicio)? 0-1** **¿En qué pueblo (ciudad)? 0-1** **¿En qué provincia estamos? 0-1** **¿En qué país (o nación, autonomía)? 0-1**	**ORIENTACIÓN ESPACIAL (Máx.5)**	
Nombre tres palabras Peseta-Caballo-Manzana (o Balón-Bandera-Arbol) a razón de 1 por segundo. Luego se pide al paciente que las repita. Esta primera repetición otorga la puntuación. Otorgue 1 punto por cada palabra correcta, pero continúe diciéndolas hasta que el sujeto repita las 3, hasta un máximo de 6 veces. **Peseta 0-1 Caballo 0-1 Manzana 0-1** **(Balón 0-1 Bandera 0-1 Árbol 0-1)**	**Nº de repeticiones necesarias** **FIJACIÓN-Recuerdo Inmediato (Máx.3)**	
Si tiene 30 pesetas y me va dando de tres en tres, ¿Cuántas le van quedando?. Detenga la prueba tras 5 sustraciones. Si el sujeto no puede realizar esta prueba, pídale que deletree la palabra MUNDO al revés. **30 0-1 27 0-1 24 0-1 21 0-1 18 0-1** **(O 0-1 D 0-1 N 0-1 U 0-1 M0-1)**	**ATENCIÓN-CÁLCULO (Máx.5)**	
Preguntar por las tres palabras mencionadas anteriormente. **Peseta 0-1 Caballo 0-1 Manzana 0-1** **(Balón 0-1 Bandera 0-1 Árbol 0-1)**	**RECUERDO diferido (Máx.3)**	
***.DENOMINACIÓN.* Mostrarle un lápiz o un bolígrafo y preguntar ¿qué es esto?. Hacer lo mismo con un reloj de pulsera. Lápiz 0-1 Reloj 0-1** ***.REPETICIÓN.* Pedirle que repita la frase: "*ni sí, ni no, ni pero*" (o "*En un trigal había 5 perros*") 0-1** ***.ÓRDENES.* Pedirle que siga la orden: "*coja un papel con la mano derecha, dóblelo por la mitad, y póngalo en el suelo*".** **Coje con mano d. 0-1 dobla por mitad 0-1 pone en suelo 0-1** ***.LECTURA.* Escriba legiblemente en un papel "*Cierre los ojos*". Pídale que lo lea y haga lo que dice la frase 0-1** ***.ESCRITURA.* Que escriba una frase (con sujeto y predicado) 0-1** ***.COPIA.* Dibuje 2 pentágonos intersectados y pida al sujeto que los copie tal cual. Para otorgar un punto deben estar presentes los 10 ángulos y la intersección. 0-1**	**LENGUAJE (Máx.9)**	
Puntuaciones de referencia 27 ó más: normal **24 ó menos: sospecha patológica 12-24: deterioro** **9-12 : demencia**	**Puntuación Total (Máx.: 30 puntos)**	

APPENDIX M. BARTHEL INDEX

ÍNDICE DE BARTHEL			
Comida:			
	10	Independiente. Capaz de comer por sí solo en un tiempo razonable. La comida puede ser cocinada y servida por otra persona	
	5	Necesita ayuda para cortar la carne, extender la mantequilla.. pero es capaz de comer sólo/a	
	0	Dependiente. Necesita ser alimentado por otra persona	
Lavado (baño)			
	5	Independiente. Capaz de lavarse entero, de entrar y salir del baño sin ayuda y de hacerlo sin que una persona supervise	
	0	Dependiente. Necesita algún tipo de ayuda o supervisión	
Vestido			
	10	Independiente. Capaz de ponerse y quitarse la ropa sin ayuda	
	5	Necesita ayuda. Realiza sin ayuda más de la mitad de estas tareas en un tiempo razonable	
	0	Dependiente. Necesita ayuda para las mismas	
Arreglo			
	5	Independiente. Realiza todas las actividades personales sin ayuda alguna, los complementos necesarios pueden ser provistos por alguna persona	
	0	Dependiente. Necesita alguna ayuda	
Deposición			
	10	Continente. No presenta episodios de incontinencia	
	5	Accidente ocasional. Menos de una vez por semana o necesita ayuda para colocar enemas o supositorios.	
	0	Incontinente. Más de un episodio semanal	
Micción			
	10	Continente. No presenta episodios. Capaz de utilizar cualquier dispositivo por si solo/a (botella, sonda, orinal ...).	
	5	Accidente ocasional. Presenta un máximo de un episodio en 24 horas o requiere ayuda para la manipulación de sondas o de otros dispositivos.	
	0	Incontinente. Más de un episodio en 24 horas	
Ir al retrete			
	10	Independiente. Entra y sale solo y no necesita ayuda alguna por parte de otra persona	
	5	Necesita ayuda. Capaz de manejarse con una pequeña ayuda; es capaz de usar el cuarto de baño. Puede limpiarse solo/a.	
	0	Dependiente. Incapaz de acceder a él o de utilizarlo sin ayuda mayor	
Transferencia (traslado cama/sillón)			
	15	Independiente. No requiere ayuda para sentarse o levantarse de una silla ni para entrar o salir de la cama.	
	10	Mínima ayuda. Incluye una supervisión o una pequeña ayuda física.	
	5	Gran ayuda. Precisa ayuda de una persona fuerte o entrenada.	
	0	Dependiente. Necesita una grúa o el alzamiento por dos personas. Es incapaz de permanecer sentado	
Deambulación			
	15	Independiente. Puede andar 50 metros o su equivalente en casa sin ayuda supervisión. Puede utilizar cualquier ayuda mecánica excepto un andador. Si utiliza una prótesis, puede ponérsela y quitársela solo/a.	
	10	Necesita ayuda. Necesita supervisión o una pequeña ayuda física por parte de otra persona o utiliza andador.	
	5	Independiente en silla de ruedas. No requiere ayuda ni supervisión	
	0	Dependiente	
Subir y bajar escaleras			
	10	Independiente. Capaz de subir y bajar un piso sin ayuda ni supervisión de otra persona.	
	5	Necesita ayuda. Necesita ayuda o supervisión.	
	0	Dependiente. Es incapaz de salvar escalones	

La incapacidad funcional se valora como:	* Severa: < 45 puntos. * Grave: 45 - 59 puntos. **ASISTIDO/A**	* Moderada: 60 - 80 puntos. * Ligera: 80 - 100 puntos. **VÁLIDO/A**	**Puntuación Total:**

APPENDIX N. LAWTON AND BRODY IADLs SCALE

Escala de Lawton y Brody para las actividades instrumentales de la vida diaria (AIVD)

Mide capacidad y tienen un buen coeficiente de reproductibilidad (0,94)

Paciente……..Edad……..Sexo……

Anotar con la ayuda del cuidador principal, cuál es la situación concreta personal del paciente, respecto a estos 8 ítems de actividades instrumentales de la vida diaria

		Puntos
A.	**CAPACIDAD PARA USAR EL TELÉFONO**	
1.	Utiliza el teléfono a iniciativa propia, busca y márca los números, etc	
2.	Marca unos cuantos números bien conocidos	1
3.	Contesta el teléfono pero no marca	1
4.	No usa el teléfono	0
B.	**IR DE COMPRAS**	
1.	Realiza todas las compras necesarias con independencia	1
2.	Compra con independencia pequeñas cosas	0
3.	Necesita compañía para realizar cualquier compra	0
4.	Completamente incapaz de ir de compras	0
C.	**PREPARACIÓN DE LA COMIDA**	
1.	Planea, prepara y sirve las comidas adecuadas con independencia	1
2.	Prepara las comidas si se le dan los ingredientes	0
3.	Calienta y sirve las comidas pero no mantiene una dieta adecuada	0
4.	Necesita que se le prepare y sirva la comida	0
D.	**CUIDAR LA CASA**	
1.	Cuida la casa sólo o con ayuda ocasional (ej. Trabajos pesados)	1
2.	Realiza tareas domésticas ligeras como fregar o hacer cama	1
3.	Realiza tareas domésticas ligeras pero no puede mantener un nivel de limpieza aceptable	1
4.	Necesita ayuda en todas las tareas de la casa	1
5.	No participa en ninguna tarea doméstica	0
E.	**LAVADO DE ROPA**	
1.	Realiza completamente el lavado de ropa personal	1
2.	Lava ropa pequeña	1
3.	Necesita que otro se ocupe del lavado	0
F.	**MEDIO DE TRANSPORTE**	
1.	Viaja con independencia en transportes públicos o conduce su coche	1
2.	Capaz de organizar su propio transporte en taxi, pero no usa transporte público	1
3.	Viaja en transportes públicos si le acompaña otra persona	1
4.	Sólo viaja en taxi o automóvil con ayuda de otros	0
5.	No viaja	0
G.	**RESPONSABILIDAD SOBRE LA MEDICACIÓN**	
1.	Es responsable en el uso de la medicación, dosis y horas correctas	1
2.	Toma responsablemente la medicación si se le prepara con anticipación en dosis preparadas	0
3.	No es capaz de responsabilizarse de su propia medicación	0
H.	**CAPACIDAD DE UTILIZAR EL DINERO**	
1.	Maneja los asuntos financieros con independencia, recoge y conoce sus ingresos	1
2.	Maneja los gastos cotidianos pero necesita ayuda para ir al banco, grandes gastos, etc	1
3.	Incapaz de manejar el dinero	0

Máxima dependencia: 0 puntos
Independencia total: 8 puntos

APPENDIX O. HEALTH STATUS QUESTIONNAIRE

CUESTIONARIO DE SALUD

Nombre: _____Fecha:_____
Fecha de Nacimiento: _____Centro: _____

Antecedentes familiares: Refiera si en la familia directa alguien padece o ha padecido:

- Tensión arterial alta (hipertensión)
- Problemas de corazón:
- Diabetes (Tipo):
- Niveles altos de colesterol:
  (200-250 Hipercolesterolemia leve; 250-300 moderada; >300 grave)
- Sobrepeso/obesidad (IMC 25-30; IMC >30):
- Artritis
- Artrosis
- Osteoporosis
- Alergias o asma
- Cáncer (tipo):
- Problemas emocionales o psiquiátricos. Epilepsia
- Muerte repentina
- Enfermedades hereditarias (hemofilia, síndrome de Marfan, etc)

Antecedentes personales: Si padece o ha padecido alguno de los siguientes problemas:

1- Relacionados con trastornos cardiovasculares:

- Hipertensión arterial (tensión arterial alta: > 140-90)
- Tensión arterial baja (tensión arterial baja: <120-80)
- Problemas de corazón (tipo; arterias coronarias, válvulas, etc):
- Marcapasos
- Varices (enfermedad vascular periférica)
- Aterosclerosis
- Arritmias
- Aneurisma
- Accidente cerebrovascular (ictus)
- Insuficiencia cardiaca congestiva
- Infarto agudo de miocardio (ataque de corazón)
- Angina de pecho
- Trombosis venosa profunda y embolia pulmonares

2- Relacionados con trastornos metabólicos:

- Diabetes (Tipo):
- Niveles altos de colesterol:
  (200-250 Hipercolesterolemia leve; 250-300 moderada; >300 grave)
- Sobrepeso/obesidad (IMC 25-30; IMC >30):
- Insuficiencia renal
- Hepatitis o ictericia
- Hipertiroidismo
- Hipotiroidismo

3-Relacionados con trastornos óseos:

- Artrosis (desgaste óseo)
- Artritis (inflamación articular)
- Osteoporosis
- Prótesis (tipo, lugar, desde cuándo)
- Fracturas óseas (sin prótesis)
- Hernia discal
- Fractura vertebral

4- Relacionados con trastornos inmunológicos:

- Alergias (tipo)
- Asma
- Urticaria
- Lupus
- Artritis reumatoide
- Dermatitis
- Rinitis
- Esclerosis Múltiple
- Conjuntivitis
- Psoriasis

5- Relacionados con trastornos intestinales:

- Problemas de digestión
- Problemas intestinales
- Gastritis
- Úlceras
- Estreñimiento (problemas de evaluación)
- Incontinencia urinaria
- Problemas de próstata

6- Relacionados con trastornos musculoesqueléticos:

- Dolor lumbar frecuente (Lumbalgia)
- Dolor cervical frecuente (Cervicalgia)
- Problemas hombro (síndrome subacromial, hombro congelado, etc):
- Problemas codo (epicondilitis, epitrocleítis, bursitis):
- Síndrome del túnel carpiano
- Síndrome de DeQuervain
- Hipercifosis
- Escoliosis

7- Relacionados con trastornos psicológicos:

- ☐ Depresión
- ☐ Ansiedad
- ☐ Trastorno obsesivo-compulsivo
- ☐ Hipocondría
- ☐ Trastornos del sueño
- ☐ Algún tipo de fobia

8- Relacionados con la alimentación:

- ☐ Toma suplementos nutritivos actualmente (vitaminas, hierro, calcio, etc)
- ☐ Toma bebidas alcohólicas habitualmente. ¿Cuántas?
- ☐ Toma café ¿Cuántos al día?
- ☐ Toma bebidas con cafeína ¿Cuántas al día?

9- Otros:

- ☐ Fuma (Cigarrillos/día):
- ☐ Terapia Sustitutiva o de Reemplazo Hormonal (TRH)
- ☐ Problemas de piel como picor, enrojecimiento, erupciones
- ☐ Intervenciones quirúrgicas en el pasado
- ☐ Cataratas
- ☐ Fibromialgia
- ☐ Problemas de visión:
- ☐ Epilepsia o convulsiones
- ☐ Anemia
- ☐ Cáncer (tipo):
- ☐ Otras enfermedades:
- ☐ Algún problema de salud no mencionado hasta ahora:

10- Medicación que toma:

Firma:

APPENDIX P. ATTENDANCE RECORD SHEET

CMAPM – BENICALAP

Horario: Lunes y miércoles 11:45- 12:45 horas (Noviembre)

	NOMBRE	L-27	X-29	L-3	X-5	L-10	X-12	L-17	X-19	L-24	X-27
1	Cabello P										
2	Magdalen										
3	Carmen M										
4	Carmen R										
5	Ester Lor										
6	Angeles F										
7	Amparo C										
8	Pilar Mar										
9	Josefina S										
10	Virtudes I										
11	Celia Mar										
12	Gabriel F										
13	Ana Tole										
14	Ilda Fern										
15	José Seis										
17	Margarita										
18	Julia Esq										
19	Josefina I										
20	Pilar Garc										
21	María Lop										
22	Julia Este										
23	Amparo F										
24	Carmen T										
25	Patrocinio										
26	Mª Luisa										
27	Mª Pieda										
28	Ignasia M										
29	Angelines										
30	Victoria N										
31	Pilar Dor										
32	Diego Sán										
33	Josefa Mu										
34	José Pavi										
35	Desampar										
36	Lucia Pér										
37	Mª Pilar M										
38	María Gar										
39	Carmen F										
40	Gregoria J										

APPENDIX Q. CHECKLIST FOR SUPERVISE TRAINING SESSIONS

CMAPM:	**N° sesión:**	**Fecha:**	
		SI	**NO**
1. ¿El instructor revisa el estado de las bandas elásticas entregadas a los participantes?			
2. ¿Da aviso a los directivos del centro del inicio de la sesión?			
3. ¿Revisa y ajusta la temperatura de la sala?			
4. ¿Realiza el control de asistencia de los participantes?			
5. ¿Entrega las bandas elásticas correspondientes a cada adulto mayor?			
6. ¿Solicita la revisión del estado de las bandas por parte de los participantes?			
7. ¿Se lleva a cabo el calentamiento el tiempo estipulado y siguiendo el protocolo correspondiente a la sesión?			
8. ¿Realiza los ejercicios de entrenamiento correspondientes a la sesión?			
9. ¿Recuerda la técnica de ejecución de cada ejercicio?			
10. ¿Recuerda y/o educa control de la respiración?			
11. ¿Corrige y/o solicita al intructor de referencia la corrección de los adultos mayores que no realizan la técnica de ejercicio adecuadamente?			
12. ¿Cumple el tiempo de pausa activa?			
13. ¿Realiza e control de la intensidad con OMNI-RES al iniciar cada ejercicio?			
14. ¿Registra las variaciones de ancho de agarre y color de banda elástica (de existir) utilizado por cada participante?			
15. ¿Otorga los tiempos de hidratación correspondientes?			
16. ¿Cumple con el tiempo de elongación y protocolo de elongación?			
17. ¿Recoge y guarda el material utilizado?			
18. ¿Desecha (de producirse el caso) las bandas elásticas rotas?			
19. ¿Da aviso a los directivos del fin de la sesión y la asistencia del día?			

APPENDIX R. CLINICALTRIAL PROTOCOL REGISTRATION

ClinicalTrials.gov PRS
Protocol Registration and Results System

ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: March 8, 2018

ClinicalTrials.gov ID: NCT03455179

Study Identification

Unique Protocol ID:	H1508742840440
Brief Title:	Effects of Slow-speed Traditional Resistance Training, High-speed Resistance Training and Multicomponent Training With Variable Resistances on Molecular, Body Composition, Neuromuscular, Physical Function and Quality of Life Variables in Older Adults.
Official Title:	Effects of Slow-speed Traditional Resistance Training, High-speed Resistance Training and Multicomponent Training With Variable Resistances on Molecular, Body Composition, Neuromuscular, Physical Function and Quality of Life Variables in Older Adults.
Secondary IDs:	

APPENDIX S. ETHICS COMMITTEE APPROVAL

VNIVERSITAT DE VALÈNCIA Vicerectorat d'Investigació i Política Científica

D. José María Montiel Company, Profesor Contratado Doctor Interino del departamento de Estomatología, y Secretario del Comité Ético de Investigación en Humanos de la Comisión de Ética en Investigación Experimental de la Universitat de València,

CERTIFICA:

Que el Comité Ético de Investigación en Humanos, en la reunión celebrada el día 6 de noviembre de 2017, una vez estudiado el proyecto de investigación titulado: *"Efectos del entrenamiento multicomponente, de fuerza y de potencia con dispositivos elásticos sobre la densidad mineral ósea, la composición corporal, el perfil óseo, inflamatorio, lipídico, glucídico, el estrés oxidativo y la función motora en adultos mayores", número de procedimiento H1508742840440,*
cuyo responsable es D. Juan Carlos Colado Sánchez,
ha acordado informar favorablemente el mismo dado que se respetan los principios fundamentales establecidos en la Declaración de Helsinki, en el Convenio del Consejo de Europa relativo a los derechos humanos y cumple los requisitos establecidos en la legislación española en el ámbito de la investigación biomédica, la protección de datos de carácter personal y la bioética.

Y para que conste, se firma el presente certificado en Valencia, a quince de noviembre de dos mil diecisiete.

UNIVERSITAT DE VALÈNCIA

Av. Blasco Ibáñez, 13 Valencia 46010 tel. 9638 64109 fax. 9638 83221 vicerec.investigacio@uv.es www.uv.es/serinves

APPENDIX T. INFORMED CONSENT

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FORMULARIO DE CONSENTIMIENTO CON CONOCIMIENTO DE CAUSA

I.- CONSENTIMIENTO INFORMADO Y DERECHO A LA INFORMACIÓN

Sirva el presente escrito para mostrarle nuestra invitación formal a participar en el proyecto de investigación que a continuación se describe. Le rogamos que lea con atención el siguiente documento donde se le proporciona información acerca del estudio al que se le invita participar, así como información sobre sus derechos en el tratamiento y confidencialidad de los datos. Igualmente, podrá consultar con el equipo investigador todas las dudas que se le planteen o cualquier cuestión que le surja. A su vez, la firma de este documento certificará su consentimiento en la participación de dicho estudio denominado **"EFECTOS DEL ENTRENAMIENTO MULTICOMPONENTE, DE FUERZA Y DE POTENCIA CON DISPOSITIVOS ELÁSTICOS SOBRE LA DENSIDAD MINERAL ÓSEA, LA COMPOSICIÓN CORPORAL, EL PERFIL ÓSEO, INFLAMATORIO, LIPÍDICO, GLUCÍDICO, EL ESTRÉS OXIDATIVO Y LA FUNCIÓN MOTORA EN ADULTOS MAYORES."**. El estudio está dirigido por el Dr. Juan Carlos Colado Sánchez del Departamento de Educación Física y Deportiva de la Universidad de Valencia.

En caso de que colabore como grupo de no realización de ejercicio físico deberá seguir con el desarrollo habitual de su vida diaria según las consideraciones que nos indicó y por las que fue incluido en este estudio, mientras que si colabora en alguno de los grupos de ejercicio deberá desarrollar dos veces a la semana un protocolo de ejercicio para el entrenamiento de la fuerza con bandas elásticas, absteniéndose de realizar algún otro protocolo de ejercicio físico. Es importante considerar posibles efectos adversos o riesgos que puede experimentar al realizar el protocolo de ejercicio físico, como por ejemplo la aparición de dolor, rigidez, fatiga, mareos, o lesiones músculo-esqueléticas como pudiera ser una sobrecarga muscular o dolor muscular de inicio retardado (clásicas agujetas).

Para poder comprobar los efectos de los dicho protocolo de ejercicio físico, todas las personas que colaboren, incluido/a usted, deberán efectuar en dos momentos temporales (al inicio y al finalizar el programa de entrenamiento) una serie de pruebas físicas con diversos aparatos (densitómetro, dinamómetro isocinético, ecógrafo) que pretenderán medir la densidad mineral ósea de sus huesos, su composición corporal [se utilizará un densitómetro QDR Explorer Wi Hologic (USA) que le someterá a una pequeña dosis de radiación, siendo ésta menor que la equivalente a la exposición de un día a la radiación natural], su rendimiento físico (fuerza, equilibrio, agilidad, resistencia), junto con una serie de cuestionarios que pretenderán evaluar su calidad de vida y disfrute hacia el programa y actividades recibidas, siguiendo en todos los casos los protocolos científicos habituales al respecto. Entre los posibles riesgos que pudiera conllevar la realización de las valoraciones se encuentra el dolor, la fatiga, calambres, mareos y lesiones músculo-esqueléticas como pudieran ser sobrecargas musculares o dolor muscular de inicio retardado.

II.- OBTENCIÓN DE MUESTRAS BIOLÓGICAS

Además, en este estudio un aspecto de gran interés es la valoración y seguimiento del grado de envejecimiento biológico de las personas a través de la determinación de diferentes parámetros clínicos y genéticos. Para ello, junto con las pruebas anteriormente mencionadas, se llevarán a cabo análisis de sangre y orina para poder monitorizar

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parámetros génicos de estrés oxidativo (8-OHdG), así como parámetros moleculares de perfil óseo (osteocalcina y BCTX), lipídicos (colesterol, total, c-HDL, c-LDL, c-VLDL), glucídico (glucosa, hemoglobina glicosilada) y de inflamación (proteína C reactiva). Entre los posibles efectos adversos o riesgos que puede experimentar al realizar la extracción venosa se encuentra dolor, lesión nerviosa, punción de arteria, hematoma, sangrado abundante, infección, disminución de la presión sanguínea, mareo, fatiga. La manipulación de las muestras, su conservación y el tratamiento de los datos personales y resultados obtenidos se llevará a cabo siguiendo las normas de confidencialidad y éticas que se describen más abajo.

III.- PROTECCIÓN DE DATOS

1. Confidencialidad y tratamiento de datos.

La información facilitada será tratada de forma confidencial respecto a la legislación vigente en materia de protección de datos e investigación biomédica. A tal efecto y de acuerdo con La Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal, la ley 41/2002 de 14 de Noviembre, que regula la autonomía del paciente y de los derechos y obligaciones en materia de información y documentación clínica y la Ley 14/2007, de 3 de julio, de Investigación biomédica, le informamos que en cumplimiento de lo dispuesto por el Real Decreto 1720/2007, de 21 de diciembre, por el que se aprueba el Reglamento de desarrollo de la Ley Orgánica 15/1999, se adoptarán las medidas de seguridad estipuladas legalmente para garantizar la absoluta confidencialidad de la información personal y de salud a la que los investigadores tengan acceso. En todos los casos, los datos se conservarán de forma codificada en un fichero, sin ningún tipo de información que pudiera hacer posible identificarse con usted, garantizando la confidencialidad de los datos recogidos. Así, se informa que toda la información personal recibida será codificada y sólo la persona responsable podrá relacionar dichos datos con usted. Por lo tanto, su identidad no será revelada a persona alguna salvo excepciones tales como urgencia médica o requerimiento legal.

2. Uso de los datos.

Los datos e información derivada de la participación en el proyecto podrá ser utilizada para el desarrollo de funciones docentes y académicas propias de la Universidad de Valencia, tales como:

- Investigación científica
- Creación, desarrollo y transmisión de los hallazgos obtenidos a través de publicaciones científicas, asistencia a congresos, etc.
- Marketing y difusión del proyecto de investigador.

Cualquier divulgación pública de los datos obtenidos con motivo de la investigación se realizará anonimizando debidamente los datos que serán utilizados de modo que los sujetos de la investigación no resulten identificados o identificables.

3. Revocación y ejercicio de derechos.

Usted podrá revocar el presente consentimiento en cualquier momento sin justificar las razones que le hayan llevado a tal decisión. En caso de revocación, sus datos serán conservados durante 5 años conforme a lo establecido en el art. 17.1 de la Ley 41/2002 y sus muestras biológicas serán destruidas.

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Usted puede ejercer los derechos de acceso, rectificación, cancelación u oposición al tratamiento o revocar el consentimiento, mediante presentación de escrito adjuntando documento identificativo. Para ello diríjase a:

Protección de datos

Servei d'Informàtica

Avenida de Blasco Ibáñez 13.

46010, Valencia".

(Se recomienda que en su solicitud indique Vd. el título del Proyecto « _____ ».").

IV.- COMPROMISOS Y AUTORIZACIÓN

La falta a estos compromisos y a los momentos marcados de evaluación le puede hacer perder cualquier derecho de continuidad en el estudio. También queda informado de que su participación en este estudio es totalmente voluntaria, pudiéndose retirar del estudio en cualquier momento, así como que no recibirá compensación económica alguna por su participación en el mismo. Con su firma de este Consentimiento Informado, usted manifiesta explícitamente que ha entendido la descripción del tipo de ejercicio a realizar y sus posibles complicaciones, así como de las evaluaciones pertinentes. Además, usted indica que cualquier duda que haya podido surgir sobre el proceso de evaluación y sus posibles riesgos ha sido respondida con claridad, quedando satisfecho con las explicaciones aportadas. De igual forma manifiesta que se le ha informado del compromiso por parte de los responsables del estudio acerca de la confidencialidad de aquellos datos personales que respecto de su persona pueden recabar los mismos durante la realización de la investigación. Así mismo se le informa del derecho a acceder a toda información y resultados obtenidos del análisis de muestras extraídas.

Le informamos que al firmar este documento usted está AUTORIZANDO Y CONSINTIENDO DE FORMA EXPRESA E INEQUÍVOCA a:

- A participar en el estudio.
- A la obtención de muestras biológicas.
- Al tratamiento de sus datos personales y sanitarios, incluida la creación, utilización y difusión del material fotográfico y de vídeo, con los fines indicados en este documento.

En Valencia a _____de_____de 2017.

D. Dña._____

DNI_____

Firma_____

APPENDIX U. 3-DAY NUTRITION INTAKE RECORD SHEET

Nombre y apellidos:

Fechas: De ____/_____/_____ a ___/_____/_____

Por favor, lea atentamente las indicaciones que se dan a continuación para rellenar correctamente esta encuesta. No olvide completar los datos personales y las fechas.

Si tiene alguna duda u observación apúntela con detalle en el espacio para tal fin de la última hoja.

FORMA DE RECOGER LOS DATOS

1. Anote todos los alimentos consumidos durante 3 días **CONSECUTIVOS** (2 ENTRE SEMANA y 1 FIN DE SEMANA) Indique:

a) **Plato** (p.e. pollo en salsa)

b) **Ingredientes** (p.e. pechuga de pollo, tomate natural, cebolla, ajo y aceite de oliva)

c) **Cantidad** expresada según peso o porción **APROXIMADA O MEDIDA CASERA** (p.e. 200 gramos o ½ pechuga; un cazo sopero de lentejas o una cucharada de aceite, etc). Si son galletas, o alimentos que se puedan contar por unidades, indicar el número de unidades (p.e. 3 galletas; 3 rebanadas de pan; 4 varitas de merluza; 1 longaniza; 5 nueces; etc).

(*NOTA:* a continuación tiene dos hojas con información sobre medidas caseras para facilitarle esta labor).

d) **Marca del producto** (p.e. Gullón, Hacendado, Bimbo, Galletas Príncipe).

2. **Indique el aceite utilizado** en la preparación del plato.

3. **Registre la leche y bebidas consumidas** (que no sea agua). Exprese la cantidad aproximada según el vaso o taza en el que se sirvió (p.e. vaso de agua, taza de desayuno). No olvide anotar si añadió azúcar u otro tipo de edulcorante a la bebida.

Correlación de medidas caseras de los alimentos			
Grupo de alimentos	**Alimentos**	**Medida casera**	**Ración**
Leche y derivados	Leche Yogur Queso fresco Queso curado Flan, natillas	1 vaso 1 unidad 1 loncha 1 loncha 1 unidad	200 mL 125 g 30 g 40 g 120 g
Pan, cereales y féculas	Arroz, pasta Patata Pan Legumbres Cereales Frutos secos	1 plato 1 unidad mediana 1 rebanada 1 plato 1 bol 1 bol	180-240 g 180 g 20 g 200 g 45 g 125 g
Carne, pescados, huevos	Carne/pescado Huevos Embutido	1 ración pequeña 1 unidad 1 loncha	80-100 g 50 g 20 g
Frutas	Fruta fresca o seca Zumos	1 pieza mediana 1 brik	100-200 g 200 mL
Verduras y hortalizas	Hervidas, en puré o en ensalada	1 plato	100-200 g
Grasas	Aceites vegetales Mantequilla Margarina Nata, crema de leche	1 cucharada sopera 1 cucharada sopera 1 cucharada sopera 1 cucharada sopera	10 g 10 g 10 g 10 g
Refrescos y otras bebidas	Refrescos de cola, energéticos, cítricos, con gas, etc.	Ver etiquetado del fabricante	
Otros	Pastelería industrial, snacks, chucherías, etc.	Ver etiquetado del fabricante	

Medida casera			Ración
Cucharada	Café		3 g
	Postre		5 g
	Sopera		10-15 g
Taza	Café	  	50 mL
	De leche		150-200 mL
	Tazón		250-300 mL
Vaso	Pequeño	  	50 mL
	De agua		200 mL
	Copa		100 mL
Plato	De postre	  	75-100 g
	Llano		150-250 g
	Hondo		200-300 g
Punta de cuchillo	Ej: mantequilla		5 g

Medida Casera			**Ración**
Cucharada	sopera colmada		20 g
	Sopera rasa		15 g
	Postre colmada		7 g
	Postre rasa		5 g
	Café colmada		4 g
	Café rasa		2 g

DÍA 0: Ejemplo

Fecha: ___/_____/_____

	Plato	Ingredientes	Cantidad	Marca del producto
Desayuno	Vaso de leche con cereales	Leche semidesnatada	200ml	Hacendado
		Cereales	3 c.s	Chocapic
		Cacao soluble	1 c.p	Hacendado
Almuerzo	Bocadillo de jamón serrano y zumo	Pan blanco	5 dedos	Hacendado
		Jamón serrano	2 lonchas	Navidul
		Aceite de oliva	1 c.p*	Hacendado
		Zumo de melocotón	Brick 200 ml	Hacendado
Comida	Paella Fanta y Naranja	Arroz	Plato pequeño	Hacendado
		Judías	3-4 unidades	
		Alubias	3-4 unidades	
		Costillas de cerdo	2-3 unidades	
		Muslo/alita de pollo	1-2 unidades	
		Aceite de oliva	2 c.s*	
		Pimiento rojo	2 tiras	
		Albóndigas	2	
		Fanta de naranja	2 vasos	Fanta
		Naranja	Mediana	
Merienda	Yogur y galletas	Yogur con cereales	125g (1)	Hacendado
		Galletas de chocolate	3	Príncipe
Cena	Pechuga rebozada, pan integral, ensalada de tomate y pera	Pechuga	1 filete	
		Harina	1 c.s	Hacendado
		Aceite de oliva	2 c.s	
		Pan integral	3 dedos	Hacendado
		Tomate	1 mediano	
		Pera	1 mediana	
Entre Horas	Leche con galletas	Leche	Brick 200ml	Puleva
		Galletas	6 unidades	Gullón

*c.c → cuchara café
c.p → cuchara postre
c.s → cuchara sopera

DÍA 1

Fecha: ___/_____/_____

	Plato	Ingredientes	Cantidad	Marca del producto
Desayuno				
Almuerzo				
Comida				
Merienda				
Cena				
Entre Horas				

DÍA 2

Fecha: ___/_____/_____

	Plato	Ingredientes	Cantidad	Marca del producto
Desayuno				
Almuerzo				
Comida				
Merienda				
Cena				
Entre Horas				

DÍA 3

Fecha: ___/_____/_____

	Plato	Ingredientes	Cantidad	Marca del producto
Desayuno				
Almuerzo				
Comida				
Merienda				
Cena				
Entre Horas				

COMENTARIOS/OBSERVACIONES

a) Consumo de sal

¿Añade sal en la preparación de las comidas?

SÍ ( ) NO ( ) A VECES ( )

¿Añade sal en las comidas cuando el plato ya está en la mesa?

SÍ ( ) NO ( ) A VECES ( )

b) Consumo de alcohol

SÍ ( ) NO ( )

Frecuencia:…….

Cantidad:……

Tipo:……..

c) Consumo de suplementos vitamínicos y minerales

SÍ ( ) NO ( )

Marca comercial……

APPENDIX V. GPAQ

Actividad física

A continuación voy a preguntarle por el tiempo que pasa realizando diferentes tipos de actividad física. Le ruego que intente contestar a las preguntas aunque no se considere una persona activa.

Piense primero en el tiempo que pasa en el trabajo, que se trate de un empleo remunerado o no, de estudiar, de mantener su casa, de cosechar, de pescar, de cazar o de buscar trabajo *[inserte otros ejemplos si es necesario]*. En estas preguntas, las "actividades físicas intensas" se refieren a aquéllas que implican un esfuerzo físico importante y que causan una gran aceleración de la respiración o del ritmo cardíaco. Por otra parte, las "actividades físicas de intensidad moderada" son aquéllas que implican un esfuerzo físico moderado y causan una ligera aceleración de la respiración o del ritmo cardíaco.

	Pregunta	Respuesta	Código
En el trabajo			
49	¿Exige su trabajo una actividad física intensa que implica una aceleración importante de la respiración o del ritmo cardíaco, como [*levantar pesos, cavar o trabajos de construcción*] durante al menos 10 minutos consecutivos? *(INSERTAR EJEMPLOS Y UTILIZAR LAS CARTILLAS DE IMÁGENES)*	Sí 1 No 2 *Si No, Saltar a P 4*	P1
50	En una semana típica, ¿cuántos días realiza usted actividades físicas intensas en su trabajo?	Número de días ⌊__⌋	P2
51	En uno de esos días en los que realiza actividades físicas intensas, ¿cuánto tiempo suele dedicar a esas actividades?	Horas : minutos ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P3 (a-b)
52	¿Exige su trabajo una actividad de intensidad moderada que implica una ligera aceleración de la respiración o del ritmo cardíaco, como caminar deprisa *[o transportar pesos ligeros]* durante al menos 10 minutos consecutivos? *(INSERTAR EJEMPLOS Y UTILIZAR LAS CARTILLAS DE IMÁGENES)*	Sí 1 No 2 *Si No, Saltar a P7*	P4
53	En una semana típica, ¿cuántos días realiza usted actividades de intensidad moderada en su trabajo?	Número de días ⌊__⌋	P5
54	En uno de esos días en los que realiza actividades físicas de intensidad moderada, ¿cuánto tiempo suele dedicar a esas actividades?	Horas : minutos ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P6 (a-b)
Para desplazarse			
En las siguientes preguntas, dejaremos de lado las actividades físicas en el trabajo, de las que ya hemos tratado. Ahora me gustaría saber cómo se desplaza de un sitio a otro. Por ejemplo, cómo va al trabajo, de compras, al mercado, al lugar de culto [*insertar otros ejemplos si es necesario*]			
55	¿Camina usted o usa usted una bicicleta al menos 10 minutos consecutivos en sus desplazamientos?	Sí 1 No 2 *Si No, Saltar a P 10*	P7
56	En una semana típica, ¿cuántos días camina o va en bicicleta al menos 10 minutos consecutivos en sus desplazamientos?	Número de días ⌊__⌋	P8
57	En un día típico, ¿cuánto tiempo pasa caminando o yendo en bicicleta para desplazarse?	Horas : minutos ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P9 (a-b)
En el tiempo libre			
Las preguntas que van a continuación excluyen la actividad física en el trabajo y para desplazarse, que ya hemos mencionado. Ahora me gustaría tratar de deportes, fitness u otras actividades físicas que practica en su tiempo libre [inserte otros ejemplos si llega el caso].			
58	¿En su tiempo libre, practica usted deportes/fitness intensos que implican una aceleración importante de la respiración o del ritmo cardíaco como [*correr, jugar al fútbol*] durante al menos 10 minutos consecutivos? *(INSERTAR EJEMPLOS Y UTILIZAR LAS CARTILLAS DE IMÁGENES)*	Sí 1 No 2 *Si No, Saltar a P 13*	P10
59	En una semana típica, ¿cuántos días practica usted deportes/fitness intensos en su tiempo libre?	Número de días ⌊__⌋	P11
60	En uno de esos días en los que practica deportes/fitness intensos, ¿cuánto tiempo suele dedicar a esas actividades?	Horas : minutos ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P12 (a-b)

SECCIÓN PRINCIPAL: Actividad física (en el tiempo libre) sigue.			
Pregunta		**Respuesta**	**Código**
61	¿En su tiempo libre practica usted alguna actividad de intensidad moderada que implica una ligera aceleración de la respiración o del ritmo cardíaco, como caminar deprisa, [*ir en bicicleta, nadar, jugar al volleybal*] durante al menos 10 minutos consecutivos? *(INSERTAR EJEMPLOS Y UTILIZAR LAS CARTILLAS DE IMÁGENES)*	Si 1 No 2 *Si No, Saltar a P16*	P13
62	En una semana típica, ¿cuántos días practica usted actividades físicas de intensidad moderada en su tiempo libre?	Número de días ⌊__⌋	P14
63	En uno de esos días en los que practica actividades físicas de intensidad moderada, ¿cuánto tiempo suele dedicar a esas actividades?	Horas : minutos ⌊__⌋ : ⌊__⌋ hrs mins	P15 (a-b)
Comportamiento sedentario			
La siguiente pregunta se refiere al tiempo que suele pasar sentado o recostado en el trabajo, en casa, en los desplazamientos o con sus amigos. Se incluye el tiempo pasado [ante una mesa de trabajo, sentado con los amigos, viajando en autobús o en tren, jugando a las cartas o viendo la televisión], pero no se incluye el tiempo pasado durmiendo. *(INSERTAR EJEMPLOS) (UTILIZAR LAS CARTILLAS DE IMÁGENES)*			
64	¿Cuándo tiempo suele pasar sentado o recostado en un día típico?	Horas : minutos ⌊__⌋ : ⌊__⌋ hrs mins	P16 (a-b)

APPENDIX W. OASIS SCALE

Los siguientes ítems preguntan sobre ansiedad y miedo. Para cada ítem, selecciona el número que mejor describe tu experiencia **durante la última semana**.

1. Durante la última semana, ¿con qué frecuencia te has sentido ansioso?

0 **= *No me sentí ansioso*** durante la última semana.

1 = ***Ansiedad infrecuente***. Me sentí ansioso en algunos momentos.

2 = ***Ansiedad ocasional***. La mitad del tiempo me sentí ansioso y la otra mitad no. Me costó relajarme.

3 = ***Ansiedad frecuente***. Me sentí ansioso la mayor parte del tiempo. Me resultó muy difícil relajarme.

4 = ***Ansiedad constante***. Me sentí ansioso todo el tiempo y nunca llegué a relajarme.

2. Durante la última semana, cuando te sentiste ansioso, ¿en qué medida tu ansiedad fue intensa o severa?

0 = ***Poco o nada***. La ansiedad estuvo ausente o casi no la noté.

1 = ***Leve.*** La ansiedad fue de baja intensidad. Pude relajarme cuando lo intenté. Los síntomas físicos fueron sólo un poco molestos.

2 = ***Moderada***. La ansiedad me generó malestar en algunos momentos. Me resultó difícil relajarme o concentrarme, pero pude hacerlo cuando lo intenté. Los síntomas físicos fueron molestos.

3 = ***Severa***. La ansiedad fue intensa la mayor parte del tiempo. Me resultó muy difícil relajarme o concentrarme en cualquier otra cosa. Los síntomas físicos fueron enormemente molestos.

4 = ***Extrema.*** La ansiedad me sobrepasó. Me fue totalmente imposible relajarme. Los síntomas físicos fueron insoportables.

3. Durante la última semana, ¿con qué frecuencia evitaste situaciones, lugares, objetos o actividades debido a tu ansiedad o miedo?

0 = ***Ninguna.*** No evité lugares, situaciones, actividades o cosas por miedo.

1 = ***Infrecuente***. Evité algunas cosas de vez en cuando, pero por lo general me enfrenté a las situaciones u objetos. Mi estilo de vida no se vio afectado.

2 = ***Ocasional.*** Tuve algo de miedo a ciertas situaciones, lugares u objetos, pero todavía pudo manejarlos. Mi estilo de vida sufrió pocos cambios. Siempre o casi siempre evité las cosas que me dan miedo si estaba solo, pero las pude manejar si alguien venía conmigo.

3 = ***Frecuente.*** Tuve bastante miedo y realmente intenté evitar las cosas que me asustan. He hecho cambios significativos en mi estilo de vida para evitar objetos, situaciones, actividades o lugares.

4 = ***Todo el tiempo***. Evitar objetos, situaciones, actividades o lugares ha ocupado gran parte de mi vida. Mi estilo de vida se ha visto enormemente afectado y ya no hago cosas con las que solía disfrutar.

4. Durante la última semana, ¿en qué medida ha interferido la ansiedad en tu capacidad para hacer las cosas que tenías que hacer respecto al trabajo, el colegio o tu hogar?

0 = ***Nada.*** La ansiedad no interfirió en mi trabajo/hogar/colegio.

1 = ***Leve.*** La ansiedad me causó algo de interferencia en mi trabajo/hogar/colegio. Las cosas eran más difíciles, pero pude realizar todo lo que necesitaba hacer.

2 = ***Moderada***. La ansiedad definitivamente interfirió en mis tareas. He podido realizar la mayoría de las cosas, pero sólo algunas las he hecho tan bien como en el pasado.

3 = ***Severa.*** La ansiedad verdaderamente ha cambiado mi capacidad para hacer las cosas. Algunas cosas las he podido realizar, pero otras no. Mi rendimiento se ha visto definitivamente afectado.

4 = ***Extrema***. La ansiedad ha llegado a ser incapacitante. He sido incapaz de completar mis tareas y he tenido que irme del colegio, he dejado o me han despedido de mi trabajo o he sido incapaz de completar las tareas del hogar y he sufrido consecuencias como desalojos, cobradores, etc.

5. Durante la última semana, ¿en qué medida ha interferido la ansiedad en tu vida social y en tus relaciones?

0 = ***Nada.*** La ansiedad no interfirió en mis relaciones.

1 = ***Leve***. La ansiedad apenas interfirió en mis relaciones. Algunas de mis amistades y otras relaciones se han visto afectadas, pero en conjunto mi vida social sigue siendo satisfactoria.

2 = ***Moderada***. La ansiedad interfirió algo en mi vida social, pero sigo teniendo algunas relaciones cercanas. No paso tanto tiempo con otros como en el pasado, pero sigo teniendo relaciones sociales algunas veces.

3 = ***Severa***. Mis amistades y otras relaciones se han visto muy afectadas a causa de mi ansiedad. No disfruto de las actividades sociales. Tengo muy pocas relaciones sociales.

4 = ***Extrema***. La ansiedad ha alterado completamente mis actividades sociales. Todas mis relaciones se han visto afectadas o han finalizado. Mi vida familiar es extremadamente tensa

APPENDIX Y. ODSIS SCALE

Los siguientes ítems preguntan sobre depresión. Para cada ítem, selecciona el número que mejor describe tu experiencia **durante la última semana**.

1. Durante la última semana, ¿con qué frecuencia te has sentido deprimido?

0 **= *No me sentí deprimido*** durante la última semana.

1 = ***Depresión infrecuente***. Me sentí deprimido en algunos momentos.

2 = ***Depresión ocasional***. La mitad del tiempo me sentí deprimido y la otra mitad no.

3 = ***Depresión frecuente***. Me sentí deprimido la mayor parte del tiempo.

4 = ***Depresión constante***. Me sentí deprimido todo el tiempo.

2. Durante la última semana, cuando te sentiste deprimido, ¿en qué medida tu depresión fue intensa o severa?

0 = ***Poco o nada***. La depresión estuvo ausente o casi no la noté.

1 = ***Leve.*** La depresión fue de baja intensidad.

2 = ***Moderada***. La depresión me generó malestar en algunos momentos.

3 = ***Severa***. La depresión fue intensa la mayor parte del tiempo.

4 = ***Extrema.*** La depresión me sobrepasó.

3. Durante la última semana, ¿con qué frecuencia tuviste dificultad para realizar o interesarte en actividades que normalmente disfrutas debido a tu depresión?

0 = ***Ninguna.*** No tuve dificultades para realizar o interesarme en actividades que normalmente disfruto debido a la depresión.

1 = ***Infrecuente***. Algunas veces tuve dificultades para realizar actividades o interesarme en actividades que normalmente disfruto, debido a la depresión. Mi estilo de vida no se vio afectado.

2 = ***Ocasional.*** Tuve algunas dificultades para realizar actividades o interesarme en actividades que normalmente disfruto, debido a la depresión. Mi estilo de vida sufrió pocos cambios.

3 = ***Frecuente.*** Tuve bastantes dificultades para realizar actividades o interesarme en actividades que normalmente disfruto, debido a la depresión. He realizado cambios significativos en mi estilo de vida por no poder interesarme en actividades que solía disfrutar.

4 = ***Todo el tiempo***. No he podido participar o interesarme en actividades que normalmente disfruto, debido a la depresión. Mi estilo de vida se ha visto enormemente afectado y ya no hago cosas que solía disfrutar.

4. Durante la última semana, ¿en qué medida ha interferido la depresión en tu capacidad para hacer las cosas que tenías que hacer respecto al trabajo, el colegio o tu hogar?

0 = ***Nada.*** La depresión no interfirió en mi trabajo/hogar/colegio.

1 = ***Leve.*** La depresión me causó algo de interferencia en mi trabajo/hogar/colegio. Las cosas fueron más difíciles, pero pude realizar todo lo que necesitaba hacer.

2 = ***Moderada***. La depresión definitivamente interfirió en mis tareas. He podido realizar la mayoría de las cosas, pero sólo algunas las he hecho tan bien como en el pasado.

3 = ***Severa.*** La depresión verdaderamente ha interferido en mis tareas. Algunas tareas las he podido realizar, pero muchas otras no. Mi rendimiento se ha visto definitivamente afectado.

4 = ***Extrema***. La depresión ha llegado a ser incapacitante. He sido incapaz de completar mis tareas y he tenido que irme del colegio, he dejado o me han despedido de mi trabajo o he sido incapaz de completar las tareas del hogar y he sufrido consecuencias como desalojos, cobradores de cuentas, etc.

5. Durante la última semana, ¿en qué medida ha interferido la depresión en tu vida social y en tus relaciones?

0 = ***Nada.*** La depresión no interfirió en mis relaciones.

1 = ***Leve***. La depresión apenas interfirió en mis relaciones. Algunas de mis amistades y otras relaciones se han visto afectadas, pero en conjunto mi vida social sigue siendo satisfactoria.

2 = ***Moderada***. La depresión ha interferido algo en mi vida social, pero sigo teniendo algunas relaciones cercanas. No paso tanto tiempo con otros como en el pasado, pero sigo manteniendo relaciones sociales algunas veces.

3 = ***Severa***. Mis amistades y otras relaciones se han visto muy afectadas a causa de mi depresión. No disfruto de las actividades sociales. Tengo muy pocas relaciones sociales.

4 = ***Extrema***. La depresión ha alterado completamente mis actividades sociales. Todas mis relaciones se han visto afectadas o han finalizado. Mi vida familiar es extremadamente tensa.

6. Durante la última semana, ¿Con qué frecuencia has tenido pensamientos sobre suicidio?

0= ***Nada***. No he tenido pensamientos de suicidio.

1= ***Infrecuente***. En alguna ocasión he tenido pensamientos de suicidio, pero de forma esporádica.

2= ***Ocasional***. Algunas veces he tenido pensamientos de suicidio.

3= ***Frecuente***. En muchas ocasiones he tenido pensamientos de suicidio.

4= ***Todo el tiempo***. Casi la mayor parte del tiempo he tenido pensamientos de suicidio

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