VNIVERSITAT DE VALÈNCIA

Facultat de Fisioteràpia

BIOPSYCHOSOCIAL FACTORS IN CARPAL TUNNEL SYNDROME

DOCTORAL THESIS - DOCTORAL PROGRAM: PHYSIOTHERAPY (3165)

Author:
Rodrigo Núñez Cortés

Supervision:
Dra. Sofía Pérez Alenda
Dr. Claudio Tapia Malebrán
Dr. Joaquín Calatayud Villalba

VALENCIA, SEPTEMBER, 2023

Dra. Dña. Sofía Pérez Alenda, Profesora Titular de la Universitat de València, adscrita al Departament de Fisioteràpia

Dr. D. Claudio Tapia Malebrán, Profesor Asistente del Departamento de Kinesiología de la Universidad de Chile.

Dr. D. Joaquín Calatayud Villalba, Profesor Contratado Doctor de la Universitat de València, adscrito al Departament de Fisioteràpia

HACEN CONSTAR:

Que el presente trabajo titulado "***Biopsychosocial factors in carpal tunnel syndrome***" ha sido realizado bajo su dirección, por D. Rodrigo Núñez Cortés, para optar al grado de Doctor por la Universitat de València. Habiéndose concluido, y reuniendo a su juicio las condiciones de originalidad y rigor científico necesarias, autorizan su presentación a fin de que pueda ser defendido ante el tribunal correspondiente.

Y para que así conste, expiden y firman la presente documentación en València a 04 de Septiembre de 2023.



Dra. S. Pérez Alenda Dr. C. Tapia Malebrán Dr. J. Calatayud Villalba

Deseo expresar mi agradecimiento:

A mis directores, Sofía Pérez, Claudio Tapia y Joaquín Calatayud, por la confianza depositada en mi, el apoyo incondicional y por compartir su sabiduría. Me siento afortunado de contar con su guía durante este largo proceso.

A todos los coautores que formaron parte de este compendio de artículos, en especial a Rodrigo Torres, Maritza Ortega, Serghio Torreblanca y Lars Andersen, cuya contribución ha sido fundamental para concretar este proyecto.

A mi amigo Carlos Cruz, quien además de ser un pilar fundamental de esta tesis, ha sido quien confió en mi desde un principio y me motivó a seguir el camino de la investigación.

A todos los pacientes que aceptaron participar de este proyecto he hicieron posible su ejecución.

A mi madre y hermana, que a pesar de estar lejos durante este proceso, trasmiten su amor y preocupación día a día, gracias por creer en mí y por ayudarme a ser quien soy.

A Clau, mi compañera en esta aventura, gracias por todo el amor que me has dado y por los bellos momentos en Valencia que recordaremos por siempre.

Preface

This Doctoral thesis has been carried out at the Faculty of Physiotherapy of the University of Valencia, with an international mention after a research stay at the "National Research Centre for the Working Environment", Copenhagen, Denmark. The supervisors of this research are Dra. Sofía Pérez Alenda, Dr. Joaquín Calatayud Villalba and Dr. Claudio Tapia Malebrán. The clinical studies were approved by the local ethics committee and were conducted in accordance with the ethical standards of the Declaration of Helsinki. The ethical approval document is included in the Appendix at the end of the main text. Rodrigo Núñez Cortés is funded by a grant from the National Agency for Research and Development (ANID)/Scholarship Program/DOCTORADO BECAS CHILE/2020−72210026.

List of studies

This doctoral thesis is a compendium of the following three studies:

Núñez-Cortés R, Cruz-Montecinos C, Torres-Castro R, Tapia C, Püschel TA, Pérez-Alenda S. Effects of Cognitive and Mental Health Factors on the Outcomes Following Carpal Tunnel Release: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil. 2022 Aug;103(8):1615-1627. **JCR 2022 Impact Factor 4.3, Category 8/68 REHABILITATION, Q1)**

Núñez-Cortés R, Cruz-Montecinos C, Torreblanca-Vargas S, Andersen LL, Tapia C, Ortega-Palavecinos M, López-Bueno R, Calatayud J, Pérez-Alenda S. Social determinants of health and physical activity are related to pain intensity and mental health in patients with carpal tunnel syndrome. Musculoskelet Sci Pract. 2023 Feb;63:102723. **JCR 2022 Impact Factor 2.3, Category 25/68 REHABILITATION, Q2)**

Núñez-Cortés R, Cruz-Montecinos C, Torreblanca-Vargas S, Tapia C, Gutiérrez-Jiménez M, Torres-Gangas P, Calatayud J, Pérez-Alenda S. Effectiveness of adding pain neuroscience education to telerehabilitation in patients with carpal tunnel syndrome: A randomized controlled trial. Musculoskelet Sci Pract. 2023. DOI: https://doi.org/10.1016/j.msksp.2023.102835. **JCR 2022 Impact Factor 2.3, Category 25/68 REHABILITATION, Q2)**

Other publications related to this doctoral thesis:

Núñez-Cortés R, Cruz-Montecinos C, Antúnez-Riveros MA, Pérez-Alenda S. Does the educational level of women influence hand grip and pinch strength in carpal tunnel syndrome? Med Hypotheses. 2020 Feb;135:109474.

Núñez-Cortés R, Cruz-Montecinos C, Tapia C, Pommer PP, Pérez-Alenda S. Carpal tunnel syndrome and pain. Features and Assessments of Pain, Anaesthesia, and Analgesia. 2022 Pages 275-283 https://doi.org/10.1016/b978-0-12-818988-7.00031-5

Núñez-Cortés R, Espin A, Pérez-Alenda S, López-Bueno R, Cruz-Montecinos C, Vincents-Seeberg KG, Püschel TA, Calatayud J, Andersen LL. Association between pain coping and symptoms of anxiety and depression, and work absenteeism in people with upper limb musculoskeletal disorders: A systematic review and meta-analysis. Arch Phys Med Rehabil. 2023 Jul 23:S0003-9993(23)00409-4. doi: 10.1016/j.apmr.2023.07.003.

List of abbreviations

BCTQ	Boston Carpal Tunnel Questionnaire
BDI-II	Beck depression Inventory
BMI	Body mass index
CES-D	Center of Epidemiologic Studies-Depression
CTS	Carpal tunnel syndrome
CTS-6	6-item Boston Carpal Tunnel Questionnaire
CTR	Carpal tunnel release
DASH	Disabilities of the Arm, Shoulder, and Hand
EQ-5D	EuroQol5-dimensions
HADS	Hospital Anxiety and Depression scale
NPRS	Numeric Pain Rating Scale
PASS	Pain Anxiety Symptoms Scale
PCS	Pain Catastrophizing Scale
PGICS	Patient Global Impression of Change Scale
PHQ4	Patient Health Questionnaire-4
PNE	Pain Neuroscience Education
RCT	Randomized controlled trial
SDH	Social Determinants of Health
SUS	System Usability Scale
TSK-11	Tampa Scale for Kinesiophobia-11
VAS	Visual Analogue Scale

Table of Contents

List of Tables

List of Figures

English Summary

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity, causing disability, reducing quality of life and limiting daily activities and work capacity. The clinical presentation of CTS is usually characterised by pain, tingling and numbness in the region of the median nerve and weakness of the thumb. In particular, persistent pain is a fairly common symptom of CTS. Currently, the most empirical approach to persistent pain is the biopsychosocial model, which proposes that pain is the result of the interaction of biological, psychological and social factors. Therefore, understanding and addressing these factors in a comprehensive manner could help in the assessment and effective treatment of people with CTS.

The purpose of this thesis was to evaluate the role of psychological and social factors on physical and mental health outcomes in patients with CTS during the pre- and post-operative periods, and to determine the efficacy of adding a biopsychosocial approach to telerehabilitation in patients with CTS awaiting surgery. To this end, three studies were proposed to specifically address the following objectives. Study I) The aim was to determine the association of catastrophising, kinesiophobia, self-efficacy, fear avoidance, and mental health factors (anxiety symptoms and depression) with outcomes after CRT, at least 3 months after surgery;

Study II) The aim was to analyse the association between social determinants of health (SDH) and physical activity with pain intensity and mental health in patients with CTR awaiting surgery; Study III) The aim was to determine the effectiveness of adding a biopsychosocial approach to telerehabilitation in patients with CTS awaiting surgery by comparing a 6-week telerehabilitation programme based on pain neuroscience education (PNE) plus exercise versus exercise alone on patient-reported outcomes at the end of treatment (week 6) and at the 6-week post-treatment follow-up (week 12).

Study I: We conducted a systematic review and meta-analysis by systematically searching Embase, Pubmed/MEDLINE, Web of Science, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL) databases from their inception to 14 August 2021. Randomised controlled trials and observational studies of patients with carpal tunnel release were included. We included studies that assessed the relationship between cognitive (catastrophic thinking, kinesiophobia and self-efficacy) or mental health (anxiety and depressive symptoms) factors and postoperative outcomes (pain, function, symptom severity, satisfaction) at least three months after surgery. Two independent reviewers extracted data and assessed risk of bias. Random-effects models were used for meta-analysis. A total of fifteen studies involving 2599 patients were included. The majority of studies indicate a

significant association between the cognitive or mental health factors and outcomes following CTR. Quantitative analysis showed a moderate association of symptoms of depression on symptom severity (n = 531, r = 0.347, 95% CI: 0.205 to 0.475, p<0.0001), function (n = 386, r = 0.307, 95% CI: 0.132 to 0.464, p=0.0008), and pain (n = 344, r = 0.431, 95% CI: 0.286 to 0.558, p<0.0001). Symptoms of anxiety, catastrophic thinking and self-efficacy were also important indicators of poor postoperative outcomes.

Study II: A cross-sectional study was conducted in patients with CTS awaiting surgery in two public hospitals in Chile. The SDH collected included: employment status, educational level and monetary income. The level of physical activity was defined according to compliance with WHO recommendations. Outcome measures included: Pain intensity (Visual Analogue Scale), Symptoms of anxiety and depression (Hospital Anxiety and Depression Scale), and catastrophic thinking (Pain Catastrophizing Scale). The adjusted regression coefficient (β) for the association between SDH and physical activity with each outcome was obtained using multivariable linear regression models controlling for age, sex, body mass index and symptom duration. Eighty-six participants were included (mean age 50.9 ± 10 years, 94% women). A high level of physical activity was associated with a 12.41 mm decrease in pain intensity (β=-12.41, 95% CI: -23.87 to -0.95) and a 3.29 points decrease in depressive symptoms (β=-3.29, 95%CI: -

5.52 to -1.06). In addition, being employed was associated with a 2.30 points decrease in anxiety symptoms (β=-2.30; 95%CI: -4.41 to -0.19) and a high educational level was associated with a 7.71 points decrease in catastrophizing (β=-7.71; 95%CI: -14.06 to -1.36);

Study III: A single-blind randomised controlled trial was conducted. Twenty-five patients with CTS were assigned to either the PNE plus exercise or the exercise-only group. The PNE was conducted through an interactive video conference with visual support. The exercise program included aerobic exercises, digital flexor tendon gliding, neurodynamic exercises and stretching. Outcome measures included pain intensity, pain catastrophizing, kinesiophobia, symptom severity, function, symptoms of anxiety and depression, quality of life, self-perception of improvement. Inferential analyses of the data were performed using a two-factor (intergroup x time) mixed analysis of variance. A significant intergroup x time point interaction with a large effect size was observed for kinesiophobia ($F=6.67$, $p=0.005$, $\eta p^2=0.225$) and symptom severity ($F=4.82$, $p=0.013$, $\eta p^2=0.173$). No significant interaction was observed for the other variables ($p>0.05$). Significant differences were observed in favour of the PNE plus exercise group after treatment on the self-perception of improvement ($p<0.05$). Although there were significant and clinically relevant improvements within the PNE plus exercise group in pain, catastrophizing and symptoms of

anxiety, there were no significant differences between the groups.

In conclusion, this thesis highlights the importance of addressing psychosocial factors in patients with carpal tunnel syndrome, both in assessment and treatment. First, we found that depressive symptoms, anxiety symptoms, catastrophic thinking and self-efficacy were important indicators of poor postoperative outcomes. Therefore, preoperative assessment of these variables could help identify patients at risk of poor surgical outcomes and provide timely treatment.

Secondly, a high level of physical activity was associated with a decrease in pain intensity and depressive symptoms in patients with CTS awaiting surgery. In addition, being employed was associated with a decrease in anxiety symptoms and having a high educational level was associated with a decrease in catastrophizing. Thus, a comprehensive assessment of these variables may be relevant to identify cases of increased psychosocial risk and to plan strategies to reduce pain and improve the mental health of patients with CTS awaiting surgery, e.g., physical activity programs guided by WHO recommendations.

Finally, the addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity in patients with CTS awaiting surgery.

There were also significant and clinically relevant improvements in pain intensity, catastrophizing and anxiety symptoms in the PNE plus exercise group. These results highlighted the benefits of including a biopsychosocial approach in telerehabilitation interventions.

Spanish Summary

El síndrome del túnel carpiano (STC) es la neuropatía por atrapamiento más frecuente de la extremidad superior, que provoca discapacidad, reduce la calidad de vida y limita las actividades cotidianas y la capacidad laboral de las personas afectadas. La presentación clínica del STC suele caracterizarse por dolor, hormigueo y entumecimiento en la región del nervio mediano y debilidad del pulgar. En particular, el dolor persistente en particular es un síntoma bastante común del STC. Actualmente, el enfoque más empírico del dolor persistente es el modelo biopsicosocial, que propone que el dolor es el resultado de la interacción de factores biológicos, psicológicos y sociales. Por lo tanto, comprender y abordar estos factores de forma integral podría ayudar en la evaluación y en el tratamiento eficaz de las personas con STC.

El propósito de esta tesis fue evaluar el papel de los factores psicológicos y sociales en los resultados de salud física y mental en pacientes con STC durante los períodos pre y postoperatorio, y determinar la eficacia de añadir un enfoque biopsicosocial a la telerehabilitación en pacientes con STC en espera de cirugía. Para ello, se propusieron tres estudios que abordaban específicamente los siguientes objetivos. Estudio I) El objetivo fue determinar la asociación entre la

catastrofización, la kinesiofobia, la autoeficacia, evitación por miedo y los factores de salud mental (síntomas de ansiedad y depresión) y los resultados tras la cirugía, al menos 3 meses después de esta; Estudio II) El objetivo fue analizar la asociación entre los determinantes sociales de la salud (DSS) y la actividad física con la intensidad del dolor y la salud mental en pacientes con STC pendientes de cirugía; Estudio III) El objetivo fue determinar la eficacia de añadir un enfoque biopsicosocial a la telerrehabilitación en pacientes con STC en espera de cirugía mediante la comparación de un programa de telerrehabilitación de 6 semanas basado en educación del dolor más ejercicio frente al ejercicio solo sobre los resultados informados por los pacientes al final del tratamiento (semana 6) y en el seguimiento de 6 semanas posterior al tratamiento (semana 12).

Estudio I: Se realizó una revisión sistemática y un metanálisis mediante búsquedas sistemáticas en las bases de datos Embase, Pubmed/MEDLINE, Web of Science, CINAHL y el Registro Cochrane Central de Ensayos Controlados (CENTRAL) desde su inicio hasta el 14 de agosto de 2021. Se incluyeron los estudios que evaluaron la relación entre los factores cognitivos (pensamiento catastrófico, kinesiofobia y autoeficacia) o de salud mental (ansiedad y síntomas depresivos) con los resultados de la cirugía (dolor, función severidad de síntomas, satisfacción) al menos tres meses después de esta. Dos revisores independientes extrajeron los

datos y evaluaron el riesgo de sesgo. Se utilizaron modelos de efectos aleatorios para el metanálisis. Se incluyeron un total de quince estudios con 2599 pacientes. La mayoría de los estudios indicaron una asociación significativa entre los factores cognitivos o de salud mental y los resultados tras la cirugía. El análisis cuantitativo mostró una asociación moderada de los síntomas de depresión con la gravedad de los síntomas (n = 531, r = 0,347, IC 95%: 0,205 a 0,475, p<0,0001), la función (n = 386, r = 0,307, IC 95%: 0,132 a 0,464, p=0,0008) y el dolor (n = 344, r = 0,431, IC 95%: 0,286 a 0,558, p<0,0001). Los síntomas de ansiedad, pensamiento catastrófico y autoeficacia también fueron indicadores importantes de malos resultados postoperatorios.

Estudio II: Se realizó un estudio transversal en pacientes con STC en espera de cirugía en dos hospitales públicos de Chile. Los DSS recogidos incluyeron: situación laboral, nivel educativo e ingresos monetarios. El nivel de actividad física se definió según el cumplimiento de las recomendaciones de la OMS. Las medidas de resultado incluyeron: Intensidad del dolor (Escala Visual Analógica), Síntomas de ansiedad y depresión (Escala Hospitalaria de Ansiedad y Depresión), y pensamiento catastrófico (Escala de Catastrofización del Dolor). El coeficiente de regresión ajustado (β) para la asociación entre DSS y actividad física con cada resultado se obtuvo utilizando modelos de regresión lineal multivariable controlando la edad, el sexo, el índice de masa corporal y la

duración de los síntomas. Se incluyeron 86 participantes (edad media 50,9 ± 10 años, 94% mujeres). Un alto nivel de actividad física se asoció con una disminución de 12,41 mm en la intensidad del dolor (β=-12,41; IC 95%: -23,87 a -0,95) y una disminución de 3,29 puntos en los síntomas depresivos (β=-3,29; IC 95%: -5,52 a -1,06). Además, estar empleado se asoció con una disminución de 2,30 puntos en los síntomas de ansiedad (β=-2,30; IC 95%: -4,41 a -0,19) y un nivel educativo alto se asoció con una disminución de 7,71 puntos en la catastrofización (β=-7,71; IC 95%: -14,06 a -1,36).

Estudio III: Se llevó a cabo un ensayo controlado aleatorizado simple ciego. Veinticinco pacientes con STC fueron asignados al grupo de educación del dolor más ejercicio o al de sólo ejercicio. La educación del dolor se realizó a través de una videoconferencia interactiva con apoyo visual. El programa de ejercicios incluía ejercicios aeróbicos, deslizamiento del tendón flexor digital, ejercicios neurodinámicos y estiramientos. Las medidas de resultado incluyeron la intensidad del dolor, la catastrofización del dolor, la kinesiofobia, la gravedad de los síntomas, la función, los síntomas de ansiedad y depresión, la calidad de vida y la autopercepción de mejoría. Los análisis inferenciales de los datos se realizaron mediante un análisis de varianza mixta de dos factores (intergrupo x tiempo). Se observó una interacción significativa intergrupo x punto temporal con un gran tamaño del efecto para la kinesiofobia (F=6,67; p=0,005; ηp^2=0,225) y

la gravedad de los síntomas ($F=4,82$; $p=0,013$; $\eta p^2=0,173$). No se observó ninguna interacción significativa para las demás variables ($p>0,05$). Se observaron diferencias significativas a favor del grupo tras el tratamiento combinado en la autopercepción de mejoría ($p<0,05$). Aunque se produjeron mejoras significativas y clínicamente relevantes en el grupo experimental en la intensidad del dolor, la catastrofización y los síntomas de ansiedad, no hubo diferencias significativas entre los grupos.

En conclusión, esta tesis destaca la importancia de abordar los factores psicosociales en pacientes con síndrome del túnel carpiano, tanto en la evaluación como en el tratamiento. En primer lugar, encontramos que los síntomas depresivos, los síntomas de ansiedad, el pensamiento catastrófico y la autoeficacia fueron indicadores importantes de malos resultados postoperatorios. Por lo tanto, una evaluación preoperatoria de estas variables podría ayudar a identificar a los pacientes con riesgo de malos resultados quirúrgicos y proporcionar un tratamiento oportuno.

En segundo lugar, un alto nivel de actividad física se asoció con una disminución de la intensidad del dolor y de los síntomas depresivos en pacientes con STC en espera de cirugía. Además, tener un empleo se asoció con una disminución de los síntomas de ansiedad y tener un nivel educativo alto se asoció con una disminución de la

catastrofización. Por lo tanto, una evaluación exhaustiva de estas variables puede ser relevante para identificar casos de mayor riesgo psicosocial y planificar estrategias para reducir el dolor y mejorar la salud mental de los pacientes con STC pendientes de cirugía, por ejemplo, implementar programas de actividad física guiados por las recomendaciones de la OMS.

Por último, la adición de la educación del dolor a un programa de ejercicios de telerehabilitación mostró mejoras a corto plazo en la kinesiofobia y la gravedad de los síntomas en pacientes con STC en espera de cirugía. También hubo mejoras significativas y clínicamente relevantes en la intensidad del dolor, la catastrofización y los síntomas de ansiedad en el grupo de educación del dolor más ejercicio. Estos resultados pusieron de relieve los beneficios de incluir un enfoque biopsicosocial en las intervenciones de telerrehabilitación.

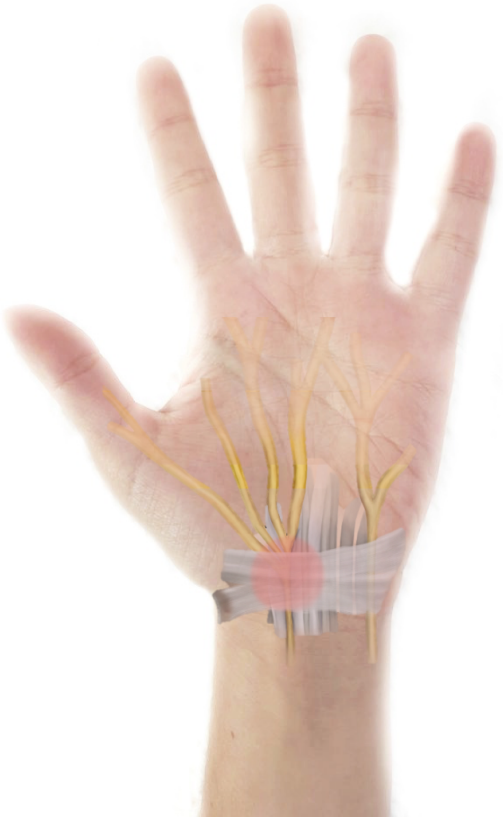
1. Introduction

1. Introduction

1.1 General aspects of carpal tunnel syndrome

The carpal tunnel is an anatomical structure located on the anterior aspect of the wrist, between the carpal bones and the transverse carpal ligament, containing the flexor tendons of the fingers and the median nerve (Figure 1). The median nerve is the most superficial structure of the carpal tunnel and can be compressed by an increase in the volume of its contents (e.g. flexor synovitis) or by a decrease in the surrounding volume (e.g. thickening of the flexor retinaculum) (1,2). Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity, caused by compression of the median nerve at the level of the carpal tunnel (3,4). Estimates of the prevalence of CTS vary widely in the literature, from 6.3% to 11.7%, depending on the diagnostic criteria used (5,6). Although more common in women and between the ages of 40 and 60, the condition may occur in people of all ages (2).

Figure 1. Carpal tunnel and median nerve



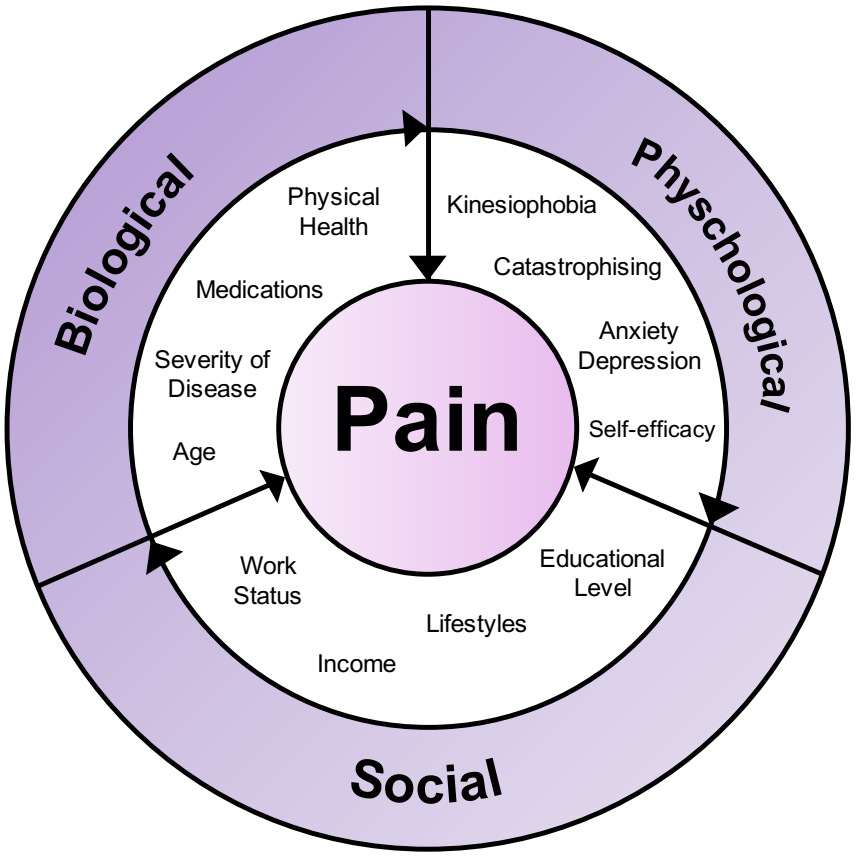
The illustration shows the median nerve as the most superficial structure of the carpal tunnel and therefore most vulnerable to compression.
Source: Figure modified from Núñez-Cortés R, et al. Carpal tunnel syndrome and pain. Features and Assessments of Pain, Anaesthesia, and Analgesia. 2022. p. 275–83.

Carpal tunnel syndrome is a common cause of disability and reduced quality of life, affecting a person's daily activities and ability to work (5,7,8). The clinical presentation of CTS is usually characterised by pain, tingling and numbness in the

region of the median nerve and weakness of the thumb (1, 9). In particular, pain is a common symptom of CTS, present in 58% of cases according to a multicentre study of 1,123 patients (10). Reducing the suffering caused by persistent pain and curbing the growing number of harms associated with the use of opioid medicines are currently two major public health challenges (11).

Recently, the International Association for the Study of Pain (IASP) has provided a revised definition of pain, describing it as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (12). Currently, the most empirical approach to persistent pain is the biopsychosocial model (13). The model proposes that pain is the result of the interaction between biological, psychological and social factors (Figure 2). Correlations between disability and pain intensity with physical and psychosocial factors in patients with CTS support that the biopsychosocial model should be considered for both pain and disability (14). Therefore, understanding and addressing these factors in a comprehensive manner could help in the assessment and effective treatment of people with CTS.

Figure 2. Exemplification of the biopsychosocial model.



Source: own elaboration

1.2. Biological factors

Several pathological factors are involved in the development of CTS. Substantial compression of the median nerve can cause disruption of intraneural blood flow and contribute to intraneural oedema, fibrosis and disruption of the normal gliding kinematics of the nerve (15–17). Thus, prolonged

ischaemia and mechanical injury can eventually lead to effects such as demyelination and ultimately axonal degeneration (18). On the other hand, peripheral nerve injuries can trigger changes in the central nervous system. For example, pain-related contributions to CTS include central sensitization mechanisms and, in some cases, generalised hyperalgesia (19,20). In this regard, hypoaesthesia and increased thermal and mechanical pain scores are the dominant sensory phenotype in these patients (21).

The frequency of symptoms seems to be a factor that distinguishes mild from moderate CTS, i.e. mild refers to more intermittent symptoms and moderate to more constant or repetitive symptoms. As for severe CTS, it is characterised by the presence of muscle atrophy in the thenar eminence (2). Other intrinsic (or biological) factors linked to CTS include obesity, age and female sex (2). Metabolic changes associated with obesity may cause endoneuronal oedema and inflammation of the median nerve (22). In addition, physiological changes associated with ageing predispose to CTS (e.g. vascular abnormalities, slower conduction velocity) (23). Female sex also increases the risk by 1.5 to 4 times compared to male sex, which could be explained by hormonal mechanisms as well as the smaller cross-section of the carpal tunnel compared to men (2,24).

Carpal tunnel release (CTR) is indicated mainly in severe cases (e.g. persistent hypoesthesia and motor impairment) (25). In this procedure, the median nerve is surgically released by cutting the flexor retinaculum in the palmar region to reduce pressure on the median nerve (26). The unfavourable outcome after CTR may also be due to pain associated with the surgical scar (27). According to the Center for Epidemiology at the Swedish National Board for Health and Welfare, it is estimated that 65% of people diagnosed with CTS will eventually require surgery, and the incidence of CTR per 100,000 person-years is 151 in women and 65 in men (28), making it one of the most common upper extremity surgeries. Although most patients improve after surgery, approximately 5% have persistent symptoms and require revision CTR in the first year after surgery (29). Electrodiagnostic tests provide a quantitative measure of physiological function of the median nerve. However, the degree of electrodiagnostic value may not be related to the benefit of surgery (30). For this reason, other non-biological prognostic factors should also be investigated.

1.3. Psychological factors

Psychological factors include a heterogeneous set of factors related to mental health (e.g. anxiety and depressive symptoms) and cognitions and coping strategies (e.g. catastrophic thinking, kinesiophobia, self-efficacy, fear avoidance). These variables may influence recovery and

response to rehabilitation in patients with chronic musculoskeletal pain (31,32). Furthermore, identification of these factors is also important for optimising postoperative outcomes (33,34).

In this regard, the fear-avoidance model proposes that patients with pain catastrophizing tend to interpret certain experiences as threatening, avoid these activities and develop disuse, disability and depression (35). In particular, catastrophizing, self-efficacy, pain-related anxiety, depression and anxiety have gained importance in recent decades due to their strong association with postoperative pain and function (33,34). Recent systematic reviews have shown that these factors are associated with worse postoperative outcomes in shoulder surgery (33,36), spine surgery (34,37,38), and knee arthroplasty (34,39,40). Nevertheless, the relevance of cognitive and mental health factors as predictors of recovery from carpal tunnel release is controversial (41).

There is a growing body of literature supporting the role of modifiable cognitive and mental health factors in CTR (42–48). However, assessment of these factors has not been included in recent clinical practice guidelines for patients with CTR (2), when the majority of patients may ultimately require surgery (28). A better understanding of the association between cognitive and mental health factors and surgical outcomes could also help to provide more specialised interventions,

including the expertise of psychologists, physiotherapists, occupational therapists and physicians in the preoperative and postoperative periods. In addition, the economic costs associated with mental health disorders and postoperative pain reinforce the need to examine these risk factors in detail with a rigorous narrative approach and quantitative synthesis of the available evidence.

1.4. Social factors

Social factors related to pain have important implications for policy and clinical practice (49). Social determinants of health (SDH) include the conditions in which people are born, grow, live, learn, work and age, and the social inequalities that explain differences in health outcomes (e.g. educational level, monetary income and employment status) (50). The literature has shown that SDH, such as low educational attainment, is associated with negative beliefs about pain (e.g. catastrophizing) in women with CTS, which could lead to altered physical measures (e.g. lower handgrip strength) (51). Adults with pain who have low educational attainment may also be less likely to have good mental health (52).

Additionally, SDH, such as low educational attainment and unemployment, were associated with higher levels of pain in patients with musculoskeletal disorders in the shoulder and low back region (53–55). A recent meta-analysis found that

low socioeconomic status (in terms of educational level, income or employment status) was moderately associated with an increased risk of chronic pain, although none of the included studies focused on patients with painful hand conditions (56).

On the other hand, physical activity (as a lifestyle indicator) is an environmental health behaviour that could also be influenced by SDH (57), such as having the financial means to enrol in an exercise class, or having adequate education or health literacy to understand the benefits of physical activity. Physical activity has been shown to have a protective effect on mental health in adults and to promote positive coping strategies (e.g. self-efficacy) (58,59). Furthermore, in other neurological conditions (e.g. spinal cord injury), healthier lifestyles (e.g. increased physical activity) have been associated with lower levels of pain and depressive symptoms (60).

The COVID-19 outbreak led to a high demand for healthcare that limited access to quality pain management care (61). In this context, the approach to pain management was mainly biomedical (e.g. pharmacological treatment), with less consideration of psychosocial aspects (62). Therefore, clinical assessment of more severe cases of CTS (e.g. those awaiting surgery) should also take full account of social stressors, particularly their impact on pain and mental health. However,

the role of SDH in this population has been little studied, and preoperative assessment of these variables may be useful to identify those most at risk and thus develop more specific perioperative interventions to reduce pain and improve mental health.

1.5. Physiotherapy and rehabilitation

Previous literature supports that conservative treatment should be considered prior to surgery, even in severe cases of CTS (63). Nerve and tendon gliding exercises are often included as part of multimodal treatment to improve function and reduce pain and symptom severity (63–65). In fact, exercise-based physical therapy can produce similar results to surgery in terms of pain and function (63). In addition, encouraging physical activity may be a valuable strategy for reducing pain intensity and depressive symptoms in patients with CTS awaiting surgery (66).

In the context of the COVID-19 pandemic, the use of telerehabilitation has improved the accessibility of rehabilitation care by providing physiotherapists with an accessible and cost-effective way to educate patients, improve exercise compliance and monitor the progress of patients with musculoskeletal conditions through remote consultations (67,68). Indeed, telerehabilitation has been shown to be as effective as face-to-face interventions for some clinical and

functional outcomes, making it a good alternative to improve the accessibility of rehabilitation care in a context of social distance (69). Nevertheless, to our knowledge, telerehabilitation in patients with CTS remains unexplored.

The high prevalence of CTS, its impact on quality of life and the socioeconomic costs to healthcare systems make it crucial to identify research priorities (e.g. new telerehabilitation approaches) to be addressed in clinical trials (70). Considering that CTS symptoms may be modulated by various psychosocial variables (71–73), treatment approaches, including telerehabilitation, should move away from the biomedical bubble (74). Thus, pain neuroscience education (PNE), which aims to help individuals change their negative beliefs about pain, may be a promising alternative (75,76). Recent meta-analyses have concluded that PNE has positive short-term effects on pain, disability, kinesiophobia and catastrophizing in patients with chronic musculoskeletal disorders, especially when combined with exercise (77,78). Although international clinical guidelines recommend exercise as a key element in the treatment of chronic musculoskeletal pain (79), the effects of combining exercise with PNE in telerehabilitation programmes have been little studied. Thus, the addition of PNE to an exercise-based telerehabilitation programme may be an innovative alternative to address psychosocial variables related to pain (80), improving the

physical and mental health of patients with CTS who have not been able to access face-to-face treatment.

1.6. Relevance and justification

An increasing number of publications highlight the role of psychosocial factors in patients with chronic musculoskeletal pain (31,32,34,56). However, there is little information on how these variables may interact and how they relate to the physical and mental health of people with CTS. Furthermore, a recent scoping review found that physiotherapists lack the confidence and ability to identify psychosocial factors (81). Therefore, the management of patients with CTS requires a broader understanding of the relevance of these factors and how they relate to clinical outcomes in the pre- and post-operative periods.

In a previous cross-sectional study (51), we tested the hypothesis that social determinants, in particular educational level, might affect both the physical and mental health of patients with CTS awaiting surgery, as assessed by handgrip strength and catastrophizing, respectively (Figure 3). The results showed clinical and significant differences in handgrip strength and catastrophizing between patients with higher and lower levels of education. These differences in strength were independent of individual factors (age, BMI, duration of symptoms and type of work). Moreover, pain education can

also improve self-perceived safety in performing active therapies such as exercise, so incorporating this intervention into a multimodal treatment that includes exercise may lead to improved clinical outcomes. In this context, a recent study identified reductions in kinesiophobia and central sensitisation-related distress following PNE combined with exercise as significant mediators of changes in disability and pain medication use (82). Thus, this preliminary evidence justifies the importance of continuing to investigate the implications of the biopsychosocial model for clinical practice in patients with CTS, both in the identification of cases with greater psychosocial risk and in the design of tailor-made treatments.

Figure 3. Biopsychosocial model applied to carpal tunnel syndrome.

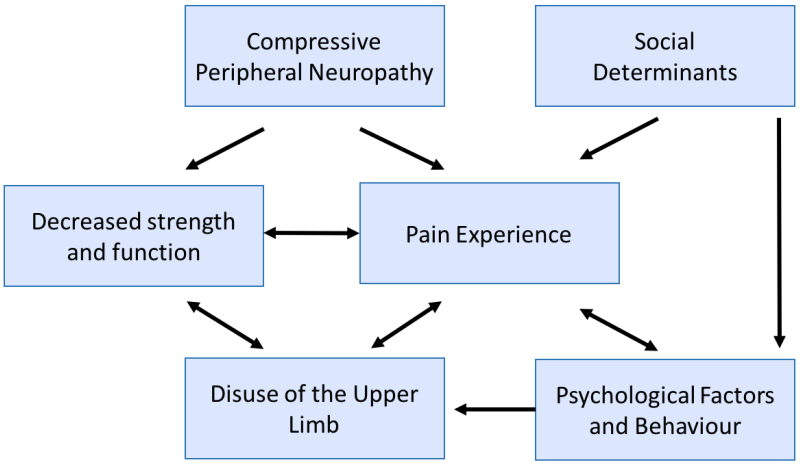


Figure modified from Núñez-Cortés R, Cruz-Montecinos C, Antúnez-Riveros MA, Pérez-Alenda S. Does the educational level of women influence hand grip and pinch strength in carpal tunnel syndrome? Med Hypotheses. 2020 Feb;135:109474 (Ref 51).

1.7. Objectives and hypotheses

The overall aim was to assess the role of psychological and social factors on physical and mental health in patients with CTS during the pre- and post-operative periods, and to determine the efficacy of adding a biopsychosocial approach to telerehabilitation in patients with CTS awaiting surgery. The specific aims for each of the different studies conducted were:

- **Study I:** To determine the association of catastrophizing, kinesiophobia, self-efficacy, fear avoidance, and mental health factors (anxiety symptoms and depression) with outcomes after CRT, at least 3 months after surgery. It was hypothesised that the chosen cognitive and mental health factors would correlate with pain, function, symptom severity, return to work and satisfaction after surgery, 3 months after surgery and afterwards.

- **Study II:** To analyse the association between SDH and physical activity with pain intensity and mental health in patients with CTS awaiting surgery. It was hypothesised that SDH and physical activity would be associated with pain severity and mental health in patients with CTS before surgery.

- **Study III:** To compare the effectiveness of a 6-week telerehabilitation programme based on PNE plus exercise versus exercise alone on patient-reported outcomes after treatment (week 6) and at six weeks' post-treatment follow-up (week 12) in patients with CTS awaiting surgery. We hypothesised that the addition of a biopsychosocial approach (i.e. PNE) to exercise-based telerehabilitation would lead to better patient-reported outcomes after treatment compared with exercise alone in patients with CTS awaiting surgery.

2. Methods

2. Methods

The methodology used in the studies that compose this thesis is explained in detail in the original articles (Appendix 1, 2 and 3). This section describes the most relevant data. Table 1 provides an overview of the methodology used in each study.

Table 1. Overview of the methodology used (studies I, II and III).

Study	Design	Subjects	Study variables
I	Systematic review and meta-analysis	Patients with CTR (open or endoscopic surgery).	*Independent variables:* Pain-related cognitive factors (catastrophic thinking, kinesiophobia, self-efficacy, fear avoidance) and mental health factors (anxiety and depressive symptoms). *Dependent variables:* Functional limitations and symptom severity, pain intensity, patient satisfaction, work participation.
II	Cross-sectional	Patients with CTS awaiting surgery in two public hospitals in Chile.	*Independent variables:* Social determinants of health (educational level, employment status, monetary income) and physical activity). *Dependent variables:* Pain intensity, depressive symptoms, anxiety symptoms, catastrophizing.
III	Randomised controlled trial	Patients with CTS awaiting surgery in two public hospitals in Chile.	*Intra-subject factor:* Three time measures (baseline, week 6 and week 12). *Between-subject factor:* PNE+exercise or exercise only. *Dependent variables:* Pain intensity, pain catastrophizing, kinesiophobia, symptom severity, function, symptoms of anxiety and depression, quality of life, self-perception of improvement.

2.1. Study I (Effects of Cognitive and Mental Health Factors on the Outcomes Following Carpal Tunnel Release: A Systematic Review and Meta-analysis)

2.1.1. Protocols and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (83). The meta-analysis was conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) (84). The protocol was previously registered on the International Prospective Register of Systematic Reviews PROSPERO (CRD42020181709) in July 2020.

2.1.2. Selection criteria

Randomised controlled trials (RCTs) and observational studies (cross-sectional, longitudinal, case control and cohort) of patients with CTR (open or endoscopic surgery) were included. The included studies aimed to determine the effect of the chosen cognitive or mental health factors on the outcomes at least three months post-CTR. The cognitive factors related to pain (i.e. catastrophic thinking, kinesiophobia, self-efficacy and fear avoidance) and mental health factors (i.e. symptoms of anxiety and depression)

should have been assessed using an objective measure. On the other hand, studies with at least one of the following outcomes after surgery were included: functional limitations and symptoms, pain intensity, patient satisfaction, work participation, physical measures of recovery, including grip and pinch strengths and range of motion. The assessment instrument included for each prognostic factor and outcome is described in the original article (Appendix 1). We included studies in any language published between January 1950 and August 2021. All editorials, letters to the editor, review articles, systematic review, and meta-analysis, in vivo and in vitro studies were excluded.

2.1.3. Search strategy

A systematic review of the literature was conducted to identify the studies that investigate the effect of the chosen cognitive and mental health factors on the outcomes following carpal tunnel release. We reviewed the Embase, Pubmed/MEDLINE, Web of Science, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) databases, from inception to August 14, 2021. The terms used in the search strategy are described in the original article (Appendix 1). We supplemented our search with the reference lists of all included studies to identify potentially relevant articles from other sources. All references were analysed using the Rayyan web software (85).

2.1.4. Reviewing procedure and data extraction

First, the titles and abstracts of all identified studies were reviewed by two investigators. The irrelevant references were removed. Any disagreements were solved by consensus. Second, the full text versions of the articles selected in the first stage were read and checked against the eligibility criteria. Any disagreements were solved by a third reviewer.

Then, two investigators extracted the data independently using a standardised protocol and reporting forms. The following information was extracted from each included study: design, population characteristics, type of surgery, follow-up time, prognostic factor, postoperative outcomes, results of univariate analysis and results of multivariate analysis. If some relevant data were not included in the study, the authors were contacted to obtain the information.

2.1.5. Methodological quality assessment

The risk of bias in the included studies was assessed using the Quality in Prognosis Studies (QUIPS) risk-of-bias tool (86). Two authors carried out this evaluation independently, and discrepancies were resolved by consensus.

2.1.6. Quantitative synthesis

The meta-analyses were performed in R v. 4.0.2 (87). For the quantitative synthesis, the prognostic factors that were evaluated by three or more studies were considered to avoid performing low-power analyses. Studies that operationalized the risk factor in a markedly different way than most other studies were excluded from the estimate. The quantitative synthesis was carried out in the following steps: I) The original data (e.g., correlations, regression coefficients, and odds ratios) were converted to Pearson's r using standard formulas (88). To maintain consistency, the associations were recalculated so that they were in the same direction; II) The data were converted into Fisher's z using the escalc() function from the *'metafor'* v. 3.0-2 R package (89); III) different random-effects models were fitted to synthesise the quantitative results of the published studies for each one the effect sizes under study (i.e., correlational data on prognostic factors and postoperative results). These models were computed using the rma() function from the same package (i.e. *'metafor'* v. 3.0-2); IV) The result of each meta-analysis was transformed back into Pearson's r for final interpretation. The effect size magnitude of r can be interpreted as follows: r=0.1, small; r=0.3, moderate; r=0.5, large (90). Statistical heterogeneity was assessed using I^2 and classified as might not be important (I^2 = 0-40%), moderate (I^2= 30–60%), substantial (I^2 = 50–90%) or considerable (I^2 = 75-100%) (91).

Forest plots were generated to visualise the effect sizes and 95% confidence intervals (95% CI) of the studies considered, together with the calculated summary effect size.

2.2. Study II (Social Determinants of Health and Physical Activity are Related to Pain Intensity and Mental Health in Patients With Carpal Tunnel Syndrome)

2.2.1. Study setting, design and participants

A cross-sectional study was conducted in patients with CTS who were awaiting surgery in two public hospitals in Chile (Hospital Clínico La Florida and Hospital Provincia Cordillera), between February and July 2022. Both institutions were located in an urban area composed mainly of families of middle socioeconomic status. Inclusion criteria were the following: over 18 years of age, medical diagnosis of moderate or severe CTS according to the clinical practice guideline of the Academy of Orthopaedic Physical Therapy and the Academy of Hand and Upper Extremity Physical Therapy (i.e. history, medical examination and tests/measurements) (2), remain on the hospital's official waiting list for CTR for at least 3 months or more, and accept to participate in the study. Exclusion criteria were: inability to understand instructions (e.g. illiteracy), neurological conditions of the central nervous system (e.g. stroke, spinal cord injury), and previous surgery in the upper limb. The study was conducted according to the

guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of the two participating hospitals. Written informed consent was obtained from all participants after explanation of the objectives of the study. This study was conducted in accordance with the guidelines "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) (92).

2.2.2. Social determinants of health

Participants were interviewed face-to-face at each hospital. Data collected included: I) Employment status: employed versus unemployed (only for working-age participants); II) Educational level: participants were assigned to the lower educational level if they had not completed secondary education and to the higher educational level if they had completed secondary education or university studies; III) Monetary income was categorised according to individual monthly taxable income. The cut-off point was set at USD 320, which corresponds to the minimum wage in Chile (year 2020) and determines the degree of coverage of the Chilean public health system (year 2021).

2.2.3. Physical activity

Participants reported the minutes and type of physical activities (moderate or vigorous) they performed as part of their daily life during the last seven days. Participants were classified according to the recommendations of the World Health Organization (WHO) 2020 guidelines on physical activity (93). Therefore, a level ≥ 150 minutes of moderate-intensity physical activity per week, or ≥ 75 minutes of vigorous-intensity physical activity per week, was used as the cut-off point (high vs. low level) (93).

2.2.4. Outcomes

Outcome measures included the following self-reported assessments: I) Pain intensity, assessed using the Visual Analogue Scale (VAS), a valid and reliable measure for pain assessment and widely used in patients with CTS (94,95). Participants were asked to rate their average pain during the seven days prior to assessment on a scale defined from 0 to 100 millimetres, where 0 is “no pain” and 100 is “the worst pain imaginable”. II) Mental health, assessed with the Spanish version of the Hospital Anxiety and Depression Scale (HADS) (96), which evaluates the level of anxiety and depression by means of two subscales of 0 to 21 points each. Higher values represent a worse outcome. In addition, catastrophic thinking

in response to pain was assessed using the Spanish version of the Pain Catastrophizing Scale (PCS) (97). PCS has 13 items of four possible choices from 1 "not at all" to 4 "all the time," a higher score indicating greater catastrophic thinking, with a maximum score of 52 points (98).

2.2.5. Covariates

Data collected included: I) Sociodemographic variables (age and sex); II) Body Mass Index was obtained from the ratio between weight and height squared ($kg \cdot m^2$); III) Duration of symptoms associated with CTS (years).

2.2.6. Sample size calculation

The sample size calculation was determined by considering a minimum of 10 participants for each independent variable entered in the multivariable linear regression. Considering a total of eight independent variables (four exposure factors and four covariates), the minimum sample size was set at 80 patients. Post-hoc power was calculated in the G*Power software, version 3.1.9.2 (Universität Düsseldorf, Germany) using the statistical test of multiple linear regression, one-tailed with an α err prob = 0.05. The post-hoc power was >80% for each of the models tested.

2.2.7. Statistical analyses

The normality of the data was tested using the Shapiro-Wilk test. Means and standard deviations (SD) were calculated for quantitative variables with a normal distribution, and percentages for categorical variables. For the employment status variable, only cases of working age (n=75) were considered for the analysis. Considering the aim of our study, multivariable linear regression analysis was performed for each dependent variable (pain intensity, depressive symptoms, anxiety symptoms, catastrophizing). Dummy codes were used for the exposure factors, and unemployed, low educational level, low income and low physical activity were established as reference categories. Multivariable linear regression analysis examined the association of each of the exposure factors (educational level, employment status, monetary income, and physical activity) with each outcome, while controlling for each of the other exposure factors (i.e., mutually adjusted) and possible confounders (age, sex, body mass index, and symptom duration). For each analysis, the crude and adjusted regression coefficient (β) was obtained, with a 95% confidence interval (95% CI). All statistical analyses were performed in SPSS version 22.0 (IBM Corporation, Armonk, New York). Statistical significance was set at $p < 0.05$.

2.3. Study III (Effectiveness of Adding Pain Neuroscience Education to Telerehabilitation in Patients with Carpal Tunnel Syndrome: A randomised controlled trial)

2.3.1. Participants and design

A randomised controlled trial (RCT) with two parallel groups was performed. Participants with a diagnosis of severe CTS awaiting surgery in two hospitals of the Chilean public health system (Hospital Clínico la Florida and Hospital Provincia Cordillera), who were invited to participate between January and June 2022, were candidates for the present study. The inclusion criteria were: age between 18 and 60 years, diagnosis of moderate or severe CTS according to international guidelines (i.e. history, physical examination and tests/measurements) (2), symptoms of at least three months duration, unilateral or bilateral symptoms, availability of a smartphone with Internet access, and agreement to participate in the study. Exclusion criteria were: inability to understand instructions, uncontrolled mental pathology, cognitive problems, patients on treatment with alternative therapies, previous participation in a telerehabilitation programme, and previous surgery on the affected upper limb. All participants were informed about the objective and procedures of the research and gave written informed consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics

Committee of the South East Metropolitan Health Service (ID: CEC-08-04/RAD-03), Santiago de Chile (Appendix 4). The study was registered on ClinicalTrials.gov (NCT05184413) and adheres to the CONSORT Statement (99).

2.3.2. Randomization and allocation

After receiving the surgical waiting list from a physician not involved in the study in each hospital, the investigator involved in the recruitment process randomly contacted potential participants by telephone. The first 30 participants who agreed to participate and met the selection criteria were randomised following a simple randomization procedure using the Randomization software (www.randomization.com). A 1:1 allocation ratio to a PNE plus exercise group or to an exercise only group was considered. Allocation remained concealed and stored in the cloud until the end of the intervention and collection of all study data. When a participant was enrolled in the study, the external research assistant informed the therapist of the assigned intervention group.

2.3.3. Telerehabilitation programme

The telerehabilitation program was conducted using a smartphone videoconferencing method via WhatsApp™ and lasted 6 weeks. Both groups received three telerehabilitation sessions supervised by physiotherapists every 15 days. In the

first session, all participants received an individual self-managed exercise program (see below). The PNE+exercise group also received three individual PNE sessions before each exercise session (on the same day). Participants in the study did not have to stop taking any pain medication at the time of the study.

2.3.4. Exercise programme

The type and amount of exercises were the same for both groups. The exercise was multimodal and included aerobic exercise (100), digital flexor tendon gliding (65), neurodynamic home exercises (64), and self-stretching (101) (Table 2). Each participant received printed material with the different types of exercises and videos of the execution of each exercise as reinforcement. In the first videoconference, the physiotherapist demonstrated the exercises and corrected each participant to ensure correct technique and to check that participants were confident to perform the exercises independently at home. Each participant received on the day of the initial assessment a folder with printed material with the different types of exercises and a sheet to record compliance and prescription of each exercise (Appendix 5). Each exercise session lasted approximately 30 minutes. A total of 18 exercise sessions were performed (15 self-managed and 3 supervised). Supervization of the exercises was performed every 15 days.

In case of bilateral symptoms, participants were instructed to perform the exercises with both upper extremities.

2.3.5. Pain Neuroscience Education

The PNE+exercise group additionally received three individual 40-minute PNE sessions every 15 days for 6 weeks, via WhatsApp™ video conferencing. The intervention was performed by a physiotherapist with seven years of clinical experience and training in PNE (102). Participants were instructed to be in a room with no distractions for the videoconferencing session. In addition, audiovisual material was sent between each session (i.e., videos with examples and metaphors, 6 minutes each) to reinforce the key contents of the PNE (Appendix 6). The total duration of the intervention was 132 minutes (120 minutes of synchronous pain education and 12 minutes of asynchronous material). The key concepts addressed during the online sessions are presented in Table 2. At the end of the last session, as feedback, a multiple-choice and true/false questionnaire was used to assess perceived knowledge and self-management skills. This assessment has not yet been validated and was suggested by Ziegler et al. to motivate patients/participants to learn. For evaluation purposes in our study, the percentage of correct answers was reported (103).

Table 2. Intervention characteristics.

INTERVENTIONS	WEEKS						CHARACTERISTICS
Brisk walking (all patients) [a]	**1**	**2**	**3**	**4**	**5**	**6**	
15 minutes at moderate intensity	●	●					Moderate intensity was determined by the Talk test (i.e. can hold a conversation but not sing).
20 minutes at moderate intensity			●	●			
25 minutes at moderate intensity					●	●	
Digital flexor tendon gliding exercises (all patients) [a]							
Straight	●	●	●	●	●	●	Maximum number of repetitions up to a perceived exertion on the Borg CR10 scale of 4/10 (week 1-2), 5/10 (week 3-4) and 6/10 (week 5-6).
Hook	●	●	●	●	●	●	
Fist	●	●	●	●	●	●	
Table top	●	●	●	●	●	●	
Stretching (all patients) [a]							
Scalene muscles	●	●					45 seconds 2 times
Transverse carpal ligament			●	●	●	●	30 seconds 4 times
Lumbrical muscles			●	●	●	●	45 seconds 2 times
Neurodynamic exercise (all patients) [a]							
Median nerve gliding exercise	●	●					Each exercise included 3 sets of 10 repetitions.
Busy bee flexion shape of (Z) exercise			●	●			
Free the bird exercise					●	●	
Pain Neuroscience Education (only in experimental group)							
Neurobiology concepts.	●						Three synchronous individual sessions of 40 minutes by interactive videoconference plus asynchronous reinforcement videos between each session (two 6-minute videos). Theoretical information was illustrated with images, examples and metaphors (visual support)
Examples on “Pain does not always equate to tissue injury”.	●						
Pain is a nerve sensitivity.	●						
Reinforcement videos (asynchronous).		●					
Review of content covered in previous sessions; Dispelling common misconceptions about pain.			●				
Influencing/sustaining factors.			●				
Examples of neuroplastic changes due to experience and learning.			●				
Reinforcement videos (asynchronous).				●			
Review of content covered in previous sessions.					●		
Concepts related to self-management perception.					●		
Learning assessment [b]					●		

[a] Three days a week (self-managed), each session was separated by 48 hours. Supervision for reinforcement and adjustment of progressions every 15 days by interactive videoconference via WhatsApp™. Restriction: Pain intensity >4 during exercise, on a numerical pain rating scale (0-10).

At the end of each treatment, all participants completed the System Usability Scale (SUS) to assess their experience with the telerehabilitation system (104), to ensure that both groups perceived the same subjective usability of telerehabilitation. The SUS is a simple 10-item scale that provides an overview of subjective usability evaluations (range, 0-100). Scores between 68 and 80 suggest a "good" usable interactive system and scores above 80 can be considered "excellent" (105).

2.3.6. Clinical outcome measures

The evaluations of the participants were performed by an evaluator from each hospital who was unaware of the group allocation. The physiotherapist who performed the interventions was not involved in the evaluation process. In the first interview, participants completed self-reported information regarding age, sex, duration of CTS (months), educational level (primary, secondary or higher), analgesic intake and minutes of moderate physical activity per week. Participants were assessed before starting treatment (baseline) and reassessed after treatment (week 6) and at six weeks' post-treatment follow-up (week 12). If there were symptoms in both hands, the hand with the more severe symptoms was evaluated because it was the hand that was to be operated on. Compliance with the exercise program was assessed by means of a record sheet to be filled out by the patient at home. To define 100% adherence to the exercise program, both the

number of sessions completed (out of a total of 18 sessions) and the number of exercises completed within each session were considered.

Pain intensity: The primary outcome measure was pain intensity assessed using the numeric pain rating scale (NPRS) (106). Participants were asked to rate the average pain intensity during the seven days prior to the assessment on a defined 0 to 10-point scale, where 0 represents "no pain" and 10 is "worst pain imaginable." The minimum clinically important difference (MCID) for this scale is 2 points (107).

Pain catastrophizing: The Pain Catastrophizing Scale (PCS) was used to measure catastrophic thinking in response to pain through 13 statements with four possible options, from 1 "not at all" to 4 "all the time" (108). Higher scores (range, 0-52) indicate greater pain catastrophizing. The Spanish version of the PCS has shown adequate internal consistency and test-retest reliability (97). The minimum detectable change (MDC) of the PCS is 10.45 points (97).

Kinesiophobia: The Spanish version of the Tampa Scale for Kinesiophobia-11 (TSK-11) was used to measure fear of movement (109). The TSK-11 has demonstrated acceptable consistency and validity (109). Total scores range from 11 to 44, with higher values representing worse outcome (i.e. greater interference of pain with fear avoidance behavior). The

MDC for the TSK-11 is 5.6 points in people with chronic pain (110).

Severity of symptoms and function: The Boston Carpal Tunnel Questionnaire (BCTQ) measures self-reported functional status (BCTQ-FS) and severity of symptoms (BCTQ-SSS) (111). The BCTQ-SSS consists of 11 questions, each question provides 5 response choices, from 1 (no symptoms) to 5 (most severe/often). The BCTQ-FS includes 8 questions assessing difficulty with daily tasks. These responses are also scored on a 5-point scale (1-5). The MCID has been determined to be 0.74 points for the function subscale and 1.14 points for the symptom severity subscale (112).

Mental health: The Hospital Anxiety and Depression Scale (HADS) was used to assess mental health using two 0-21 point subscales (anxiety and depression) (113). The score is obtained by summing the items of each subscale, with higher values representing a worse outcome. A score of 0-7 is considered normal, 8-10 is considered a possible case and ≥11 indicates a probable clinical case of anxiety or depression (113). The MCID is 1.67 points for the anxiety subscale and 1.85 for the depression subscale (114).

Quality of life: The EuroQol5-dimensions (EQ-5D) was used as a self-assessed health-related quality of life questionnaire (115). The EQ-5D essentially consists of two pages: First, the

EQ-5D description system, which provides a single index value for health status where a score of 1 represents "perfect health", 0 is a health state equivalent to death and values below 0 represent "worse than death" states. Second, a visual analogue scale (EQ-VAS) numbered from 0 "the worst health you can imagine" to 100 "the best health you can imagine".

Self-perception of improvement: The Patient Global Impression of Change Scale (PGICS) consists of two subscales, one categorical and one quantitative (116). The categorical scale is a 7-point verbal scale with the following options: i) "very much improved", ii) "much improved", ii) "minimally improved", iv) "no change", v) "worse", vi) "much worse", and vii) "very much worse". The categories "very much improved" and "much improved" are considered a clinically significant improvement (116). The quantitative scale consists of a line from 0 to 10, where 0 = much better and 10 = much worse.

2.3.7. Sample size calculation

An a priori sample size calculation was performed in G*Power software (version 3.1, Universität Düsseldorf, Germany) using the fixed effects ANOVA statistical test. An effect size of f = 0.685 was estimated based on a previous study on the effectiveness of PNE (117), which found a between-group difference greater than the MCID of 2 points on the NPRS with

a large effect size (d = 1.37). The effect size transformation was performed with an online calculator. With α err prob = 0.05 and power (β-1 err prob) = 0.8, a total of 24 patients were required. The sample size was increased by 20% to account for potential dropouts during the follow-up period. The resulting sample size was 30 participants.

2.3.8. Statistical analyses

Statistical analysis was performed with SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The normality of the data was tested using the Shapiro-Wilk test. Mean ± standard deviation (SD) or median and interquartile range (IQR) values were calculated for continuous data according to parametric or nonparametric distribution, respectively. The significance level was set at 0.05 for all statistical analyses. Baseline differences between groups were compared using the Chi-square test for distributions of categorical variables and the independent t-test for continuous variables. If the data did not have a normal distribution, the Mann Whitney U test was used. The mean difference (MD) between groups was calculated with a 95% confidence interval (95% CI). Inferential analyses of the data were performed using a two-factor mixed analysis of variance (ANOVA): i) a between-subjects factor with two categories (two treatment groups); ii) a within-subject factor with three categories (three measures of time). When a significant

interaction between factors was found, the simple mean effect (one-way ANOVA for each group) and simple pairwise comparisons (unpaired t-test between the two groups) were used. The chi-square test and independent t-test were used to explore differences between groups for the categorical and continuous PGICS, respectively, at each time measurement. Differences between usability and adherence at the end of treatment were tested with the independent t-test or Mann Whitney U-test according to the distribution. The partial eta squared ($\eta p2$) values were calculated as a measure of the effect size and the results were interpreted as small (>0.01), medium (>0.06) and large (>0.14).

3. Results

3. Results

The following is a general summary of the main findings of each of the studies that make up this thesis (Appendix 1, 2 and 3).

3.1. Study I (Effects of Cognitive and Mental Health Factors on the Outcomes Following Carpal Tunnel Release: A Systematic Review and Meta-analysis)

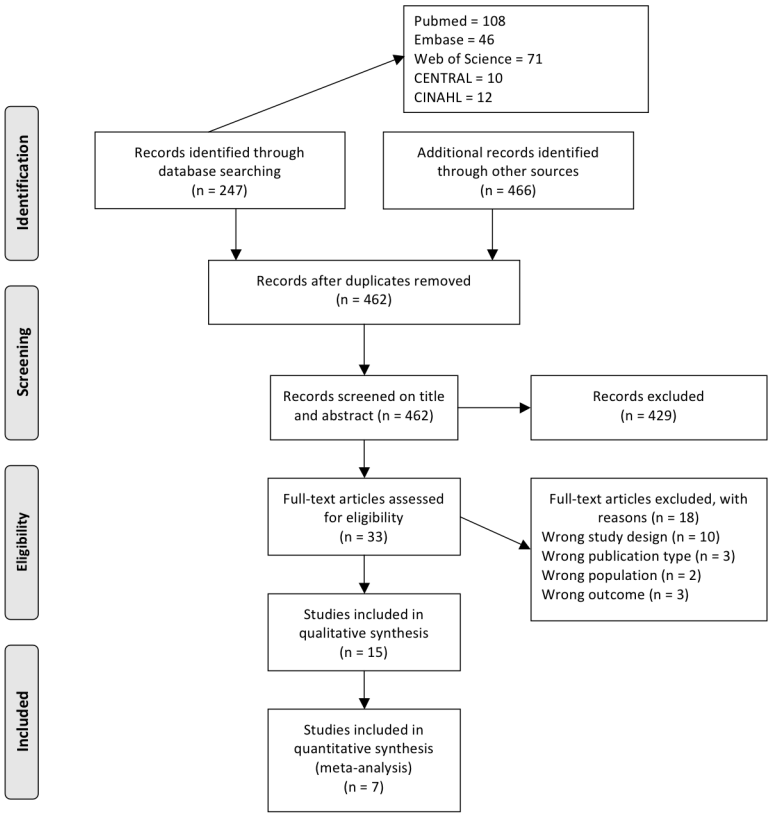
3.1.1. Selection of studies

Fifteen articles were included in this review (43,46,118–130). The study selection process is detailed in Figure 4.

3.1.2. Study characteristics

A total of 2,599 patients were included, with a mean age that varied between 46 ± 9 and 62 ± 12 years respectively. Eight articles included open CTR (43,119–124,130) and five articles included open and endoscopic CTR (125–129), while two articles did not report the type of surgery (46,118). The total time of the follow-up ranged from three months after CTR (43,120,124) to two years (119). The characteristics of the articles included are given in the original study (Appendix 1).

Figure 4. Study selection process.

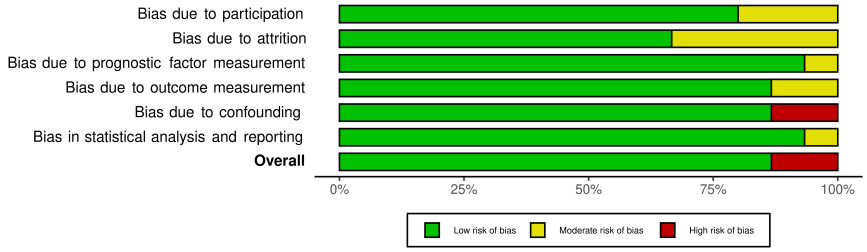


Abbreviations: CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health.

3.1.3. Methodological quality assessment

The assessment of risk of bias using the QUIPS tool for each study is provided in the original study (Appendix 1). In general, the risk of bias in the included studies was low. Figure 5 shows the summary of each 'Risk of bias' domain.

Figure 5. Risk of bias



Proportion of included studies with low, high, or moderate risk of bias using the Quality in Prognosis Studies tool.

3.1.4. Narrative synthesis

Estimates of the association between prognostic factors and outcomes after CTR are shown in the original study (Appendix 1). Most of the predictors were associated with the symptom severity, function, pain, satisfaction or return to work after CTR, both in the bivariate and multivariate analysis. Regarding the severity of symptoms, symptoms of depression were associated with higher severity of symptoms in 71% of the studies that considered this prognostic factor, followed by symptoms of anxiety (66%). Regarding the function, pain catastrophizing was associated with higher functional impairment in 100% of the studies that considered this prognostic factor, followed by symptoms of depression (57%) and symptoms of anxiety (0%). Regarding pain, symptoms of depression were associated with higher pain intensity in 100% of the studies that considered this prognostic factor, followed

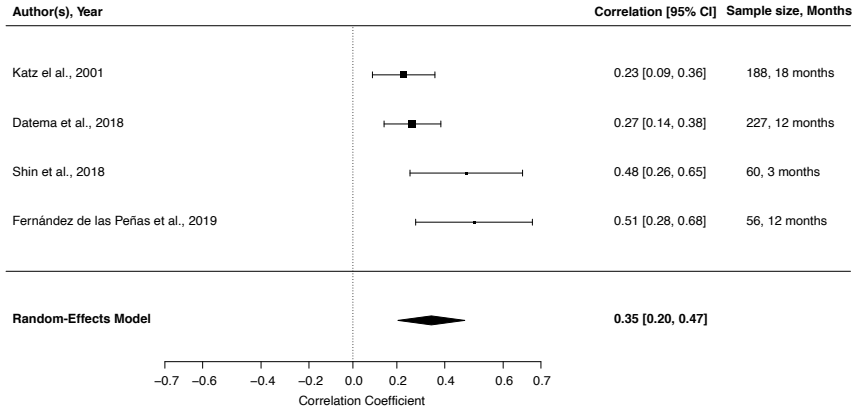
by symptoms of anxiety (0%). Regarding patient satisfaction, symptoms of depression were associated with higher satisfaction in 60% of the studies that considered this prognostic factor, followed by pain catastrophizing (33%) and symptoms of anxiety (25%). Regarding return to work, lower pain catastrophizing was associated with early return to work in 100% of the studies that considered this prognostic factor, followed by symptoms of anxiety (100%) and symptoms of depression (33%).

3.1.5. Quantitative synthesis (Meta-analyses)

The meta-analyses included estimates of the predictive role of symptoms of depression on symptom severity, function, pain, and satisfaction. We decided not to pool data from studies evaluating symptoms of anxiety, self-efficacy, and pain catastrophizing. In all these variables, there were not enough articles to analyse their operationalizations separately.

Four studies reported estimates of the depressive symptoms on symptom severity (n = 531). The overall result of the random effects model was r = 0.347 (95% CI = 0.205 to 0.475, p = <0.0001) (Figure 6). Heterogeneity between studies was substantial (I^2= 63.13%).

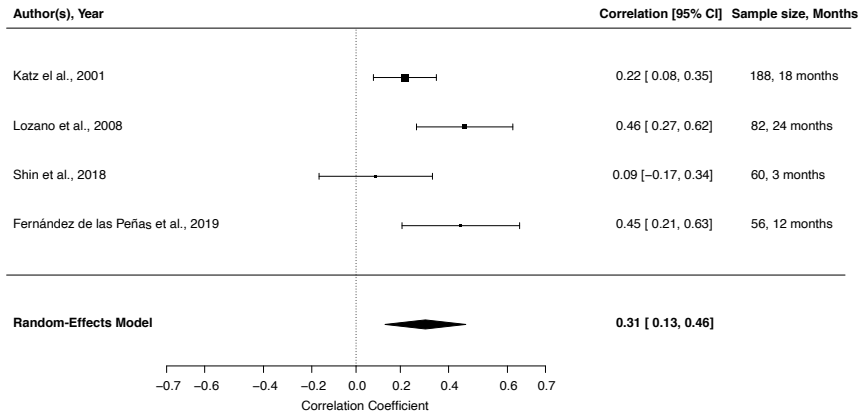
Figure 6. Forest plot of the relationship between symptoms of depression and symptom severity.



Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

Four studies reported estimates of the depressive symptoms on function (n = 386). The overall result of the random effects model was r = 0.307 (95% CI = 0.132 to 0.464, p = 0.0008) (Figure 7). Heterogeneity between studies was substantial (I^2= 65.51%).

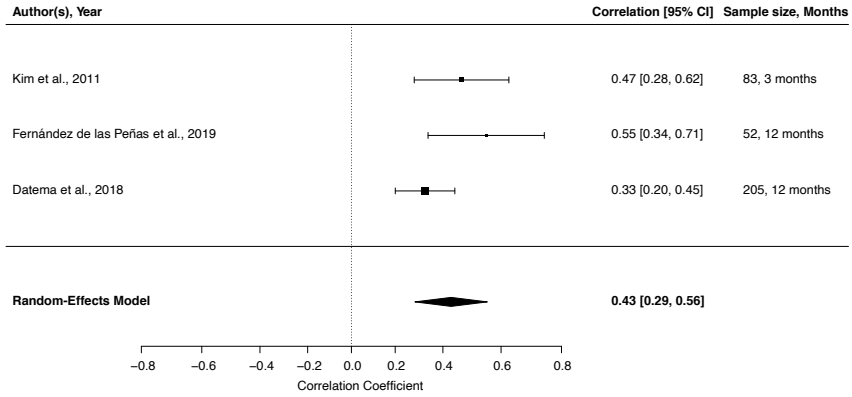
Figure 7. Forest plot of the relationship between symptoms of depression and function.



Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

Three studies reported estimates of the depressive symptoms on pain intensity (n = 344). The overall result of the random effects model was r = 0.431 (95% CI = 0.286 to 0.558, p = <0.0001) (Figure 8). Heterogeneity between studies was moderate (I^2= 51.29%).

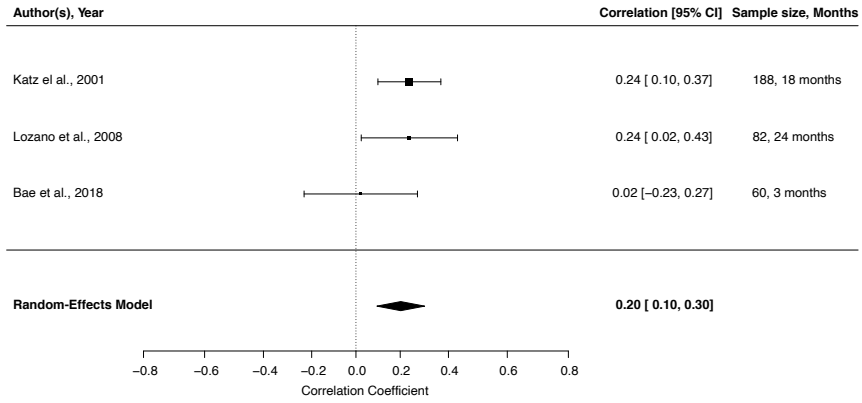
Figure 8. Forest plot of the relationship between symptoms of depression and pain intensity.



Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

Three studies reported estimates of the depressive symptoms on satisfaction (n = 330). The overall result of the random effects model was r = 0.202 (95% CI = 0.096 to 0.305, p = 0.0002) (Figure 9). Heterogeneity between studies was extremely low (I^2= 0.01%).

Figure 9. Forest plot of the relationship between symptoms of depression and dissatisfaction.



Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

3.2. Study II (Social Determinants of Health and Physical Activity are Related to Pain Intensity and Mental Health in Patients With Carpal Tunnel Syndrome)

A total of 92 patients were assessed for eligibility. Six participants were excluded for the following reasons: refusal to participate (n=4), previous upper extremity surgery (n=2). Finally, a total of 86 subjects were included in this study (Figure 10). Ninety-four percent were women and the mean age was 50.9 ± 10 years. The mean duration of symptoms was 3.2 ± 2.5 years. The socio-demographic data, the SDH and the outcomes of the total sample are summarised in Table 3.

Figure 10. Patient flow diagram (Study II).

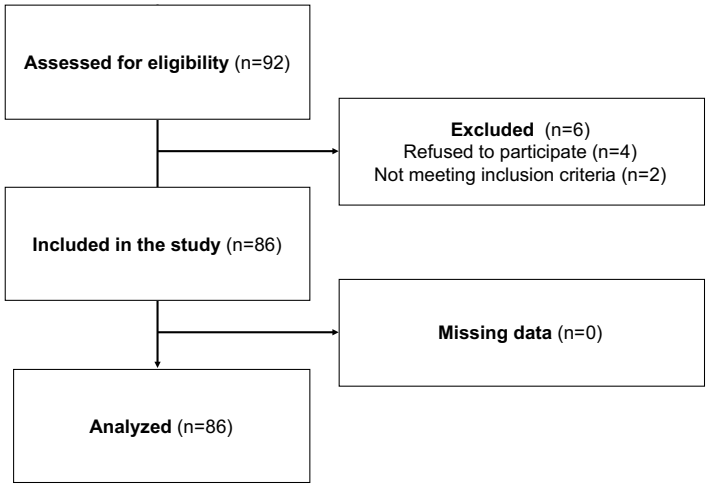


Table 3. Characterization of Patients (n=86).

Characteristics	Value
Age (years)	50.9 ± 10.0
Sex	
Male	5 (5.8%)
Female	81 (94.2%)
BMI (kg/m^2)	31.7 ± 6.2
Duration of CTS (years)	3.2 ± 2.5
Educational level	
Low level	43 (50%)
High level	43 (50%)
Employment status	
Unemployed	31 (36.0%)
Employed	44 (51.2%)
Non-working age	11 (12.8%)
Monetary Income	
≤ 320 USD	49 (57%)
> 320 USD	37 (43%)
Physical Activity	
Low level	66 (76.7%)
High level	20 (23.3%)
VAS (0-100)	66.0 ± 20.8
HADS-D (0-21)	8.0 ± 4.5
HADS-A (0-21)	9.0 ± 4.2
PCS (0-52)	27.3 ± 13.0

Abbreviations: BMI, Body Mass Index; HADS, Hospital Anxiety and Depression Scale (D, depression; A, anxiety); PCS, Pain Catastrophizing Scale; USD, US dollar; VAS, Visual Analogue Scale.

Data are expressed as percentages or mean ± SD.

3.2.1. Pain intensity

Multivariable linear regression analysis for pain intensity showed that a high level of physical activity was associated with a 12.41 mm decrease in VAS (R^2 = 0.101; β = -12.41; CI 95%: -23.87 to -0.95). No significant associations were found for the other exposure factors (Table 4).

Table 4. Multivariable associations for Pain Intensity (Visual Analogue Scale 0-100).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	-3.41 [-12.94 to 6.12]	0.96 [-9.38 to 11.31]
Low education	ref.	ref.
High education	-7.21 [-16.05 to 1.63]	-2.83 [-13.31 to 7.64]
Low income	ref.	ref.
High income	-5.5 [-14.49 to 3.49]	-2.60 [-13.04 to 7.84]
Low physical activity	ref.	ref.
High physical activity	**-12.64 [-22.91 to -2.37]***	**-12.41 [-23.87 to -0.95]***

Data are shown as regression coefficient (β) and 95% confidence intervals (95%CI). Significant values are in bold; *Statistically-significant difference ($p < 0.05$); Notes: ref. = reference category; [a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

3.2.2. Mental health

Depressive symptoms: Multivariable linear regression analysis for depressive symptoms showed that a high level of physical activity was associated with a decrease of 3.29 points on the HADS (Depression subscale) ($R^2 = 0.264$; β = -3,29; CI: 95%: -5,52 to -1,06). No significant associations were found for the other exposure factors (Table 5).

Anxiety symptoms: Multivariable linear regression analysis for anxiety symptoms showed that being employed was associated with a decrease of 2.30 points on the HADS (Anxiety subscale) ($R^2 = 0.142$; β = -2.30; 95% CI: -4.41 to -0.19). No significant associations were found for the other exposure factors (Table 6).

Table 5. Multivariable associations for Depressive Symptoms (Hospital Anxiety and Depression Scale 0-21)

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	0.15 [-1.9 to 2.21]	1.01 [-1.01 to 3.03]
Low education	ref.	ref.
High education	-1.16 [-3.07 to 0.74]	-0.51 [-2.56 to 1.53]
Low income	ref.	ref.
High income	-0.90 [-2.83 to 1.03]	-0.36 [-2.39 to 1.67]
Low physical activity	ref.	ref.
High physical activity	**-3.39 [-5.54 to -1.23]****	**-3.29 [-5.52 to -1.06]****

Data are shown as regression coefficient (β) and 95% confidence intervals (95%CI). Significant values are in bold; *Statistically-significant difference ($p < 0.05$); Notes: ref. = reference category; [a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

Table 6. Multivariable associations for Anxiety Symptoms (Hospital Anxiety and Depression Scale 0-21).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	**-2.06 [-4.00 to -0.12]***	**-2.30 [-4.41 to -0.19]***
Low education	ref.	ref.
High education	-1.07 [-2.86 to 0.72]	0.14 [-1.99 to 2.28]
Low income	ref.	ref.
High income	0.09 [-1.74 to 1.91]	0.68 [-1.45 to 2.81]
Low physical activity	ref.	ref.
High physical activity	-0.95 [-3.08 to 1.18]	0.12 [-2.22 to 2.45]

Data are shown as regression coefficient (β) and 95% confidence intervals (95%CI). Significant values are in bold; *Statistically-significant difference ($p < 0.05$); Notes: ref. = reference category; [a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

Catastrophizing: Multivariable linear regression analysis for catastrophizing showed that a high educational level was associated with a decrease of 7.71 points on the PCS scale (R^2 = 0.216; β = -7.71; 95% CI: -14.06 to -1.36). No significant associations were found for the other exposure factors (Table 7).

Table 7. Multivariable associations for Catastrophizing (Pain Catastrophizing Scale 0-52).

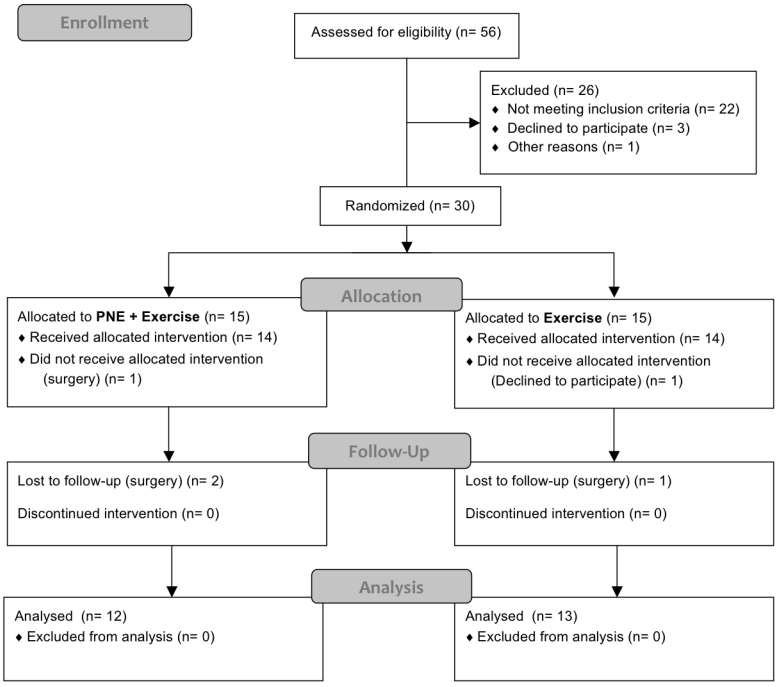
Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	0.55 [-5.66 to 6.75]	3.08 [-3.20 to 9.35]
Low education	1.0	ref.
High education	**-7.47 [-12.85 to -2.09]****	**-7.71 [-14.06 to -1.36]***
Low income	ref.	ref.
High income	-2.02 [-7.67 to 3.64]	-2.91 [-9.24 to 3.42]
Low physical activity	ref.	ref.
High physical activity	-4.67 [-11.25 to 1.89]	-3.92 [-10.86 to 3.03]

Data are shown as regression coefficient (β) and 95% confidence intervals (95%CI). Significant values are in bold; *Statistically-significant difference ($p < 0.05$); Notes: ref. = reference category; [a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

2.3. Study III (Effectiveness of Adding Pain Neuroscience Education to Telerehabilitation in Patients with Carpal Tunnel Syndrome: A randomised controlled trial)

Twenty-five participants completed the study and their data were used in the final analyses (Figure 11). No significant differences were observed between the PNE plus exercise group and the exercise group before starting the intervention (Table 8). The mean usability of the interaction system for telerehabilitation was "excellent" in both groups (SUS score > 80). No significant differences were observed between groups ($p>0.05$) (Table 9). Compliance with the telerehabilitation program was over 80% in both groups, with no significant differences ($p>0.05$) (Table 9). In the PNE plus exercise group, the assessment of learning after pain education was 88% (IQR=19) for the assessment of knowledge of key concepts and 100% (IQR=17) for perceived self-management (Table 10).

Figure 11. CONSORT flowchart for the selection of participants



Note: PNE, Pain Neuroscience Education

Table 8. Baseline comparison between groups.

Characteristics	PNE+Exercise (n=12)	Exercise (n=13)	Valor-p
Age (years)	45.9 ± 7.5	43.6 ± 8.1	0.469
Female gender (%)	91.7%	92.3%	0.740
BMI (kg/m^2)	29.7 ± 5.2	33.3 ± 7.3	0.177
Duration of CTS (months)	36 (51)	43 (45)	0.810
Educational level (%)			
Primary	41.7%	53.8%	0.418
Secondary/Higher	58.3%	46.2%	
Physical Activity (minutes)	37.5 (150)	45 (165)	0.810
Patients taking analgesics (%)	50%	69%	0.327
NPRS (0-10)	6.8 ± 1.9	5.8 ± 2.1	0.234
PCS (0-52)	25.5 ± 11.8	26.4 ± 15.9	0.866
TSK-11 (0-44)	31.1 ± 5.6	29.4 ± 4.3	0.404
BCTQ-FS (0-5)	3.0 ± 0.6	3.1 ± 0.5	0.769
BCTQ-SSS (0-5)	3.4 ± 0.7	3.0 ± 0.5	0.059
HADS-A (0-21)	10.4 ± 4.2	9.5 ± 4.3	0.580
HADS-D (0-21)	7.5 ± 4.4	5.7 ± 3.9	0.284
EQ5D (0-1)	0.5 ± 0.2	0.6 ± 0.2	0.424
EQVAS (0-100)	56.3 ± 13.9	57.2 ± 16.4	0.883

Data are expressed as mean ± SD or median (interquartile range)
Abbreviations: BMI, Body Mass Index; BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11,Tampa Scale for Kinesiophobia-11.

Table 9. Comparison between groups for impression of change, usability and adherence.

Outcome	PNE + TE (n=12)	TE (n=13)	Valor-p	Effect size
Week 6 (after treatment)				
PGIC (0-10)	3.1 ± 1.6	4.3 ± 1.1	**0.037***	0.893
PGIC (%)[a]	66.7	23.1	**0.028***	1.050
SUS (0-100)	83.8 ± 10.7	81.2 ± 8.6	0.508	0.270
Adherence (%)	84.0 (7.5)	92.0 (27.5)	0.406	0.153
Week 12 (follow-up)				
PGIC (0-10)	3.7 ± 2.7	3.8 ± 2.2	0.857	0.073
PGIC (%)[a]	50	38.5	0.561	0.259

Data are expressed as mean ± SD or median (interquartile range)

[a] Percentage of patients in the category "very much improved" or "much improved"

Abbreviation: SUS, System Usability Scale; PNE, Pain Neuroscience Education; PGIC, Patients' Global Impression of Chang scale; TE, Therapeutic Exercise. The parametric (d) and nonparametric (r) effect size of d and r can be interpreted as follows: d=0.2 and r=0.1, small; d=0.5 and r=0.3, medium; d=0.8 and r=0.5, large, respectively. Bold type denotes statistically significant differences.

Table 10. Evaluation of learning following pain education.

	Knowledge	Perceived self-management
Subject 1	94%	100%
Subject 2	94%	83%
Subject 3	88%	100%
Subject 4	63%	66%
Subject 5	88%	83%
Subject 6	69%	66%
Subject 7	75%	100%
Subject 8	100%	100%
Subject 9	94%	100%
Subject 10	88%	100%
Subject 11	100%	100%
Subject 12	75%	83%
Total (median [IQR])	**88 (19)**	**100 (17)**

Knowledge was assessed by means of a 16-item questionnaire containing ten multiple choices and six true/false questions. Data are presented as a percentage of correct answers. Perceived self-management-related pain education concepts were assessed by six Yes/No/Unsure questions. Data are presented as a percentage of affirmative responses.

3.3.1. Pain intensity

The ANOVA model indicated a significant main effect of the time factor ($F=3.52$, $p=0.038$, $\eta p^2=0.133$) but not of the group factor ($p>0.05$). There was no significant time x group interaction ($F=1.81$, $p=0.174$, $\eta p^2=0.073$). Significant and clinically relevant differences in NPRS were observed at week 6 in the PNE+exercise group (MD: -2.0 points, 95% CI: -3.8 to -0.2). The exercise group showed no improvement at any time point (Table 11, Figure 12).

3.3.2. Pain catastrophizing

The ANOVA model indicated a significant main effect of the time factor (F=9.43, p<0.001, ηp^2=0.291) but not of the group factor (p>0.05). There was no significant time x group interaction (F=2.27, p=0.115, ηp^2=0.090). Significant and clinically relevant differences from baseline were observed in PCS at week 6 (MD: -13.2 points 95%CI: -21.4 to -4.9) and week 12 (MD: -8.8 points, 95%CI: -17.1 to -0.4) in the PNE+exercise group. The exercise group showed no improvement at any time point (Table 11, Figure 12).

3.3.3. Kinesiophobia

The ANOVA model indicated a significant main effect of the time factor (F=6.65, p=0.003, ηp^2=0.221) and on the group factor (F=5.41, p=0.022, ηp^2=0.074). Additionally, a significant time x group interaction with a large effect size was observed (F=6.67, p=0.005, ηp^2=0.225). Significant and clinically relevant differences from baseline were observed in TSK-11 at week 6 (MD: -6.1 points 95%CI: -10.3 to -1.8) and week 12 (MD: -7.7 points, 95%CI: -12.8 to -2.4) in the PNE+exercise group. The exercise group showed no improvement at any time point (Table 11, Figure 12). At weeks 6 and 12, the mean between-group difference in TSK-11 was -5.2 points [95% CI: -9.7 to -0.6; p=0.028] and -5.7 points [95% CI: -10.8 to -0.5; p=0.034], respectively.

3.3.4. Function and Severity of Symptoms

The ANOVA model indicated a significant main effect of the time factor (F=5.02, p=0.014, ηp^2=0.179) but not of the group factor (p>0.05). There was no significant time x group interaction. Significant differences from baseline were observed in BCTQ-FS at week 6 in the PNE+exercise group but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 11, Figure 12).

The ANOVA model indicated a significant main effect of the time factor (F=11.32, p=0.003, ηp^2=0.330). In addition, a significant time x group interaction with a large effect size was observed (F=4.82, p=0.013, ηp^2=0.173). Significant differences from baseline were observed in BCTQ-SSS at week 6 and week 12 in the PNE+exercise group. The exercise group showed no improvement at any time point (Table 11, Figure 12).

3.3.5. Mental health

The ANOVA model indicated a non-significant main effect of the time factor and group factor in both subscales (p>0.05). Additionally, a non-significant time x group interaction was observed for both subscales. Clinically relevant improvements in both subscales of the HADS were observed at week 6 in the

PNE+exercise group, but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 11, Figure 12).

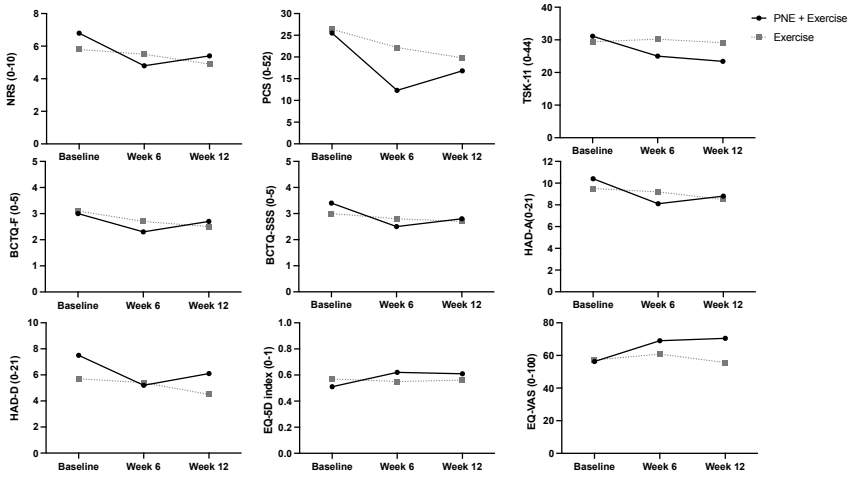
3.3.6. Quality of life

The ANOVA model indicated a non-significant main effect of the time factor in both subscales ($p>0.05$). Only a significant main effect of the group factor on the EQ-VAS was observed ($F=5.56$, $p=0.021$, $\eta p^2=0.075$), but a non-significant time x group interaction was observed for both EQ-5D ($F=1.47$, $p=0.240$, $\eta p^2=0.060$) and EQ-VAS ($F=2.93$, $p=0.063$, $\eta p^2=0.113$) (Table 11, Figure 12). At week 12, a mean difference between groups of 15.7 points [95% CI: 3.57 to 27.85, $p=0.013$] was obtained on the EQ-VAS.

3.3.7. Self-perception of improvement

Significant differences were observed in favour of the PNE plus exercise group after treatment on the continuous subscale (0-10) of the PGICS (3.1 ± 1.6 vs 4.3 ± 1.1, $p=0.037$, ES=0.893). Furthermore, on the categorical subscale, 66.7% of patients in the PNE plus exercise group reported clinically significant improvement (i.e. categories "very much improved" and “much improved”), compared to 23.1% in the exercise group (chi-square=4.812, $p=0.023$). No significant differences were observed between groups at week 12 ($p>0.05$) (Table 9).

Figure 12. Effect of intervention by time and group.



Data are expressed as mean

Abbreviations: BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analogue Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11, Tampa Scale for Kinesiophobia-11.

Table 11. Outcome measures during the follow-up period and results of the time x group comparative analysis.

Outcome	Follow-up	PNE+Exercise (n=12)		Exercise (n=13)		ANOVA Interaction Effect		
		Mean ± SD	Mean within-group difference [95% CI]	Mean ± SD	Mean within-group difference [95% CI]	F	p-value	η^2p
NPRS (0-10)	Baseline	6.8 ± 1.9		5.8 ± 2.1		1.81	0.174	0.073
	Week 6	4.8 ± 1.7	-2.0 [-3.8 to -0.2]	5.5 ± 1.4	-0.2 [-1.9 to 1.5]			
	Week 12	5.4 ± 2.0	-1.3 [-3.4 to 0.8]	4.9 ± 2.5	-0.9 [-2.8 to 1.2]			
PCS (0-52)	Baseline	25.5 ± 11.8		26.4 ± 15.9		2.27	0.115	0.090
	Week 6	12.3 ± 6.8	-13.2 [-21.4 to -4.9]	22.2 ± 13.8	-4.2 [-12.2 to 3.6]			
	Week 12	16.8 ± 11.5	-8.8 [-17.1 to -0.4]	19.8 ± 15.7	-6.6 [-14.6 to 1.4]			
TSK-11 (0-44)	Baseline	31.1 ± 5.6		29.4 ± 4.3		6.67	**0.005****	0.225
	Week 6	25.0 ± 5.3	-6.1 [-10.3 to -1.8]	30.2 ± 5.7	0.8 [-3.3 to 4.8]			
	Week 12	23.4 ± 5.9	-7.7 [-12.8 to-2.4]	29.1 ± 6.6	-0.3 [-5.2 to 4.6]			
BCTQ-FS (0-5)	Baseline	3.0 ± 0.6		3.1 ± 0.5		1.25	0.296	0.051
	Week 6	2.3 ± 0.5	-0.7 [-1.2 to -0.1]	2.7 ± 0.7	-0.4 [-0.8 to 0.2]			
	Week 12	2.7 ± 0.8	-0.3 [-0.9 to 0.3]	2.5 ± 0.9	-0.5 [-1.1 to 0.1]			
BCTQ-SSS (0-5)	Baseline	3.4 ± 0.7		3.0 ± 0.5		4.82	**0.013***	0.173
	Week 6	2.5 ± 0.5	-0.9 [-1.4 to -0.4]	2.8 ± 0.7	-0.2 [-0.6 to 0.3]			
	Week 12	2.8 ± 0.8	-0.6 [-1.0 to -0.2]	2.6 ± 0.8	-0.4 [-0.8 to 0.0]			
HADS-A (0-21)	Baseline	10.4 ± 4.2		9.5 ± 4.3		1.50	0.235	0.061
	Week 6	8.1 ± 3.8	-2.3 [-4.5 to -0.2]	9.2 ± 4.1	-0.3 [-2.4 to 1.7]			
	Week 12	8.8 ± 5.1	-1.6 [-3.8 to 0.6]	8.5 ± 4.8	-0.9 [-3.0 to 1.2]			
HADS-D (0-21)	Baseline	7.5 ± 4.4		5.7 ± 3.9		1.29	0.286	0.053
	Week 6	5.2 ± 3.9	-2.3 [-5.4 to 0.7]	5.4 ± 3.6	-0.3 [-3.2 to 2.6]			
	Week 12	6.1 ± 4.5	-1.4 [-3.7 to 0.8]	4.5 ± 4.1	-1.2 [-3.4 to 1.0]			
EQ5D (0-1)	Baseline	0.51 ± 0.2		0.57 ± 0.2		1.47	0.240	0.060
	Week 6	0.62 ± 0.2	0.11 [-0.1 to 0.3]	0.55 ± 0.2	-0.02 [-0.2 to 0.2]			
	Week 12	0.61 ± 0.2	0.10 [0.0 to 0.2]	0.56 ± 0.2	-0.01 [-0.2 to 0.1]			
EQVAS (0-100)	Baseline	56.3 ± 13.9		57.2 ± 16.4		2.93	0.063	0.113
	Week 6	69.0 ± 10.3	13.7 [0.2 to 27.1]	60.8 ± 16.8	3.6 [-9.3 to 16.5]			
	Week 12	70.5 ± 14.8	14.3 [0.8 to 27.7]	55.6 ± 15.9	-1.5 [-14.1 to 11.3]			

Abbreviations: BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Sympton Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11, Tampa Scale fo Kinesiophobia-11; 95%CI, 95% confidence interval. *Statistically-significant difference ($p < 0.05$); **Statistically-significant difference ($p < 0.01$); Bol type denotes statistically significant differences.

4. Discussion

4. Discussion

The overall aim of this thesis was to evaluate the role of psychological and social factors in patients with CTS during the pre- and postoperative periods, and to determine the efficacy of adding a biopsychosocial approach to telerehabilitation in patients awaiting surgery.

First, through a systematic review and meta-analysis (study I), we provided updated evidence on the association of cognitive and mental health factors with self-reported outcomes in patients with CTS undergoing surgery. Most of the studies included in the systematic review showed a significant association between catastrophizing, self-efficacy, anxiety symptoms or depressive symptoms, and outcomes after CTR. Despite the heterogeneity of the available evidence, the results were fairly consistent in the quantitative analysis of the impact of depressive symptoms on symptom severity, function and pain after CTR.

Second, a cross-sectional study (study II) analysed the association of SDH and physical activity with pain intensity and mental health in patients with CTS awaiting surgery. Although linear regression models explained only a small proportion of the variance in each outcome, a significant association of physical activity with pain intensity and depressive symptoms was identified. A significant association was also found

between work status and anxiety symptoms, and between low educational attainment and catastrophizing. Therefore, the identification of SDH, such as employment status, educational level and physical activity level, may help clinicians to develop more specific perioperative interventions for pain and mental health management in patients with CTS.

Thirdly, a RCT (study III) evaluated the potential benefit of adding a biopsychosocial approach to telerehabilitation in patients with CTS awaiting surgery in two hospitals of the Chilean public health system, comparing combined treatment with PNE plus exercise versus exercise alone. Overall, the proposed interactive telerehabilitation system had excellent usability and adherence was over 80% in both groups. Our results showed that a combined PNE+exercise program was more effective than exercise alone in reducing kinesiophobia and symptom severity. In addition, self-perceived improvement was greater in the PNE+exercise group compared to that of the exercise-only group at the end of treatment. In the last decade there have been an increasing number of systematic reviews and meta-analyses on telerehabilitation. To date, the available systematic reviews on the effects of PNE have not included RCTs in patients with CTS in a telerehabilitation setting (75–78,131–133). This study is therefore a novelty in this field.

The main findings obtained in this thesis are discussed below.

4.1 Physiological factors related to outcomes after surgery

The findings of our systematic review are consistent with previous reviews emphasising the potential impact of cognitive and mental health factors on postsurgical outcomes in individuals with chronic musculoskeletal pain (134,135). For example, symptoms of depression and anxiety, and pain catastrophizing can predict poor outcomes in patients undergoing shoulder surgery (33,36), spine surgery (38,136), and knee replacement (39,137). Therefore, physicians, physical therapists, and occupational therapists should consider evaluating cognitive and mental health factors in patients undergoing hand surgery.

An interesting finding is that most of the studies found that the level of symptoms of depression was associated more with the severity of the symptoms and postoperative pain than with functional impairment. This seems relevant since the severity of the symptoms is the most important reason for the patients to undergo surgery (138) and postoperative pain control is an essential goal in rehabilitation due to the possibility of reducing the costs associated with the use of opioids (139). On the other hand, although a quantitative analysis was not possible, symptoms of depression with self-efficacy showed a significant association with a late return to work. The early

identification of patients at greater risk of a delayed return-to-work could prevent prolonged absence from work or sub-optimal performance at work (140).

While some patients may experience improvement in their depressive symptoms after CTR (123,124), the need to treat depressive symptoms before surgery has been little studied. In other musculoskeletal pain conditions, it has been observed that depressed patients who received preoperative psychotherapy (e.g. cognitive behavioural therapy) had fewer medical complications and resource utilisation compared with those who did not receive psychotherapy (141). In addition, perioperative psychotherapy has been shown to be effective in reducing postoperative pain and functional impairment in orthopaedic surgery patients (142). Therefore, future studies should evaluate the efficacy of similar interventions in patients with CTS undergoing surgery, incorporating the approach to other aspects that negatively influence depressive symptoms, such as sleep quality (143).

On the other hand, it is not just about identifying those at risk of a poor outcome, but providing evidence to support that having more positive emotional and cognitive responses can benefit the patient and their outcomes. For example, expectations and optimism have been shown to be strong predictors of postoperative disability (144). Therefore, implementing strategies early on that reinforce these more

positive beliefs, attitudes, and behaviours could positively influence their current and future pain experience (e.g. multimodal treatments) (145). In addition, counselling patients before surgery may help them to increase their participation in the shared decision-making process and to set realistic expectations regarding postoperative outcomes, as meeting expectations is directly related to postoperative outcomes (130). Similarly, the efficacy of treatments following CTR should focus on more positive outcomes, such as quality of life (146). Future studies should consider this point, to reframe the conversation about how more positive cognitive and emotional responses can lead to better rehabilitation outcomes. For this reason, addressing the patient's emotional state and coping strategies could be an essential treatment opportunity that results in the improvement of the health of patients undergoing CTR.

4.2 Social factors and physical activity related to pain intensity

According to our results, a high level of physical activity was associated with a decrease in pain intensity. These results are consistent with the available literature in people with chronic pain. For example, Polaski et al (147) in a meta-analysis identified that physical activity and exercise (as a subset of physical activity) would be related to the analgesic effect in patients with chronic pain. Thus, one possible mechanism that

could explain our results is the relationship between physical activity levels and descending pain modulatory function (148). In fact, in healthy adults greater self-reported physical activity is associated with a greater pain inhibitory response through the conditioned modulatory pain response (148).

On the other hand, our results disagree with the available literature on the association between educational level and income with pain intensity. In other conditions affecting the hand (e.g. rheumatoid arthritis), subjects with a high level of education, according to Swedish records, experience less pain than those with a low level of education (149). In other surgical populations evaluated in North America (e.g. joint replacement), lack of university education was associated with higher pain scores before and after surgery (150). The discrepancies found in our results could be explained in part by the differences in the educational systems and realities of each country. Therefore, multinational studies may be necessary to evaluate these associations in greater depth. Additionally, previous studies have identified that income (in terms of annual household income) is also related to pain and coping strategies in people with musculoskeletal pain (151,152). This could be explained by the fact that monetary income was classified according to individual monthly taxable income and there was no information on household income.

4.3 Social factors and physical activity related to mental health

Regarding depressive symptoms, it was observed that patients who met the WHO physical activity recommendations had lower levels of depressive symptoms. In fact, these patients had a reduction of up to 3.29 points in the depression subscales of the HADS (taking as a reference the patients with a low level of physical activity). This difference exceeds the minimal clinically important difference (MCID) of 1.7 points on the HADS, established for other health conditions (114). These results are consistent with the available literature in the general population. For example, Choi et al found a protective relationship between accelerometer-based activity and depression among adults (153). The antidepressant effects of physical activity could be explained by several neuroplastic processes related to depression (e.g., activation of the endocannabinoid system, optimisation of brain-derived neurotrophic factor) and by the ability to reduce inflammation and increase resistance to oxidative and physiological stress (59,154,155). In addition, exercise promotes self-esteem, social support and self-efficacy (59). Therefore, our results reinforce the hypothesis that the promotion of physical activity (e.g., physical activity programs guided by WHO recommendations) could be a valuable strategy to reduce the risk of mental health issues (156), which could be relevant for patients with CTS while awaiting surgery. Moreover, being

employed was associated with a decrease of 2.30 points on the HADS anxiety subscale scores, which was also higher than the MCID reported in the literature of 1.7 points (114). Previous research indicates that the negative effect of unemployment on mental health is mainly explained by distress (157). Our study also raises the need for policies to focus on the welfare of the unemployed, including support for re-employment.

On the other hand, according to our results, educational level was significantly associated with catastrophizing. In fact, having a high level of education was associated with a reduction of 7.71 points on the PCS, which was higher than the MCID of 6.71 points on the PCS for patients with chronic low back pain (158). Thus, for patients with CTS awaiting surgery, a comprehensive approach that takes into account both physical limitations due to pain and psychosocial challenges may be necessary.

We should be aware that the association between SDH and outcomes might be affected in our study, as patients were evaluated during the COVID-19 outbreak. The pandemic has highlighted pre-existing inequalities in terms of gender and socio-economic status (159). In this context, the SDH as mediators of the impact caused by the pandemic (e.g., job insecurity or economic concerns), amplified the consequences on the mental health of the most vulnerable populations (159–

162). Furthermore, although CTR is a common surgical procedure (163), during the COVID-19 pandemic, hospitals around the world suspended elective or non-urgent hand surgeries to cope with the high demand for capacity caused by the health crisis (61). The cancellation of elective surgeries and limited access to quality pain management care resulted in a greater focus on biomedical treatment (e.g., pharmacological management), with less consideration of psychological aspects (62). In this context, the implementation of physical activity programmes in the pre-surgical phase could help to reduce pain and improve mental health in this population.

4.4 Adding a biopsychosocial approach to telerehabilitation

Several studies have reported positive effects of PNE on pain, function, and some psychosocial variables in patients with musculoskeletal conditions (75–78,131–133). Some of our results are consistent with the available evidence. For example, Watson et al (78) found in their meta-analysis that the effect of PNE treatment for kinesiophobia in adults with chronic musculoskeletal pain was clinically relevant in the short term. Siddall et al (77) also found in their meta-analysis that the combination of PNE and exercise resulted in greater improvements in kinesiophobia than exercise alone in the same population. Based on our results, we confirm that PNE

plus exercise as a telerehabilitation modality is a useful intervention to reduce fear of movement, which also applies to patients with CTS. This could be explained by the fact that the aim of a combined therapy is to reconceptualize pain, reducing the threat value and promoting gradual and safe exercise. This study also underlines that in this new era of telehealth, researchers and clinicians should explore new modalities of education, including PNE, to improve telerehabilitation interventions. On the other hand, there was a significant improvement in symptom severity reduction in favour of the PNE plus exercise group compared to exercise alone. However, the intra-group difference in the BCTQ-SSS was not superior to the MCID (112). In relation to self-perception of improvement after treatment, 66.7% of participants in the PNE plus exercise group considered that they had much improved or very much improved after treatment. In addition, half of the participants maintained this improvement at the 6-week follow-up, which is considered a clinically significant improvement for this variable (116). This finding is consistent with the observed trend toward better self-perceived quality of life in the PNE plus exercise group.

Although our results show that PNE plus exercise produced an improvement within the group, there was no significant difference compared to exercise alone. In contrast to these findings, most systematic reviews report improvements in pain or function with PNE in patients with chronic musculoskeletal

pain (75–78,131–133). For example, Malfliet et al (164) conclude in a multicenter RCT in patients with chronic spinal pain that combined treatment including PNE appears to be more effective than conventional physical therapy in improving pain and disability, among other outcomes. In fibromyalgia patients, Amer-Cuenca et al (165) found that higher doses of PNE (270 minutes) produced greater improvements in pain intensity than lower doses of PNE (90 minutes). In our study, 120 minutes of PNE were delivered by videoconference plus twelve minutes of reinforcement videos. With this in mind, higher doses of PNE may have improved the results of our study. Additionally, our sample included patients with severe CTS awaiting surgical intervention, most of whom had been symptomatic for longer than 30 months (Table 8). Because of COVID-19, most patients did not have access to timely treatment with a biopsychosocial approach, which may have increased uncertainty and sources of pain-related threat (62). In addition, patients in the PNE plus exercise group had a mean HADS score above the cutoff point on both subscales (ie, ≥8 points), indicating high levels of anxiety or depression in our sample (Table 8) (113). Both of these factors may negatively influence the prognosis of physical functioning after rehabilitation (166). All of these factors suggest that our study population may be a group with higher levels of vulnerability in various domains. This may also explain why the exercise-only group did not achieve positive results, despite the literature claiming that exercise-based physical therapy produces

improvements in symptoms and function in patients with CTS (63–65). Therefore, future studies should investigate the efficacy of telerehabilitation combined with the support of an interdisciplinary team (i.e., psychologist, occupational therapist, and social worker).

On the other hand, our study showed no significant improvement in the levels of catastrophizing in the PNE plus exercise group compared to the exercise group. Nevertheless, it is relevant to mention that in the PNE plus exercise group an improvement above the MCD (i.e. above 10.45) was obtained on the PCS at week 6 (97). This improvement was not sustained at the 12-week assessment (Figure 2), indicating that a greater number of sessions may be necessary to demonstrate stronger results. In terms of symptoms of depression and anxiety, our study also showed no significant differences when comparing the two treatments. Although the MCID of 1.85 and 1.67 points for the depression and anxiety subscales of the HADS were exceeded in the PNE plus exercise group (114), this improvement was also not sustained at the week 12 follow-up. In contrast to our results, Chimenti et al (167) and Barrenengoa-Cuadra et al (168), who also considered higher doses of pain education in the treatment of patients with chronic pain, found greater benefits for catastrophizing and mental health, respectively. Future research should explore the dose-response of PNE to guide

clinicians in developing telerehabilitation interventions to find the optimal duration of intervention.

Finally, our research provides additional information in the context of non-North American/Western European countries on digital support for patients with persistent pain, specifically on the effectiveness of a low-cost telerehabilitation programme focusing on biopsychosocial aspects. Additionally, clinically relevant improvements in catastrophizing and anxiety symptoms immediately after PNE should also be considered by surgeons, as both variables are important predictors of poor outcomes after surgery (169). Therefore, it would be interesting to coordinate surgery in patients with CTS immediately after completion of the 6-week pain education combined with exercise and to evaluate the long-term efficacy of the intervention. Future studies should also consider combining PNE with interdisciplinary and multimodal treatments (e.g. cognitive behavioral therapy and mindfulness), which have shown promise for these variables in other painful conditions such as fibromyalgia (170). Furthermore, these interventions should be tailored to account for social determinants of health (66) and the diverse cultural backgrounds of patients.

4.5 Limitations

The studies that make up this thesis have a number of limitations that should be taken into account when interpreting the results.

Regarding Study I, due to the lack of data, we were unable to perform a quantitative synthesis of the data for all the prognostic factors considered (i.e., anxiety symptoms, catastrophic thinking, and self-efficacy). In addition, we did not find studies that evaluated some psychosocial factors that we included in our search strategy (i.e., fear avoidance or kinesiophobia). Although kinesiophobia, for example, has been shown to have an important predictor of upper-extremity-specific disability in patients with CTS (171), its prognostic value in postoperative outcomes has not yet been considered, so future studies should evaluate this aspect. Another limitation was that we focused on evaluating psychosocial risk factors, while we know that many variables can modulate symptoms in patients with CTS. For example, educational level, intrinsic risk factors such as obesity, age and gender, and occupational risk factors such as exposure to higher manual forces (2,51). In addition, peripheral nerve injury triggers changes in the central nervous system. These changes include central sensitization and changes in cortical representations (18). A comprehensive assessment that considers all of these aspects will allow clinicians to make

more appropriate decisions and deliver greater benefits to patients.

Regarding Study II, a cross-sectional design does not allow a cause-effect relationship to be established between the variables studied, so the results should be interpreted with caution. In addition, SDH and physical activity were presented as dichotomous variables, which may lead to potential bias due to residual confounding. However, our study is consistent with the available literature on the importance of SDH in patients with CTS (172,173), and provides additional information in the context of non-North American/Western European countries. Furthermore, using these cut-off points could help clinicians to more clearly identify vulnerable groups that require further attention (e.g., unemployed, patients who have not completed secondary education). Therefore, our findings pave the way for future longitudinal investigations that may establish the directionality of the observed relationships. On the other hand, we examined self-reported physical activity (i.e minute per week), and not based on an objective measure (e.g., accelerometer-based). However, the method used is valid and easy to apply at the clinical/hospital setting (93), and allows specific recommendations to be provided to healthcare teams (e.g., design physical activity programs guided by WHO criteria). Finally, it is also important to mention that, although the results are in line with previous literature, our results only apply to the reality of one country. In addition, the high

percentage of women in the sample is a limitation for the generalisability of the results. Future studies should include a larger population with follow-up over time to investigate how SDH might also affect clinical outcomes after surgery.

Regarding Study III, the absence of a control group that did not receive any intervention did not allow the results of the two groups to be compared with the natural history of CTS. Ethical considerations make it difficult to allocate patients with persistent symptoms to a non-intervention group. Second, the effect of the intervention was only assessed in the short term (i.e. 6 weeks follow-up), so future RCTs are needed to study the long-term effects of similar interventions. On the other hand, due to the nature of the intervention, it was not possible to blind the patients about PNE. Also, the influence of treatment expectations was not assessed, which may be relevant as patients were candidates for surgery to resolve their symptoms. Finally, although the sample size was calculated, a larger sample could increase the precision, generalizability, and statistical power of their study. Future multicenter studies are needed to corroborate these findings and to address the cultural aspects of pain.

4.6 Projections

Musculoskeletal symptoms of the upper extremities, including CTS, place a large economic burden on the individual, the employer and society due to absenteeism and lost productivity. Therefore, early identification of factors that may affect timely return to work could be important to reduce costs and disability, especially in populations at high risk of work-related disorders. The findings of this doctoral thesis support the available evidence that psychosocial variables are modifiable through specific intervention strategies. In this sense, a better understanding of the association between these factors and absenteeism may help rehabilitation teams (psychologists, physiotherapists, occupational therapists and physicians) to design strategies to improve patients' physical and mental health, optimise return to work and, indirectly, decrease economic costs. As a projection of this thesis, a systematic review and meta-analysis was carried out with the aim of determining the association of selected pain coping strategies and symptoms of anxiety and depression with absenteeism from work in people with musculoskeletal disorders of the upper extremities (174).

A systematic search of PubMed, Web of Science, Embase, Cochrane Library, and Scopus databases was conducted from inception to September 23, 2022. Prospective observational studies of adults with upper limb musculoskeletal disorders

were included. Included studies had to provide data on the association of pain coping strategies (catastrophizing, kinesiophobia, self-efficacy or fear avoidance) or symptoms of anxiety and depression with work absenteeism. Study selection, data extraction and assessment of methodological quality (Newcastle Ottawa Scale) were performed by two independent authors. Random-effects models were used for quantitative synthesis. Eighteen studies (n=12,393 participants) were included. Most studies (77.8%) reported at least one significant association between one or more exposure factors (pain coping strategies or symptoms of anxiety and depression) and work absenteeism. Meta-analyses showed a statistically significant correlation between the exposure factors of catastrophizing (r=0.28, 95% CI: 0.15 to 0.40; p<0.0001) and symptoms of anxiety and depression (r=0.23, 95% CI: 0.10 to 0.34; p=0.0003) with work absenteeism. The correlation between self-efficacy and work absenteeism was non-significant (r=0.24, 95% CI: -0.02 to 0.47; p=0.0747).

In conclusion, rehabilitation teams should also consider assessing catastrophizing and symptoms of anxiety and depression to identify patients at risk for work absenteeism. Addressing these variables may also be considered in return-to-work programs for individuals with upper limb disorders.

5. Conclusions

5. Conclusions

This thesis highlights the importance of addressing psychosocial factors in patients with carpal tunnel syndrome, both in assessment and treatment. The conclusions drawn from the three studies that form part of this thesis are presented below.

Regarding Study I: depressive symptoms have a moderate association with symptom severity, function and pain after CTR. Symptoms of anxiety, catastrophizing and self-efficacy were also important indicators of poor postoperative outcomes and should be taken into account. Therefore, a preoperative assessment of this variable could help identify patients at risk for poor surgical outcomes and provide timely treatment.

Regarding Study II: a high level of physical activity was associated with a decrease in pain intensity and depressive symptoms in patients with CTS awaiting surgery. In addition, being employed was associated with a decrease in anxiety symptoms and having a high educational level was associated with a decrease in catastrophizing. Multidisciplinary care teams should be aware of the association between SDH and physical activity with physical and mental health. Therefore, a comprehensive assessment of these variables may be relevant to identify cases of increased psychosocial risk and to plan strategies to reduce pain and improve the mental

health of patients with CTS awaiting surgery, for example, physical activity programs guided by WHO recommendations.

Regarding Study III: the addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity in patients with CTS awaiting surgery. Although there were significant and clinically relevant improvements within the PNE plus exercise group in pain, catastrophizing and symptoms of anxiety, there were no significant differences between the groups. These results highlighted the benefits of including a biopsychosocial approach in telerehabilitation interventions.

6. References

6. References

1. Núñez-Cortés R, Cruz-Montecinos C, Tapia C, Pommer PP, Pérez-Alenda S. Carpal tunnel syndrome and pain. Features and Assessments of Pain, Anaesthesia, and Analgesia. 2022. p. 275–83. Available from: http://dx.doi.org/10.1016/b978-0-12-818988-7.00031-5

2. Erickson M, Lawrence M, Jansen CWS, Coker D, Amadio P, Cleary C. Hand Pain and Sensory Deficits: Carpal Tunnel Syndrome. J Orthop Sports Phys Ther. 2019 May;49(5):CPG1–85.

3. Aroori S, Spence RAJ. Carpal tunnel syndrome. Ulster Med J. 2008 Jan;77(1):6–17.

4. Nora DB, Becker J, Ehlers JA, Gomes I. What symptoms are truly caused by median nerve compression in carpal tunnel syndrome? Clin Neurophysiol. 2005 Feb;116(2):275–83.

5. Thiese MS, Gerr F, Hegmann KT, Harris-Adamson C, Dale AM, Evanoff B, et al. Effects of Varying Case Definition on Carpal Tunnel Syndrome Prevalence Estimates in a Pooled Cohort. Vol. 95, Archives of Physical Medicine and Rehabilitation. 2014. p. 2320–6. Available from: http://dx.doi.org/10.1016/j.apmr.2014.08.004

6. Dale AM, Harris-Adamson C, Rempel D, Gerr F, Hegmann K, Silverstein B, et al. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. Vol. 39, Scandinavian Journal of Work, Environment & Health. 2013. p. 495–505. Available from: http://dx.doi.org/10.5271/sjweh.3351

7. Bickel KD. Carpal Tunnel Syndrome. Vol. 35, The Journal of Hand Surgery. 2010. p. 147–52. Available from: http://dx.doi.org/10.1016/j.jhsa.2009.11.003

8. Turner JA, Franklin G, Fulton-Kehoe D, Sheppard L, Wickizer TM, Wu R, et al. Early predictors of chronic work disability associated with carpal tunnel syndrome: a longitudinal workers' compensation cohort study. Am J Ind Med. 2007 Jul;50(7):489–500.

9. Harris-Adamson C, Eisen EA, Kapellusch J, Garg A, Hegmann KT, Thiese MS, Dale AM, Evanoff B, Burt S, Bao S, Silverstein B, Merlino L, Gerr F, Rempel D. Biomechanical risk factors for carpal tunnel syndrome: a pooled study of 2474 workers. Occup Environ Med. 2015 Jan;72(1):33-41.

10. Padua L, Padua R, Lo Monaco M, Aprile I, Tonali P. Multiperspective assessment of carpal tunnel syndrome: a multicenter study. Italian CTS Study Group. Neurology.

1999 Nov 10;53(8):1654–9.

11. Bonnie RJ, Schumacher MA, Clark JD, Kesselheim AS. Pain Management and Opioid Regulation: Continuing Public Health Challenges. Am J Public Health. 2019 Jan;109(1):31–4.

12. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain. 2020 Sep 1;161(9):1976–82.

13. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychol Bull. 2007 Jul;133(4):581–624.

14. Henderson M, Kidd BL, Pearson RM, White PD. Chronic upper limb pain: an exploration of the biopsychosocial model. J Rheumatol. 2005 Jan;32(1):118–22.

15. Kuo TT, Lee MR, Liao YY, Lee WN, Hsu YW, Chen JP, et al. Assessment of median nerve mobility by ultrasound dynamic imaging in carpal tunnel syndrome diagnosis. 2013 IEEE International Ultrasonics Symposium (IUS). 2013. Available from: http://dx.doi.org/10.1109/ultsym.2013.0225

16. Uchiyama S, Itsubo T, Nakamura K, Kato H, Yasutomi T,

Momose T. Current concepts of carpal tunnel syndrome: pathophysiology, treatment, and evaluation. J Orthop Sci. 2010 Jan;15(1):1–13.

17. Erel E, Dilley A, Greening J, Morris V, Cohen B, Lynn B. Longitudinal Sliding of the Median Nerve in Patients with Carpal Tunnel Syndrome. Vol. 28, Journal of Hand Surgery. 2003. p. 439–43. Available from: http://dx.doi.org/10.1016/s0266-7681(03)00107-4

18. Schmid AB, Fundaun J, Tampin B. Entrapment neuropathies: a contemporary approach to pathophysiology, clinical assessment, and management. Pain Rep. 2020 Jul 22;5(4):e829.

19. de-la-Llave-Rincón AI, Puentedura EJ, Fernández-de-las-Peñas C. New advances in the mechanisms and etiology of carpal tunnel syndrome. Discov Med. 2012 May;13(72):343–8.

20. Fernández-de-las-Peñas C, de la Llave-Rincón AI, Fernández-Carnero J, Cuadrado ML, Arendt-Nielsen L, Pareja JA. Bilateral widespread mechanical pain sensitivity in carpal tunnel syndrome: evidence of central processing in unilateral neuropathy. Brain. 2009 Jun;132(Pt 6):1472–9.

21. Sobeeh MG, Ghozy S, Elshazli RM, Landry M. Pain mechanisms in carpal tunnel syndrome: a systematic

review and meta-analysis of quantitative sensory testing outcomes. Pain. 2022 Oct 1;163(10):e1054–94.

22. Shiri R, Pourmemari MH, Falah-Hassani K, Viikari-Juntura E. The effect of excess body mass on the risk of carpal tunnel syndrome: a meta-analysis of 58 studies. Vol. 16, Obesity Reviews. 2015. p. 1094–104. Available from: http://dx.doi.org/10.1111/obr.12324

23. Hardy M, Jimenez S, Jabaley M, Horch K. Evaluation of nerve compression with the Automated Tactile Tester. J Hand Surg Am. 1992 Sep;17(5):838–42.

24. Stevens JC, Beard CM, O'Fallon WM, Kurland LT. Conditions associated with carpal tunnel syndrome. Mayo Clin Proc. 1992 Jun;67(6):541–8.

25. Urits I, Gress K, Charipova K, Orhurhu V, Kaye AD, Viswanath O. Recent Advances in the Understanding and Management of Carpal Tunnel Syndrome: a Comprehensive Review. Vol. 23, Current Pain and Headache Reports. 2019. Available from: http://dx.doi.org/10.1007/s11916-019-0811-z

26. Louie DL, Earp BE, Collins JE, Losina E, Katz JN, Black EM, et al. Outcomes of Open Carpal Tunnel Release at a Minimum of Ten Years. Vol. 95, The Journal of Bone and Joint Surgery-American Volume. 2013. p. 1067–73. Available from: http://dx.doi.org/10.2106/jbjs.l.00903

27. Kim JK, Kim YK. Predictors of scar pain after open carpal tunnel release. J Hand Surg Am. 2011 Jun;36(6):1042–6.

28. Tadjerbashi K, Åkesson A, Atroshi I. Incidence of referred carpal tunnel syndrome and carpal tunnel release surgery in the general population: Increase over time and regional variations. Vol. 27, Journal of Orthopaedic Surgery. 2019. p. 230949901982557. Available from: http://dx.doi.org/10.1177/2309499019825572

29. Wessel LE, Gu A, Asadourian PA, Stepan JG, Fufa DT, Osei DA. The Epidemiology of Carpal Tunnel Revision Over a 1-Year Follow-Up Period. Vol. 46, The Journal of Hand Surgery. 2021. p. 758–64. Available from: http://dx.doi.org/10.1016/j.jhsa.2021.04.003

30. Rivlin M, Kachooei AR, Wang ML, Ilyas AM. Electrodiagnostic Grade and Carpal Tunnel Release Outcomes: A Prospective Analysis. J Hand Surg Am. 2018 May;43(5):425–31.

31. Chester R, Jerosch-Herold C, Lewis J, Shepstone L. Psychological factors are associated with the outcome of physiotherapy for people with shoulder pain: a multicentre longitudinal cohort study. Br J Sports Med. 2018 Feb;52(4):269–75.

32. Tseli E, Boersma K, Stålnacke BM, Enthoven P, Gerdle B, Äng BO, et al. Prognostic Factors for Physical

Functioning After Multidisciplinary Rehabilitation in Patients With Chronic Musculoskeletal Pain. Vol. 35, The Clinical Journal of Pain. 2019. p. 148–73. Available from: http://dx.doi.org/10.1097/ajp.0000000000000669

33. Innocenti T, Ristori D, Galantini P, Testa M, Bari MD. The influence of central pain modulation on postoperative outcomes after shoulder surgery: A systematic review. Acta Orthop Traumatol Turc. 2021 May;55(3):227–34.

34. Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis. Vol. 162, Pain. 2021. p. 10–30. Available from: http://dx.doi.org/10.1097/j.pain.0000000000001999

35. Leeuw M, Goossens MEJB, Linton SJ, Crombez G, Boersma K, Vlaeyen JWS. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. J Behav Med. 2007 Feb;30(1):77–94.

36. Sheikhzadeh A, Wertli MM, Weiner SS, Rasmussen-Barr E, Weiser S. Do psychological factors affect outcomes in musculoskeletal shoulder disorders? A systematic review. BMC Musculoskelet Disord. 2021 Jun 19;22(1):560.

37. Celestin J, Edwards RR, Jamison RN. Pretreatment Psychosocial Variables as Predictors of Outcomes Following Lumbar Surgery and Spinal Cord Stimulation: A

Systematic Review and Literature Synthesis. Vol. 10, Pain Medicine. 2009. p. 639–53. Available from: http://dx.doi.org/10.1111/j.1526-4637.2009.00632.x

38. Alodaibi FA, Minick KI, Fritz JM. Do preoperative fear avoidance model factors predict outcomes after lumbar disc herniation surgery? A systematic review. Chiropr Man Therap. 2013 Nov 18;21(1):40.

39. Khatib Y, Madan A, Naylor JM, Harris IA. Do Psychological Factors Predict Poor Outcome in Patients Undergoing TKA? A Systematic Review. Clin Orthop Relat Res. 2015 Aug;473(8):2630–8.

40. Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. Vol. 114, British Journal of Anaesthesia. 2015. p. 551–61. Available from: http://dx.doi.org/10.1093/bja/aeu441

41. Park JW, Gong HS, Rhee SH, Kim J, Lee YH, Baek GH. The Effect of Psychological Factors on the Outcomes of Carpal Tunnel Release: A Systematic Review. Vol. 22, The Journal of Hand Surgery (Asian-Pacific Volume). 2017. p. 131–7. Available from: http://dx.doi.org/10.1142/s0218810417300029

42. Datema M, Tannemaat MR, Hoitsma E, van Zwet EW, Smits F, van Dijk JG, et al. Outcome of Carpal Tunnel

Release and the Relation With Depression. Vol. 43, The Journal of Hand Surgery. 2018. p. 16–23. Available from: http://dx.doi.org/10.1016/j.jhsa.2017.08.020

43. Bae JY, Kim JK, Yoon JO, Kim JH, Ho BC. Preoperative predictors of patient satisfaction after carpal tunnel release. Orthop Traumatol Surg Res. 2018 Oct;104(6):907–9.

44. Fernández- de- las- Peñas C, de- la- Llave- Rincón AI, Cescon C, Barbero M, Arias- Buría JL, Falla D. Influence of Clinical, Psychological, and Psychophysical Variables on Long- term Treatment Outcomes in Carpal Tunnel Syndrome: Evidence From a Randomized Clinical Trial. Vol. 19, Pain Practice. 2019. p. 644–55. Available from: http://dx.doi.org/10.1111/papr.12788

45. Shin YH, Yoon JO, Kim YK, Kim JK. Psychological Status Is Associated With Symptom Severity in Patients With Carpal Tunnel Syndrome. Vol. 43, The Journal of Hand Surgery. 2018. p. 484.e1–484.e8. Available from: http://dx.doi.org/10.1016/j.jhsa.2017.10.031

46. Jerosch-Herold C, Shepstone L, Houghton J, Wilson ECF, Blake J. Prognostic factors for response to treatment by corticosteroid injection or surgery in carpal tunnel syndrome (palms study): A prospective multicenter cohort study. Muscle Nerve. 2019 Jul;60(1):32–40.

47. Mosegaard SB, Stilling M, Hansen TB. Higher preoperative pain catastrophizing increases the risk of low patient reported satisfaction after carpal tunnel release: a prospective study. Vol. 21, BMC Musculoskeletal Disorders. 2020. Available from: http://dx.doi.org/10.1186/s12891-020-3058-2

48. Sun PO, Walbeehm ET, Selles RW, Slijper HP, Ulrich DJO, Porsius JT, et al. Patient Mindset and the Success of Carpal Tunnel Release. Vol. 147, Plastic & Reconstructive Surgery. 2021. p. 66e – 75e. Available from: http://dx.doi.org/10.1097/prs.0000000000007441

49. Goldberg DS, McGee SJ. Pain as a global public health priority. BMC Public Health. 2011 Oct 6;11:770.

50. WHO Commission on Social Determinants of Health, World Health Organization. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health: Commission on Social Determinants of Health Final Report. World Health Organization. 2008.

51. Núñez-Cortés R, Cruz-Montecinos C, Antúnez-Riveros MA, Pérez-Alenda S. Does the educational level of women influence hand grip and pinch strength in carpal tunnel syndrome? Med Hypotheses. 2020 Feb;135:109474.

52. Axon DR, Chien J. Predictors of Mental Health Status among Older United States Adults with Pain. Behav Sci. 2021 Feb 5;11(2). Available from: http://dx.doi.org/10.3390/bs11020023

53. Fliesser M, De Witt Huberts J, Wippert PM. The choice that matters: the relative influence of socioeconomic status indicators on chronic back pain- a longitudinal study. Vol. 17, BMC Health Services Research. 2017. Available from: http://dx.doi.org/10.1186/s12913-017-2735-9

54. Karran EL, Grant AR, Lorimer Moseley G. Low back pain and the social determinants of health: a systematic review and narrative synthesis. Vol. 161, Pain. 2020. p. 2476–93. Available from: http://dx.doi.org/10.1097/j.pain.0000000000001944

55. Strube P, Schöpe T, Hölzl A, Brodt S, Matziolis G, Zippelius TK. Influence of Anxiety and Depression, Self-Rated Return-to-Work Problems, and Unemployment on the Outcome of Outpatient Rehabilitation After Shoulder Arthroscopy. Vol. 98, American Journal of Physical Medicine & Rehabilitation. 2019. p. 1118–24. Available from: http://dx.doi.org/10.1097/phm.0000000000001260

56. Prego-Domínguez J, Khazaeipour Z, Mallah N, Takkouche B. Socioeconomic status and occurrence of

chronic pain: a meta-analysis. Vol. 60, Rheumatology. 2021. p. 1091–105. Available from: http://dx.doi.org/10.1093/rheumatology/keaa758

57. Gidlow C, Johnston LH, Crone D, Ellis N, James D. A systematic review of the relationship between socio-economic position and physical activity. Health Educ J. 2006 Dec;65(4):338–67.

58. Choi KW, Chen CY, Stein MB, Klimentidis YC, Wang MJ, Koenen KC, et al. Assessment of Bidirectional Relationships Between Physical Activity and Depression Among Adults. Vol. 76, JAMA Psychiatry. 2019. p. 399. Available from: http://dx.doi.org/10.1001/jamapsychiatry.2018.4175

59. Kandola A, Ashdown-Franks G, Hendrikse J, Sabiston CM, Stubbs B. Physical activity and depression: Towards understanding the antidepressant mechanisms of physical activity. Neurosci Biobehav Rev. 2019 Dec;107:525–39.

60. Tawashy AE, Eng JJ, Lin KH, Tang PF, Hung C. Physical activity is related to lower levels of pain, fatigue and depression in individuals with spinal-cord injury: a correlational study. Spinal Cord. 2009 Apr;47(4):301–6.

61. Picardo NE, Walker H, Vanat Q, Nizar B, Madura T, Jose R. Service reconfiguration in the department of hand

surgery during the UK COVID-19 lockdown: Birmingham experience. Vol. 97, Postgraduate Medical Journal. 2021. p. 532–8. Available from: http://dx.doi.org/10.1136/postgradmedj-2020-139280

62. Karos K, McParland JL, Bunzli S, Devan H, Hirsh A, Kapos FP, et al. The social threats of COVID-19 for people with chronic pain. Pain. 2020 Oct;161(10):2229–35.

63. Fernández-de-Las Peñas C, Ortega-Santiago R, de la Llave-Rincón AI, Martínez-Perez A, Fahandezh-Saddi Díaz H, Martínez-Martín J, et al. Manual Physical Therapy Versus Surgery for Carpal Tunnel Syndrome: A Randomized Parallel-Group Trial. J Pain. 2015 Nov;16(11):1087–94.

64. Hamzeh H, Madi M, Alghwiri AA, Hawamdeh Z. The long-term effect of neurodynamics vs exercise therapy on pain and function in people with carpal tunnel syndrome: A randomized parallel-group clinical trial. J Hand Ther. 2021 Oct;34(4):521–30.

65. Horng YS, Hsieh SF, Tu YK, Lin MC, Horng YS, Wang JD. The comparative effectiveness of tendon and nerve gliding exercises in patients with carpal tunnel syndrome: a randomized trial. Am J Phys Med Rehabil. 2011 Jun;90(6):435–42.

66. Núñez-Cortés R, Cruz-Montecinos C, Torreblanca-Vargas S, Andersen LL, Tapia C, Ortega-Palavecinos M, et al. Social determinants of health and physical activity are related to pain intensity and mental health in patients with carpal tunnel syndrome. Musculoskelet Sci Pract. 2023 Feb;63:102723.

67. Turolla A, Rossettini G, Viceconti A, Palese A, Geri T. Musculoskeletal Physical Therapy During the COVID-19 Pandemic: Is Telerehabilitation the Answer? Phys Ther. 2020 Aug 12;100(8):1260–4.

68. Zhang ZY, Tian L, He K, Xu L, Wang XQ, Huang L, et al. Digital rehabilitation programs improve therapeutic exercise adherence for patients with musculoskeletal conditions: a systematic review with meta-analysis. J Orthop Sports Phys Ther. 2022 Aug 12;1–36.

69. Cifu DX, Eapen B. Telerehabilitation, An Issue of Physical Medicine and Rehabilitation Clinics of North America. Elsevier Health Sciences; 2021. 240 p.

70. Padua L, Coraci D, Erra C, Pazzaglia C, Paolasso I, Loreti C, et al. Carpal tunnel syndrome: clinical features, diagnosis, and management. Lancet Neurol. 2016 Nov;15(12):1273–84.

71. Nunez F, Vranceanu AM, Ring D. Determinants of pain in patients with carpal tunnel syndrome. Clin Orthop Relat

Res. 2010 Dec;468(12):3328–32.

72. De SD, Vranceanu AM, Ring DC. Contribution of Kinesophobia and Catastrophic Thinking to Upper-Extremity-Specific Disability. Vol. 95, Journal of Bone and Joint Surgery. 2013. p. 76–81. Available from: http://dx.doi.org/10.2106/jbjs.l.00064

73. Jerosch-Herold C, Houghton J, Blake J, Shaikh A, Wilson EC, Shepstone L. Association of psychological distress, quality of life and costs with carpal tunnel syndrome severity: a cross-sectional analysis of the PALMS cohort. BMJ Open. 2017 Nov 3;7(11):e017732.

74. The Lancet. UK life science research: time to burst the biomedical bubble. Lancet. 2018 Jul 21;392(10143):187.

75. Moseley GL, Butler DS. Fifteen Years of Explaining Pain: The Past, Present, and Future. J Pain. 2015 Sep;16(9):807–13.

76. Louw A, Zimney K, Puentedura EJ, Diener I. The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. Physiother Theory Pract. 2016 Jul;32(5):332–55.

77. Siddall B, Ram A, Jones MD, Booth J, Perriman D, Summers SJ. Short-term impact of combining pain neuroscience education with exercise for chronic

musculoskeletal pain: a systematic review and meta-analysis. Pain. 2022 Jan 1;163(1):e20–30.

78. Watson JA, Ryan CG, Cooper L, Ellington D, Whittle R, Lavender M, et al. Pain Neuroscience Education for Adults With Chronic Musculoskeletal Pain: A Mixed-Methods Systematic Review and Meta-Analysis. J Pain. 2019 Oct;20(10):1140.e1–1140.e22.

79. Daenen L, Varkey E, Kellmann M, Nijs J. Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice. Clin J Pain. 2015 Feb;31(2):108–14.

80. Taulaniemi A, Kankaanpää M, Rinne M, Tokola K, Parkkari J, Suni JH. Fear-avoidance beliefs are associated with exercise adherence: secondary analysis of a randomised controlled trial (RCT) among female healthcare workers with recurrent low back pain. BMC Sports Sci Med Rehabil. 2020 May 4;12:28.

81. Henning M, Smith M. The ability of physiotherapists to identify psychosocial factors in patients with musculoskeletal pain: A scoping review. Musculoskeletal Care. 2022 Dec 23; Available from: http://dx.doi.org/10.1002/msc.1725

82. Murillo C, Galán-Martín MÁ, Montero-Cuadrado F, Lluch E, Meeus M, Loh WW. Reductions in kinesiophobia and

distress after pain neuroscience education and exercise lead to favourable outcomes: a secondary mediation analysis of a randomized controlled trial in primary care. Pain 2023. doi:10.1097/j.pain.0000000000002929.

83. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010 Feb 18;8(5):336–41.

84. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000 Apr 19;283(15):2008–12.

85. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016 Dec 5;5(1):210.

86. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med. 2013 Feb 19;158(4):280–6.

87. R Core Team. 2017 R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. See http:// www.R-project.org/.

88. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR.

Introduction to Meta- Analysis. 2009. Available from: http://dx.doi.org/10.1002/9780470743386

89. Viechtbauer W. Conducting Meta-Analyses in*R*with the**metafor**Package. Vol. 36, Journal of Statistical Software. 2010. Available from: http://dx.doi.org/10.18637/jss.v036.i03

90. Cohen J. A power primer. Methodological issues and strategies in clinical research (4th ed.). p. 279–84. Available from: http://dx.doi.org/10.1037/14805-018

91. Higgins JPT, Thomas J. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons; 2019. 728 p.

92. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014 Dec;12(12):1495–9.

93. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020 Dec;54(24):1451–62.

94. Kahl C, Cleland JA. Visual analogue scale, numeric pain

rating scale and the McGill pain Questionnaire: an overview of psychometric properties. Vol. 10, Physical Therapy Reviews. 2005. p. 123–8. Available from: http://dx.doi.org/10.1179/108331905x55776

95. Ceceli E, Gumruk S, Okumus M, Kocaoglu S, Goksu H, Karagoz A. Comparison of 2 methods of neuropathic pain assessment in carpal tunnel syndrome and hand functions. Neurosciences. 2018 Jan;23(1):23–8.

96. Herrero MJ, Blanch J, Peri JM, De Pablo J, Pintor L, Bulbena A. A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. Gen Hosp Psychiatry. 2003 Jul;25(4):277–83.

97. García Campayo J, Rodero B, Alda M, Sobradiel N, Montero J, Moreno S. [Validation of the Spanish version of the Pain Catastrophizing Scale in fibromyalgia]. Med Clin . 2008 Oct 18;131(13):487–92.

98. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. Vol. 7, Psychological Assessment. 1995. p. 524–32. Available from: http://dx.doi.org/10.1037/1040-3590.7.4.524

99. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2012;10(1):28–55.

100. Hoffman MD, Hoffman DR. Does aerobic exercise improve pain perception and mood? A review of the evidence related to healthy and chronic pain subjects. Vol. 11, Current Pain and Headache Reports. 2007. p. 93–7. Available from: http://dx.doi.org/10.1007/s11916-007-0004-z

101. Shem K, Wong J, Dirlikov B. Effective self-stretching of carpal ligament for the treatment of carpal tunnel syndrome: A double-blinded randomized controlled study. J Hand Ther. 2020 Jul;33(3):272–80.

102. Butler DS, Lorimer Moseley G. Explain Pain 2nd Edn. Noigroup Publications; 2013. 133 p.

103. Ziegler AM, Minkalis AL, Langdon ER, Vining R. Learning the neurobiology of pain: A scoping review of pain education from an instructional design perspective. Patient Educ Couns. 2022 Jun;105(6):1379–401.

104. Jordan PW, Thomas B, McClelland IL, Weerdmeester B. Usability Evaluation In Industry. CRC Press; 1996. 252 p.

105. Bangor A, Kortum PT, Miller JT. An Empirical Evaluation of the System Usability Scale. Vol. 24, International Journal of Human-Computer Interaction. 2008. p. 574–94. Available from: http://dx.doi.org/10.1080/10447310802205776

106. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005 Jan;113(1-2):9–19.

107. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008 Feb;9(2):105–21.

108. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychol Assess. 1995;7(4):524–32.

109. Gómez-Pérez L, López-Martínez AE, Ruiz-Párraga GT. Psychometric Properties of the Spanish Version of the Tampa Scale for Kinesiophobia (TSK). J Pain. 2011 Apr;12(4):425–35.

110. Hapidou EG, O'Brien MA, Pierrynowski MR, de Las Heras E, Patel M, Patla T. Fear and Avoidance of Movement in People with Chronic Pain: Psychometric Properties of the 11-Item Tampa Scale for Kinesiophobia (TSK-11). Physiother Can. 2012 Summer;64(3):235–41.

111. Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status

in carpal tunnel syndrome. Vol. 75, The Journal of Bone & Joint Surgery. 1993. p. 1585–92. Available from: http://dx.doi.org/10.2106/00004623-199311000-00002

112. Kim JK, Jeon SH. Minimal clinically important differences in the Carpal Tunnel Questionnaire after carpal tunnel release. J Hand Surg Eur Vol. 2013 Jan;38(1):75–9.

113. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983 Jun;67(6):361–70.

114. Lemay KR, Tulloch HE, Pipe AL, Reed JL. Establishing the Minimal Clinically Important Difference for the Hospital Anxiety and Depression Scale in Patients With Cardiovascular Disease. J Cardiopulm Rehabil Prev. 2019 Nov;39(6):E6–11.

115. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy. 1990 Dec;16(3):199–208.

116. Perrot S, Lantéri-Minet M. Patients' Global Impression of Change in the management of peripheral neuropathic pain: Clinical relevance and correlations in daily practice. Eur J Pain. 2019 Jul;23(6):1117–28.

117. Bodes Pardo G, Lluch Girbés E, Roussel NA, Gallego Izquierdo T, Jiménez Penick V, Pecos Martín D. Pain

Neurophysiology Education and Therapeutic Exercise for Patients With Chronic Low Back Pain: A Single-Blind Randomized Controlled Trial. Arch Phys Med Rehabil. 2018 Feb;99(2):338-347.

118. Hobby JL, Venkatesh R, Motkur P. The effect of psychological disturbance on symptoms, self-reported disability and surgical outcome in carpal tunnel syndrome. J Bone Joint Surg Br. 2005 Feb;87(2):196–200.

119. Lozano Calderón SA, Paiva A, Ring D. Patient satisfaction after open carpal tunnel release correlates with depression. J Hand Surg Am. 2008 Mar;33(3):303–7.

120. Kim JK, Kim YK. Predictors of scar pain after open carpal tunnel release. J Hand Surg Am. 2011 Jun;36(6):1042–6.

121. Becker SJE, Makanji HS, Ring D. Expected and actual improvement of symptoms with carpal tunnel release. J Hand Surg Am. 2012 Jul;37(7):1324–9.e1–5.

122. Cowan J, Makanji H, Mudgal C, Jupiter J, Ring D. Determinants of return to work after carpal tunnel release. J Hand Surg Am. 2012 Jan;37(1):18–27.

123. Datema M, Tannemaat MR, Hoitsma E, van Zwet EW, Smits F, van Dijk JG, et al. Outcome of Carpal Tunnel Release and the Relation With Depression. J Hand Surg

Am. 2018 Jan;43(1):16–23.

124. Shin YH, Yoon JO, Kim YK, Kim JK. Psychological Status Is Associated With Symptom Severity in Patients With Carpal Tunnel Syndrome. J Hand Surg Am. 2018 May;43(5):484.e1–484.e8.

125. Fernández-de-Las-Peñas C, de-la-Llave-Rincón AI, Cescon C, Barbero M, Arias-Buría JL, Falla D. Influence of Clinical, Psychological, and Psychophysical Variables on Long-term Treatment Outcomes in Carpal Tunnel Syndrome: Evidence From a Randomized Clinical Trial. Pain Pract. 2019 Jul;19(6):644–55.

126. Mosegaard SB, Stilling M, Hansen TB. Higher preoperative pain catastrophizing increases the risk of low patient reported satisfaction after carpal tunnel release: a prospective study. BMC Musculoskelet Disord. 2020 Jan 18;21(1):42.

127. Katz JN, Losina E, Amick BC 3rd, Fossel AH, Bessette L, Keller RB. Predictors of outcomes of carpal tunnel release. Arthritis Rheum. 2001 May;44(5):1184–93.

128. Amick BC 3rd, Habeck RV, Ossmann J, Fossel AH, Keller R, Katz JN. Predictors of successful work role functioning after carpal tunnel release surgery. J Occup Environ Med. 2004 May;46(5):490–500.

129. Katz JN, Amick BC 3rd, Keller R, Fossel AH, Ossman J, Soucie V, et al. Determinants of work absence following surgery for carpal tunnel syndrome. Am J Ind Med. 2005 Feb;47(2):120–30.

130. Sun PO, Walbeehm ET, Selles RW, Slijper HP, Ulrich DJO, Porsius JT, et al. Patient Mindset and the Success of Carpal Tunnel Release. Plast Reconstr Surg. 2021 Jan 1;147(1):66e – 75e.

131. Wood L, Hendrick PA. A systematic review and meta-analysis of pain neuroscience education for chronic low back pain: Short-and long-term outcomes of pain and disability. Eur J Pain. 2019 Feb;23(2):234–49.

132. Tegner H, Frederiksen P, Esbensen BA, Juhl C. Neurophysiological Pain Education for Patients With Chronic Low Back Pain: A Systematic Review and Meta-Analysis. Clin J Pain. 2018 Aug;34(8):778–86.

133. Bülow K, Lindberg K, Vaegter HB, Juhl CB. Effectiveness of Pain Neurophysiology Education on Musculoskeletal Pain: A Systematic Review and Meta-Analysis. Pain Med. 2021 Apr 20;22(4):891–904.

134. Sobol-Kwapinska M, Bąbel P, Plotek W, Stelcer B. Psychological correlates of acute postsurgical pain: A systematic review and meta-analysis. Eur J Pain. 2016 Nov;20(10):1573–86.

135. Theunissen M, Peters ML, Bruce J, Gramke HF, Marcus MA. Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with chronic postsurgical pain. Clin J Pain. 2012 Nov;28(9):819–41.

136. Celestin J, Edwards RR, Jamison RN. Pretreatment psychosocial variables as predictors of outcomes following lumbar surgery and spinal cord stimulation: a systematic review and literature synthesis. Pain Med. 2009 May;10(4):639–53.

137. Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. Br J Anaesth. 2015 Apr;114(4):551–61.

138. Gong HS, Baek GH, Oh JH, Lee YH, Jeon SH, Chung MS. Factors affecting willingness to undergo carpal tunnel release. J Bone Joint Surg Am. 2009 Sep;91(9):2130–6.

139. Ingram J, Mauck BM, Thompson NB, Calandruccio JH. Cost, Value, and Patient Satisfaction in Carpal Tunnel Surgery. Orthop Clin North Am. 2018 Oct;49(4):503–7.

140. Loisel P, Durand MJ, Berthelette D, V??zina N, Baril R, Gagnon D, et al. Disability Prevention. Vol. 9, Disease Management and Health Outcomes. 2001. p. 351–60. Available from: http://dx.doi.org/10.2165/00115677-

200109070-00001

141. Schwartz AM, Wilson JM, Farley KX, Roberson JR, Guild GN, Bradbury TL. Modifiability of Depression's Impact on Early Revision, Narcotic Usage, and Outcomes After Total Hip Arthroplasty: The Impact of Psychotherapy. Vol. 35, The Journal of Arthroplasty. 2020. p. 2904–10.

142. Wang L, Chang Y, Kennedy SA, Hong PJ, Chow N, Couban RJ, et al. Perioperative psychotherapy for persistent post-surgical pain and physical impairment: a meta-analysis of randomised trials. Vol. 120, British Journal of Anaesthesia. 2018. p. 1304–14. Available from: http://dx.doi.org/10.1016/j.bja.2017.10.026

143. Patel A, Culbertson MD, Patel A, Hashem J, Jacob J, Edelstein D, et al. The negative effect of carpal tunnel syndrome on sleep quality. Sleep Disord. 2014 Feb 17;2014:962746.

144. Kadzielski J, Malhotra LR, Zurakowski D, Lee SGP, Jupiter JB, Ring D. Evaluation of preoperative expectations and patient satisfaction after carpal tunnel release. J Hand Surg Am. 2008 Dec;33(10):1783–8.

145. Núñez-Cortés R, Espinoza-Ordóñez C, Pommer PP, Horment-Lara G, Pérez-Alenda S, Cruz-Montecinos C. A single preoperative pain neuroscience education: Is it an effective strategy for patients with carpal tunnel

syndrome? Med Hypotheses. 2019 May;126:46–50.

146. Peters S, Page MJ, Coppieters MW, Ross M, Johnston V. Rehabilitation following carpal tunnel release. Cochrane Database Syst Rev. 2016 Feb 17;2:CD004158.

147. Polaski AM, Phelps AL, Kostek MC, Szucs KA, Kolber BJ. Exercise-induced hypoalgesia: A meta-analysis of exercise dosing for the treatment of chronic pain. PLoS One. 2019 Jan 9;14(1):e0210418.

148. Naugle KM, Riley JL 3rd. Self-reported physical activity predicts pain inhibitory and facilitatory function. Med Sci Sports Exerc. 2014 Mar;46(3):622–9.

149. Jiang X, Sandberg MEC, Saevarsdottir S, Klareskog L, Alfredsson L, Bengtsson C. Higher education is associated with a better rheumatoid arthritis outcome concerning for pain and function but not disease activity: results from the EIRA cohort and Swedish rheumatology register. Vol. 17, Arthritis Research & Therapy. 2015.

150. Goodman SM, Mandl LA, Mehta B, Navarro-Millan I, Russell LA, Parks ML, et al. Does Education Level Mitigate the Effect of Poverty on Total Knee Arthroplasty Outcomes?. Vol. 70, Arthritis Care & Research. 2018. p. 884–91.

151. Palmlöf L, Skillgate E, Alfredsson L, Vingård E,

Magnusson C, Lundberg M, et al. Does income matter for troublesome neck pain? A population-based study on risk and prognosis. J Epidemiol Community Health. 2012 Nov;66(11):1063–70.

152. Whitley MD, Herman PM, Aliyev GR, Sherbourne CD, Ryan GW, Coulter ID. Income as a Predictor of Self-Efficacy for Managing Pain and for Coping With Symptoms Among Patients With Chronic Low Back Pain. J Manipulative Physiol Ther. 2021 Aug 29;44(6):433–44.

153. Choi KW, Chen CY, Stein MB, Klimentidis YC, Wang MJ, Koenen KC, et al. Assessment of Bidirectional Relationships Between Physical Activity and Depression Among Adults: A 2-Sample Mendelian Randomization Study. JAMA Psychiatry. 2019 Apr 1;76(4):399–408.

154. Phillips C. Brain-Derived Neurotrophic Factor, Depression, and Physical Activity: Making the Neuroplastic Connection. Neural Plast. 2017 Aug 8;2017:7260130.

155. Heyman E, Gamelin FX, Goekint M, Piscitelli F, Roelands B, Leclair E, et al. Intense exercise increases circulating endocannabinoid and BDNF levels in humans—Possible implications for reward and depression. Vol. 37, Psychoneuroendocrinology. 2012. p. 844–51.

156. Mammen G, Faulkner G. Physical activity and the

prevention of depression: a systematic review of prospective studies. Am J Prev Med. 2013 Nov;45(5):649–57.

157. Paul KI, Moser K. Unemployment impairs mental health: Meta-analyses. Vol. 74, Journal of Vocational Behavior. 2009. p. 264–82.

158. Suzuki H, Aono S, Inoue S, Imajo Y, Nishida N, Funaba M, et al. Clinically significant changes in pain along the Pain Intensity Numerical Rating Scale in patients with chronic low back pain. PLoS One. 2020 Mar 3;15(3):e0229228.

159. Bernardini F, Attademo L, Rotter M, Compton MT. Social Determinants of Mental Health As Mediators and Moderators of the Mental Health Impacts of the COVID-19 Pandemic. Psychiatr Serv. 2021 May 1;72(5):598–601.

160. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. Brain Behav Immun. 2020 Oct;89:531–42.

161. Wilson JM, Lee J, Fitzgerald HN, Oosterhoff B, Sevi B, Shook NJ. Job Insecurity and Financial Concern During the COVID-19 Pandemic Are Associated With Worse Mental Health. J Occup Environ Med. 2020

Sep;62(9):686–91.

162. Campo-Arias A, De Mendieta CT. Social determinants of mental health and the COVID-19 pandemic in low-income and middle-income countries. Lancet Glob Health. 2021 Aug;9(8):e1029–30.

163. Pourmemari MH, Heliövaara M, Viikari-Juntura E, Shiri R. Carpal tunnel release: Lifetime prevalence, annual incidence, and risk factors. Muscle Nerve. 2018 Oct;58(4):497–502.

164. Malfliet A, Kregel J, Coppieters I, De Pauw R, Meeus M, Roussel N, et al. Effect of Pain Neuroscience Education Combined With Cognition-Targeted Motor Control Training on Chronic Spinal Pain: A Randomized Clinical Trial. JAMA Neurol. 2018 Jul 1;75(7):808–17.

165. Amer-Cuenca JJ, Pecos-Martín D, Martínez-Merinero P, Lluch Girbés E, Nijs J, Meeus M, et al. How Much Is Needed? Comparison of the Effectiveness of Different Pain Education Dosages in Patients with Fibromyalgia. Pain Med. 2020 Apr 1;21(4):782–93.

166. Tseli E, Boersma K, Stålnacke BM, Enthoven P, Gerdle B, Äng BO, et al. Prognostic Factors for Physical Functioning After Multidisciplinary Rehabilitation in Patients With Chronic Musculoskeletal Pain: A Systematic Review and Meta-Analysis. Clin J Pain. 2019

Feb;35(2):148–73.

167. Chimenti RL, Post AA, Rio EK, Moseley GL, Dao M, Mosby H, et al. The effects of pain science education plus exercise on pain and function in chronic Achilles tendinopathy: a blinded, placebo-controlled, explanatory, randomized trial. Pain. 2023 Jan 1;164(1):e47–65.

168. Barrenengoa-Cuadra MJ, Muñoa-Capron-Manieux M, Fernández-Luco M, Angón-Puras LÁ, Romón-Gómez AJ, Azkuenaga M, et al. Effectiveness of a structured group intervention based on pain neuroscience education for patients with fibromyalgia in primary care: A multicentre randomized open-label controlled trial. Eur J Pain. 2021 May;25(5):1137–49.

169. Núñez-Cortés R, Cruz-Montecinos C, Torres-Castro R, Tapia C, Püschel TA, Pérez-Alenda S. Effects of Cognitive and Mental Health Factors on the Outcomes Following Carpal Tunnel Release: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil. 2021 Nov 30;

170. Serrat M, Sanabria-Mazo JP, Almirall M, Musté M, Feliu-Soler A, Méndez-Ulrich JL, et al. Effectiveness of a Multicomponent Treatment Based on Pain Neuroscience Education, Therapeutic Exercise, Cognitive Behavioral Therapy, and Mindfulness in Patients With Fibromyalgia (FIBROWALK Study): A Randomized Controlled Trial.

Phys Ther. 2021 Dec 1;101(12).

171. Das De S, Vranceanu AM, Ring DC. Contribution of kinesophobia and catastrophic thinking to upper-extremity-specific disability. J Bone Joint Surg Am. 2013 Jan 2;95(1):76–81.

172. Wright MA, Beleckas CM, Calfee RP. Mental and Physical Health Disparities in Patients With Carpal Tunnel Syndrome Living With High Levels of Social Deprivation. J Hand Surg Am. 2019 Apr;44(4):335.e1–335.e9.

173. Bernstein DN, Kurucan E, Fear K, Hammert WC. Evaluating the Impact of Patient Social Deprivation on the Level of Symptom Severity at Carpal Tunnel Syndrome Presentation. Hand. 2022 Mar;17(2):339–45.

174. Núñez-Cortés R, Espin A, Pérez-Alenda S, López-Bueno R, Cruz-Montecinos C, Vincents-Seeberg KG, Püschel TA, Calatayud J, Andersen LL. Association between pain coping and symptoms of anxiety and depression, and work absenteeism in people with upper limb musculoskeletal disorders: A systematic review and meta-analysis. Arch Phys Med Rehabil. 2023 Jul 23:S0003-9993(23)00409-4.

7. Appendix

ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2022;103: 1615–27

REVIEW ARTICLE (META-ANALYSIS)

Effects of Cognitive and Mental Health Factors on the Outcomes Following Carpal Tunnel Release: A Systematic Review and Meta-analysis

Rodrigo Núñez-Cortés, PT, MSc,[a,b,c] Carlos Cruz-Montecinos, PT, MSc,[a,b,d] Rodrigo Torres-Castro, PT, MSc,[b,c] Claudio Tapia, PT, PhD,[b] Thomas A. Püschel, PhD,[e,f] Sofía Pérez-Alenda, PT, PhD[a]

From the [a]Department of Physiotherapy, Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), University of Valencia, Valencia, Spain; [b]Department of Physical Therapy, Faculty of Medicine, University of Chile, Santiago, Chile; [c]International Physiotherapy Research Network (PhysioEvidence), Barcelona, Spain; [d]Division of Research, Devolvement and Innovation in Kinesiology, Kinesiology Unit, San José Hospital, Santiago, Chile; [e]Ecology and Evolutionary Biology Division, School of Biological Sciences, University of Reading, Reading, United Kingdom; and [f]Primate Models for Behavioural Evolution Lab, Institute of Cognitive and Evolutionary Anthropology, School of Anthropology, University of Oxford, Oxford, United Kingdom.

Abstract

Objective: To determine the effects of the cognitive and mental health factors on the outcomes after carpal tunnel release (CTR).

Data Sources: Embase, PubMed/MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health, and Cochrane Central Register of Controlled Trials databases from inception to August 14, 2021.

Study Selection: Randomized controlled trials and observational studies of patients with CTR were included. The included studies aimed to determine the effect of the cognitive (catastrophic thinking, kinesiophobia, self-efficacy) or mental health factors (symptoms of anxiety and depression) on the outcomes at least 3 months post CTR.

Data Extraction: Two independent reviewers performed data extraction and assessed the risk of bias. Data were extracted using a standardized protocol and reporting forms. The risk of bias of the included studies was assessed using the Quality in Prognosis Studies risk-of-bias tool. Random-effects models were used for meta-analysis.

Data Synthesis: A total of 15 studies involving 2599 patients were included in this systematic review. The majority of studies indicate a significant association between the cognitive or mental health factors and outcomes after CTR. Quantitative analysis showed a moderate association of symptoms of depression on symptom severity (n=531; r=0.347; 95% CI, 0.205-0.475; $P \leq .0001$), function (n=386; r=0.307; 95% CI, 0.132-0.464; P=.0008), and pain (n=344; r=0.431; 95% CI, 0.286-0.558; $P \leq .0001$). In general, the risk of bias in the included studies was low.

Conclusions: This systematic review and meta-analysis showed that symptoms of depression have a moderate association with symptom severity, function, and pain after CTR. Symptoms of anxiety, catastrophic thinking, and self-efficacy are also important indicators of poor postsurgery outcomes. Physicians, physical therapists, and occupational therapists should consider evaluating these variables in patients undergoing CTR.

Archives of Physical Medicine and Rehabilitation 2022;103:1615–27

Introduction

Carpal tunnel syndrome (CTS) is the most prevalent compression neuropathy of the upper limb,[1] characterized by pain, paresthesia, and a tingling sensation in the region of the median nerve.[2] These symptoms cause significant functional impairment,[3] affecting the quality of life of the patient.[4] The prevalence of CTS ranges between

PROSPERO Registration No.: CRD42020181709.

Disclosures: R. Núñez-Cortés is funded by a grant from the National Agency for Research and Development (ANID)/Scholarship Program/DOCTORADO BECAS CHILE/2020–72210026. The other authors have nothing to disclose.

0003-9993/$36 - see front matter © 2021 by the American Congress of Rehabilitation Medicine. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)
https://doi.org/10.1016/j.apmr.2021.10.026

6.3% and 11.7%,[5] being more frequent in women than in men.[6] It is estimated that 65% of people diagnosed as having CTS eventually require surgery, and the incidence of carpal tunnel release (CTR) per 100,000 person-years is 151 in women and 65 in men.[7]

CTR is one of the most common operations performed on the upper limb, with a lifetime prevalence of 3.1%,[8] representing a considerable expense for healthcare systems.[9] CTR is indicated primarily in patients who do not respond to conservative treatment, in acute cases (eg, trauma), and in severe cases with persistent hypoesthesia of the median nerve region and motor impairment.[10] While most patients improve after surgery,[11] approximately 5% of patients report persistent symptoms and require revision CTR within the first postoperative year.[12] The unfavorable outcome after CTR may also be because of pain related to the surgical scar, which may be affected by depressive symptoms.[13,14]

In musculoskeletal diseases, identified cognitive (catastrophic thinking, kinesiophobia, self-efficacy, fear avoidance) and mental health factors (symptoms of anxiety and depression) have been reported to be relevant to optimizing the postsurgical outcomes. For instance, the patient's cognitions and emotions may affect the recovery and response to treatment in patients with chronic musculoskeletal pain.[15,16] In this context, the fear avoidance model proposes that patients with catastrophic cognitions about pain tend to interpret certain experiences as a threat, avoiding select activities and developing disuse, disability, and depression.[17]

We can find a heterogeneous set of predictors related to emotions, cognitions, and coping strategies within the cognitive and mental health factors. Among them, catastrophizing, self-efficacy, fear related to pain, depression, and anxiety have taken on greater relevance in the last few decades because of their strong relationship with postsurgical pain and function.[18,19] Previous systematic reviews have shown that these factors are associated with poorer postoperative outcomes in shoulder surgery,[18,20] spine surgery,[19,21,22,] and knee replacements.[19,23,24] However, the relevance of cognitive and mental health factors as prognostic indicators of recovery to CTR is controversial.[25]

There is a growing literature supporting the role of modifiable cognitive and mental health factors in CTR.[14,26-31] However, the assessment of these factors has not been taken into account in the recent clinical practice guidelines for patients with CTS[32] when most of the patients may end up needing surgery.[7] A better understanding of the association between cognitive and mental health factors and the surgery results could also help to provide more specialized interventions, including the expertise of psychologists, physical therapists, occupational therapists, and physicians in the perioperative and postoperative period. In addition, the economic costs associated with mental health disorders and postoperative pain reinforce the need to examine these risk factors closely with a rigorous narrative approach and a quantitative synthesis of the available evidence. This systematic review and meta-analysis aims to determine the effects of the chosen cognitive and mental health factors on the outcomes after CTR, 3 months after surgery, and beyond.

List of abbreviations:

BCTQ-F	**Boston Carpal Tunnel Questionnaire score-function**
BCTQ-S	**Boston Carpal Tunnel Questionnaire score-symptoms**
BDI-II	**Beck Depression Inventory II**
CES-D	**Center of Epidemiologic Studies-Depression scale**
CTS	**Carpal tunnel syndrome**
CTS-6	**6-item shortened Boston Carpal Tunnel Questionnaire**
CTR	**Carpal tunnel release**
DASH	**Disabilities of the Arm, Shoulder, and Hand**
HADS	**Hospital anxiety and depression scale**
MHI-5	**5-item mental health index**
PASS	**Pain Anxiety Symptoms Scale**
PCS	**Pain Catastrophizing Scale**
PHQ-4	**Patient Health Questionnaire-4**
PEM	**Patient evaluation measure**
RCT	**randomized controlled trial**

Methods

Protocols and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysesguidelines.[33] The meta-analysis was conducted according to the Meta-analysis of Observational Studies in Epidemiology.[34] The protocol was previously registered on the International Prospective Register of Systematic Reviews PROSPERO (CRD42020181709) in July 2020.

Criteria for considering studies in this review

Randomized controlled trials and observational studies (cross-sectional, longitudinal, case-control, cohort) of patients with CTR (open or endoscopic surgery) were included. The included studies aimed to determine the effect of the chosen cognitive or mental health factors on the outcomes at least 3 months post CTR. The cognitive factors related to pain (ie, catastrophic thinking, kinesiophobia, self-efficacy, fear avoidance) and mental health factors (ie, symptoms of anxiety and depression) should have been assessed using an objective measure. Therefore, we included studies with at least 1 of the following prognostic factors: (1) catastrophic thinking, measured by the Pain Catastrophizing Scale[35]; (2) kinesiophobia, measured by the Tampa Scale of Kinesiophobia[36]; (3) self-efficacy, measured by Self-Efficacy Scale[37]; (4) fear avoidance, measured by Fear Avoidance and Beliefs Questionnaire[38]; (5) symptoms of anxiety, measured by the Hospital Anxiety and Depression Scale[39] or the Pain Anxiety Symptoms Scale[40]; (6) symptoms of depression, measured by the Hospital Anxiety and Depression Scale,[39] Center for Epidemiologic Studies Depression Scale,[41] Beck Depression Inventory II,[42] 5-item Mental Health Inventory,[43] or Patient Health Questionnaire-4.[44]

On the other hand, studies with at least one of the following outcomes after surgery were included: (1) functional limitations and symptoms, measured by a patient-reported scoring systems such as the Boston Carpal Tunnel Questionnaire[45] or similar, 6-item shortened Boston Carpal Tunnel Questionnaire,[46] Disabilities of the Arm, Shoulder, and Hand,[47] Quick−Disabilities of the Arm, Shoulder, and Hand,[48] and the Michigan Hand Questionnaire[49]; (2) pain intensity, measured by a visual analog scale, numeric rating scale, or another numeric ordinal rating scale; (3) patient satisfaction, measured by a satisfaction score (Likert scale or by categorical grading); (4) work participation, measured as return to work, absenteeism, or time on benefits; and (5) physical measures of recovery, including grip and pinch strengths and range of motion. We included studies in any language published between January 1950 and August 2021. All editorials, letters to the editor, review articles, systematic reviews, meta-analyses, and in vivo and in vitro studies were excluded.

Search strategy

A systematic review of the literature was conducted to identify the studies that investigate the effect of the chosen cognitive and mental health factors on the outcomes after CTR. We reviewed the Embase, PubMed/MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health, and Cochrane Central Register of Controlled Trials databases from inception to August 14, 2021. Manual searches with the followings terms were performed: (1) for population: carpal tunnel release OR carpal tunnel decompression OR ([carpal tunnel syndrome OR median neuropathy] AND [surgery OR postoperative OR post-operative OR postsurgical OR post-surgical]); (2) for exposition: psychological OR anxiety OR fear OR avoidance OR depression OR depress* OR mood OR catastrophizing OR catastrophic thinking OR self-efficacy OR kinesiophobia OR emotional OR coping; (3) for condition: association* OR predict* OR "risk factor*" OR determinant* OR prognos*; and (4) for main outcome: symptom severity OR disability OR pain OR patient reported outcome measures OR recovery of function OR range of motion, articular OR hand strength OR hand grip OR patient satisfaction OR return to work. The terms selected were combined using Boolean logical operators (OR, AND, NOT). We supplemented our search with the reference lists of all included studies to identify potentially relevant articles from other sources. All references were analyzed using the Rayyan web software.[50]

Reviewing procedure and data extraction

First, the titles and abstracts of all identified studies were reviewed by 2 investigators (R.N.C., C.C.M.). The irrelevant references were removed. Any disagreements were solved by consensus. Second, the full-text versions of the articles selected in the first stage were read and checked against the eligibility criteria (R.N.C., C.C.M.). Any disagreements were solved by a third reviewer (R.T.C.).

Then, 2 investigators (R.N.C., C.T.) extracted the data independently using a standardized protocol and reporting forms. The following information was extracted from each included study: design, population characteristics, type of surgery, follow-up time, prognostic factor, postoperative outcomes, results of univariate analysis, and results of multivariate analysis. The authors were contacted to obtain the information if some relevant data were not included in the study.

Methodological quality assessment

The risk of bias in the included studies was assessed using the Quality in Prognosis Studies risk-of-bias tool.[51] We classified the studies as high, moderate, or low risk in relation to the domains of study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. The low risk of bias was assigned only if the majority (≥75%) of the prompting items were satisfied, moderate risk of bias if 50%-74% of the prompting items were satisfied, and a high risk of bias if ≤50% of the prompting items were satisfied. Two authors carried out this evaluation independently (R.N.C., R.T.C.), and discrepancies were resolved by consensus. The concordance was calculated using Cohen's kappa coefficient. The Robvis tool[52] was used to create risk of bias assessment plots.

Quantitative synthesis

The meta-analyses were performed in R v. 4.0.2.[53] For the quantitative synthesis, the prognostic factors that were evaluated by 3 or more studies were considered to avoid performing low-power analyses. Studies that operationalized the risk factor in a markedly different way than most other studies were excluded from the estimate. The quantitative synthesis was carried out in the following steps: (1) The original data (eg, correlations, regression coefficients, odds ratios) were converted to Pearson r using standard formulas.[54] To maintain consistency, the associations were recalculated so that they were in the same direction. (2) The data were converted into Fisher z using the escalc() function from the "metafor" v. 3.0-2 R package.[55] (3) Four different random-effects models were fitted to synthesize the quantitative results of the published studies for each one the effect sizes under study (ie, correlational data on prognostic factors and postoperative results). This kind of model was preferred because it accounts for study heterogeneity and does not assume that all studies come from a single common population that were tested under identical or quite similar conditions.[56] These models were computed using the rma() function from the same package (ie, " metafor" v. 3.0-2). (4) The result of each meta-analysis was transformed back into Pearson r for final interpretation. The effect size magnitude of r can be interpreted as follows: r=0.1, small; r=0.3, moderate; and r=0.5, large.[57] Statistical heterogeneity was assessed using I^2 and classified as might not be important (I^2=0%-40%), moderate (I^2=30%-60%), substantial (I^2=50%-90%), or considerable (I^2=75%-100%).[58] Forest plots were generated as a way to visualize the effect sizes and CIs from the considered studies, along with the computed summary effect size. These plots were produced using the forest() function also available as part of the " metafor" v. 3.0-2 R package.

Results

The initial search identified 247 potential studies through electronic databases. In addition, 466 potential studies were identified by reference screening. In total, 251 duplicate studies were eliminated, and 429 were excluded in the screening stage by their title and abstract. Thirty-three studies were assessed as full texts. Of these, 10 studies were excluded for having the wrong study design, 3 for being the wrong publication type, 2 for involving the wrong population, and 3 for having the wrong outcome. Finally, 15 studies were included in this review (fig 1).[13,14,26-31,59-65] We observed a very high concordance between the reviewers when selecting the studies (kappa=0.942, P<.001).

Study characteristics

The studies were conducted in the United States (6 studies),[60-65] South Korea (3),[13,26,27] the United Kingdom (2),[29,59] the Netherlands (2),[14,31] Spain (1),[28] and Denmark (1).[30] All of the included studies were written in English. Seven studies (47%) were published less than 5 years ago (after 2016).[14,26-31] The designs of the studies included 1 randomized controlled trial,[28] 12 prospectives,[13,14,27,29-31,59,61-65] and 2 retrospectives.[26,60] The sample sizes varied between 60 participants[26-28] and 455 participants.[29] A total of 2599 patients were included, with a mean age that varied between 46±9 and 62±12 years. Eight studies included open CTR,[13,14,26,27,31,60-62] and 5 studies included open and endoscopic CTR,[28,30,63-65] while 2 studies did not report the type of surgery.[29,59] The total time of the follow-up ranged from 3 months[13,26,27] after CTR to 2 years.[60] Table 1 is the descriptive summary of the included studies.

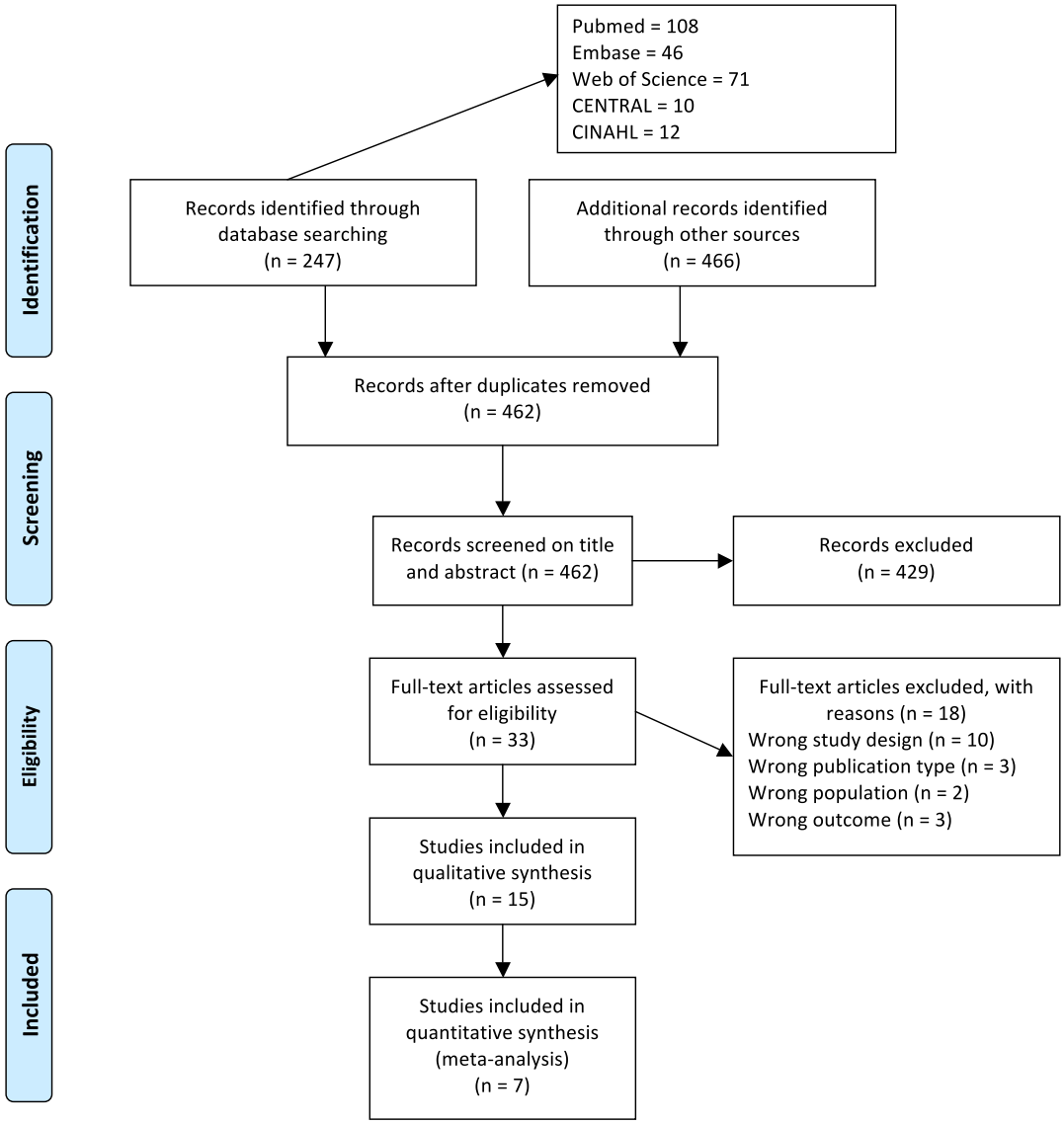


Fig 1 Study selection process. Abbreviations: CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health.

Methodological quality assessment

We assessed the risk of bias across 6 domains using the Quality in Prognosis Studies tool for the included studies (fig 2). A very high concordance between the reviewers in the quality assessment was observed (kappa=0.875, $P<.05$). In general, the risk of bias in the included studies was low. We assessed 13 studies (87%) as having a low overall risk of bias.[13,14,26-30,60-65] Figure 3 shows the summary of each Risk of Bias domain.

Narrative synthesis

Estimates of the association between prognostic factors and outcomes after CTR are shown in table 1. Most of the predictors were associated with the symptom severity, function, pain, satisfaction or return to work after CTR, both in the bivariate and multivariate analysis.

Regarding the severity of symptoms, symptoms of depression were associated with higher severity of symptoms in 71% of the studies that considered this prognostic factor, followed by symptoms of anxiety (66%). Regarding the function, pain catastrophizing was associated with higher functional impairment in 100% of the studies that considered this prognostic factor, followed by symptoms of depression (57%) and symptoms of anxiety (0%). Regarding pain, symptoms of depression were associated with higher pain intensity in 100% of the studies that considered this prognostic factor, followed by symptoms of anxiety (0%). Regarding patient satisfaction, symptoms of depression were associated with higher satisfaction in 60% of the studies that considered this prognostic factor, followed by pain catastrophizing (33%) and symptoms of anxiety (25%). Regarding return to work, lower pain catastrophizing was associated with early return to work in 100% of the studies that considered this prognostic factor, followed by symptoms of anxiety (100%) and symptoms of depression (33%). Table 2 summarizes the results and conclusions of the included studies.

Quantitative synthesis (meta-analyses)

The meta-analyses included estimates of the predictive role of symptoms of depression on symptom severity, function, pain, and

Table 1 Description of included articles

Author	Country	Design	N(M/F)	Age (y)	Type of Surgery	Follow-up(N)	Prognostic Factor	Postoperative Outcomes	Significant Result of Univariate Analysis	Significant Result of Multivariate Analysis	Overall Risk of Bias(QUIPS)
Katz et al[63]	USA	Prospective	241 (82/159)	44.6±11.5	Open or endoscopic CTR	18 mo (188)	MHI-5	BCTQ-S BCTQ-F Satisfaction	Yes Yes Yes	Yes Yes Yes	Low
Amick et al[64]	USA	Prospective	197 (NR)	NR	Open or endoscopic CTR	6 months (122)	MHI-5 Self-efficacy (4-item scale)	Return to work Return to work	Yes Yes	Yes Yes	Low
Hobby et al[59]	UK	Prospective	97 (22/75)	53.4 (21 - 85)	NR	6 mo (86)	HADS (depression) HADS (anxiety)	PEM BCTQ-S BCTQ-F Satisfaction PEM BCTQ-S BCTQ-F Satisfaction	No No No No No No No Yes		High
Katz et al[65]	USA	Prospective	181 (76/105)	45.7±9.4	Open or endoscopic CTR	6 and 12 mo (158, 157)	MHI-5 Self-efficacy (4-item scale)	Work status Work status	No, no Yes, yes	No Yes	Low
Lozano et al[60]	USA	Retrospective	82 (29/53)	61±12.8	Open CTR	2 y (82)	CES-D PASS PCS	DASH Satisfaction DASH Satisfaction DASH Satisfaction	Yes Yes No No Yes Yes	Yes Yes No No Yes No	Low
Kim et al[13]	South Korea	Prospective	83 (10/73)	54±10.4	Open CTR	3 mo (83)	CES-D PASS	Scar pain (ordinal scale) Scar pain (ordinal scale)	Yes No	Yes No	Low
Becker et al[61]	USA	Prospective	66 (17/49)	50±11	Open CTR	6±5 mo (66)	CES-D PASS PCS	DASH Satisfaction DASH Satisfaction DASH Satisfaction	No No No No No No	No No No No Yes No	Low
Cowan et al[62]	USA	Prospective	66 (17/49)	49.7±11.3	Open CTR	2-4 mo (66)	CES-D PASS PCS	Return to work Return to work Return to work	No Yes Yes	No Yes Yes	Low
Datema et al[14]	Netherlands	Prospective	227 (60/167)	58 (49-73)	Open CTR	12 mo (227)	CES-D	BCTQ Palmar pain scale (0-9)	Yes Yes	No Yes	Low
Bae et al[26]	South Korea	Retrospective	60 (7/53)	55 (36-80)	Open CTR	3 mo (60)	CES-D PASS	Satisfaction Satisfaction	Yes No	Yes No	Low
Shin et al[27]	South Korea	Prospective	60 (7/53)	55 (36-80)	Open CTR	3 mo (60)	CES-D PASS	BCTQ-S BCTQ-F BCTQ-S BCTQ-F	Yes No Yes No	Yes No Yes No	Low
Fernandez-de-Las-Peñaz et al[28]	Spain	RCT	60 (0/60)	46±9	Open or endoscopic CTR	6 and 12 mo (60,56)	BDI-II	Pain (0-10) BCTQ-S BCTQ-F		Yes, yes Yes, yes Yes, yes	Low
Jerosch-Herold et al[29]	UK	Prospective	455 (293/162)	62±12	NR	18 mo (455)	HADS (depression) HADS (anxiety)	CTS-6 GROC CTS-6 GROC	 Yes Yes 	No Yes Yes Yes	Low
Mosegaard et al[30]	Denmark	Prospective	417 (148/269)	58 (18-92)	Open or endoscopic CTR	12 mo (417)	PCS	Satisfaction	Yes	Yes	Low
Sun et al[31]	Netherlands	Prospective	307 (91/216)	56	Open CTR	6 mo (307)	PHQ-4 PCS	BCTQ BCTQ	No Yes	Yes Yes	High

NOTE. Data are shown as mean ± SD, median (IQR), n (%)

Abbreviations: F, Female; GROC, global rating of change; M, Male; NR, not reported; QUIPS, Quality in Prognosis Studies; UK United Kingdom; US, United States.

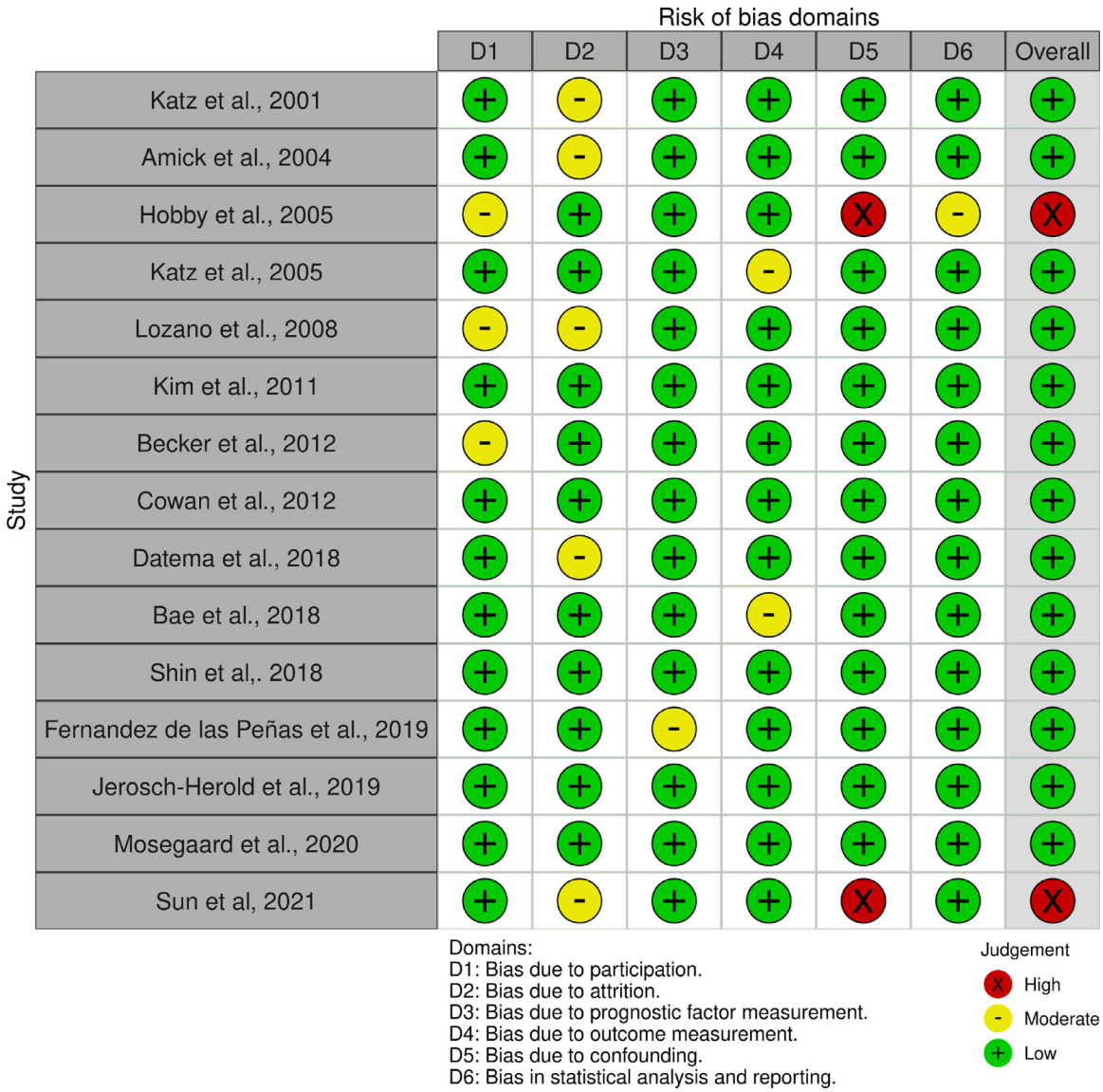


Fig 2 Summary of the risk of bias assessment using the Quality in Prognosis Studies tool.

satisfaction. We decided not to pool data from studies evaluating symptoms of anxiety, self-efficacy, and pain catastrophizing. In all these variables, there were not enough articles to analyze their operationalizations separately.

Symptoms of depression and symptom severity

Four studies reported estimates of the depressive symptoms on symptom severity (n=531). The overall result of the random-

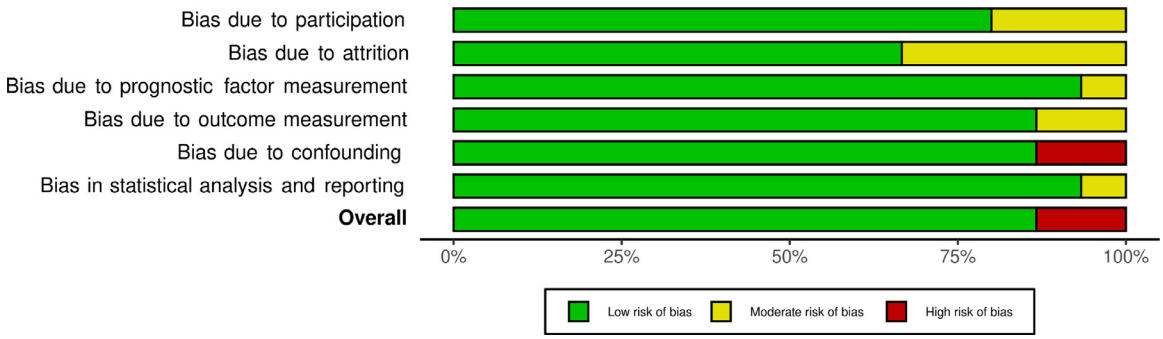


Fig 3 Proportion of included studies with low, high, or moderate risk of bias using the Quality in Prognosis Studies tool.

Table 2 Summary findings

Author	Follow-up(N)	Results	Conclusion
Katz et al[63]	18 mo (188)	Worse mental health status (MHI-5) was significantly associated with more severe symptoms (r=−0.23, P<.005), functional limitation (r=−0.22, P<.005), and lower satisfaction (r=−0.24, P<.005).	Clinicians should carefully evaluate patients' functional status, mental health status, health habits, and attorney involvement prior to performing carpal tunnel release.
Amick et al[64]	6 mo (122)	Greater likelihood of transition to successful work role functioning was related to self-efficacy improvement (χ^2=26.24, P<.001). Univariate models (self-efficacy): OR, 10.44; 95% CI, 4.17-26.17; P<.001; univariate models (depression): OR, 0.34; 95% CI, 0.17- 0.72; P=.004. In logistic regression model, only improved self-efficacy post surgery and a supportive work organization significantly predict successful work role functioning.	Significance of improved self-efficacy at 6 mo and depression at 2 mo post surgery highlights the importance of psychosocial management of musculoskeletal disorders.
Hobby et al[59]	6 mo	There was no association between the preoperative HADS and the mean score of PEM (depression: P=.2; anxiety: P=.58), BCTQ-S (depression: P=.9; anxiety: P=.79), and BCTQ-F (depression: P=.18; anxiety: P=.77). There was no difference in patient satisfaction between patients with and without depression (1.93 vs 1.53, P=.63). Patients with anxiety were less satisfied than patients without anxiety (2.05 vs 1.28, P=.005).	There was no significant difference in the outcome of CTR between patient with and without psychological disturbance.
Katz et al[65]	6 and12 mo (158, 157)	Change in self-efficacy between baseline and 2 mo was also strongly associated with work absence at 6 mo (same or better was 89% vs 11% in working vs not working respectively, P<.001). In logistic regression model, having the same or worse self-efficacy was associated with work absence at 6 mo (adjusted OR, 4.4; 95% CI, 1.4-14).	Factors associated with work absence at 6 and 12 mo after CTR included preoperative physical functional status, lower self-efficacy, workers' compensation, and less supportive organizational policies and practices.
Lozano et al[60]	2 ye (82)	Significant association between satisfaction and the CES-D score (r=−0.24, P<.05). Significant association between the DASH score and the CES-D (r=0.46, P<.01) and PCS scores (r=0.35, P<.01).	Dissatisfaction and perceived disability after CTR is predicted primarily by depression and ineffective coping skills and to a lesser degree by clinical or electrophysiologic evidence of advanced nerve damage.
Kim et al[13]	3 mo (83)	CES-D score (r=0.47, P=.001) was significantly correlated with scar pain intensity. Stepwise multivariable linear regression analysis showed that CES-D score (β=0.44, P<.001) and postoperative BCTQ-S (β=0.38, P<.01) best predicted scar pain intensity.	Depression score and postoperative symptoms predicted scar pain intensity after open CTR. However, the most important contributor to scar pain intensity variance remains unidentified.
Becker et al[61]	6±5 mo (66)	The PASS score was the only correlate of actual improvement of tingling after surgery (r=0.33, P=.009). There was no significant association between the CES-D and PASS with satisfaction with surgery and DASH scores. The best regression model for lower postoperative DASH score included men, lower PCS, and actual improvement of weakness (adjusted R^2=0.32, P<.001).	Actual relief of symptoms with CTR matched patients' expectations. Satisfaction with treatment correlated with relief of symptoms.
Cowan et al[62]	2-4 mo (66)	Earlier return to full work duty was associated with a lower PCS score (P=.028) and a lower PASS score (P=.005). CES-D was not associated with earlier return to full work duty (P=.380).	The most important determinant of return to full duty work CTR is job type, but psychological factors such as patient expectations, catastrophic thinking, and anxiety in response to pain also have a role.

(*continued on next page*)

Table 2 (*Continued*)

Author	Follow-up(N)	Results	Conclusion
Datema et al[14]	12 mo (227)	Patients with a depression had significantly less favorable outcomes than patients without depression: BCTQ: 1.1 (1.0-1.6) vs 1.4 (1.2-2.1), $P<.05$; and Palmar pain score=0: 58.4% vs 27.3%, $P<.05$. Multivariable analyses showed that preoperative CES-D had a small but statistically significant influence on palmar pain (β=0.075, $P<.05$) but not on postoperative BCTQ (β=0.005, P=.44).	Depression is not an independent predictor of residual CTS symptoms 1 y after CTR. Patients with CTS and depression may expect a somewhat higher degree of palmar pain after CTR, the clinical relevance of which is small.
Bae et al[26]	3 mo (60)	Univariate analyses demonstrated significant correlations of patient satisfaction with preoperative CES-D: OR, 0.923; 95% CI. 0.880-0.968; P=.001. Multivariate analyses showed that preoperative CES-D were significantly correlated with patient satisfaction. OR, 0.938; 95% CI, 0.895-0.982; P=.007. Age adjusted: OR, 0.922; 95% CI, 0.877-0.969; P=.001	Age and depression level were preoperative predictors influencing satisfaction after CTR.
Shin et al[27]	3 mo (60)	Postoperative CES-D (r=0.48, $P<.05$) and PASS (r=0.27, $P<.05$) were significantly correlated with postoperative BCTQ-S. In a multivariable linear regression model, the CES-D (β=6.679; 95% CI, 3.462-9.895; $P<.05$) and PASS (β=6.300; 95% CI, 0.404-12.195; $P<.05$) were significantly associated with the postoperative BCTQ-S.	Depression level and pain anxiety of patients with CTS are associated with the symptom severity of CTS in both the preoperative and the postoperative period.
Fernandez-de-Las-Peñaz et al[28]	6 and 12 mo (60, 56)	Depressive symptoms (BDI-II) were significantly and negatively correlated with pain intensity, BCTQ-S and BCTQ-F at 6 and 12 mo (all $P<.001$). Higher depressive symptoms at baseline contributed to poorer outcomes post intervention (from 5%-15% of the variance).	Baseline localized pressure pain sensitivity and depression were predictive of long-term clinical outcomes in women with CTS after surgery,
Jerosch-Herold et al[29]	18 mo (455)	A general linear model identified that lower anxiety is associated with lower symptom severity in CTS-6 (β=−0.02; 95% CI, 0.01-0.04; $P<.001$).	Multivariable modeling identified, independent of symptom severity at outset, higher health utility, fewer comorbidities, and lower anxiety as significant predictors of better outcome from CTR.
Mosegaard et al[30]	12 mo (417)	Risk of low patient-reported satisfaction for patients with preoperative PCS>30 compared with patients with PCS≤30 was unadjusted: OR, 2.24; 95% CI, 1.27-3.96; P=.005; adjusted for demographics: OR, 2.56; 95% CI, 1.38-4.74; P=.003).	Higher preoperative PCS seems to have a negative effect on postoperative patient-reported satisfaction after CTR.
Sun et al[31]	6 mo (307)	Association between BCTQ total score post surgery and baseline pain catastrophizing was statistically significant (β=0.008; 95% CI, 0-0.01). In multivariable linear regression model, only before adding illness perceptions and expectations to the model, pain catastrophizing was significantly associated with outcome.	Effects of pain catastrophizing on CTR outcome may be captured by the mindset about the efficacy of CTS and the mindset regarding CTS.

NOTE. Data are shown as mean ± SD, median (IQR), n (%)

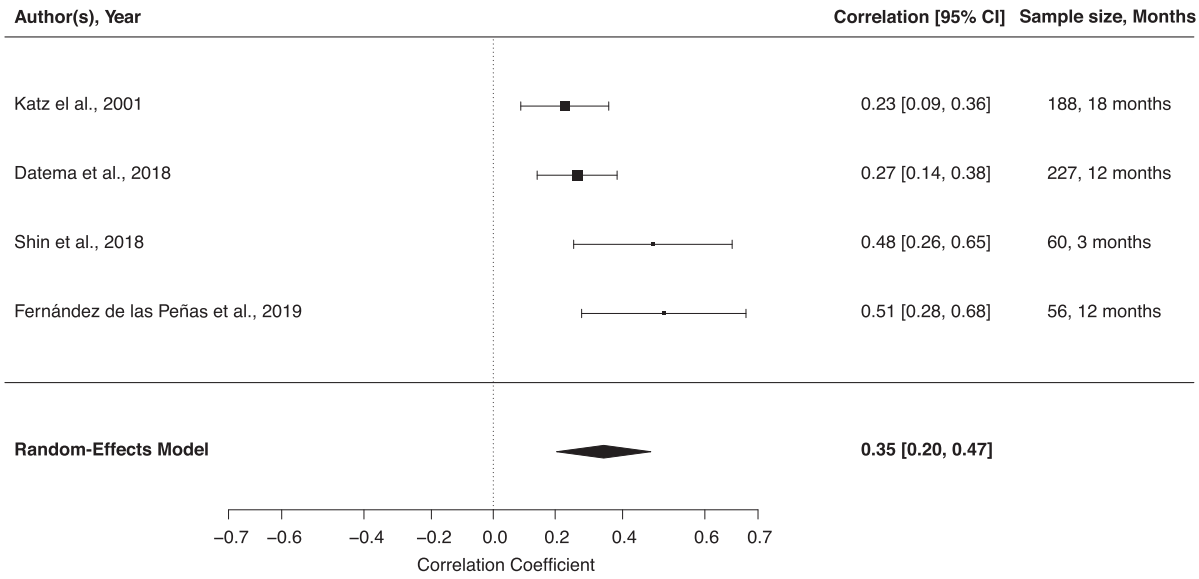


Fig 4 Forest plot of the relationship between symptoms of depression and symptom severity. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

effects model was r=0.347 (95% CI, 0.205-0.475; $P \leq .0001$) (fig 4). Heterogeneity between studies was substantial (I^2=63.13%).

Symptoms of depression and function

Four studies reported estimates of the depressive symptoms on function (n=386). The overall result of the random-effects model was r=0.307 (95% CI, 0.132-0.464; P=.0008) (fig 5). Heterogeneity between studies was substantial (I^2=65.51%).

Symptoms of depression and pain

Three studies reported estimates of the depressive symptoms on pain intensity (n=344). The overall result of the random-effects model was r=0.431 (95% CI, 0.286-0.558; $P \leq .0001$) (fig 6). Heterogeneity between studies was moderate (I^2=51.29%).

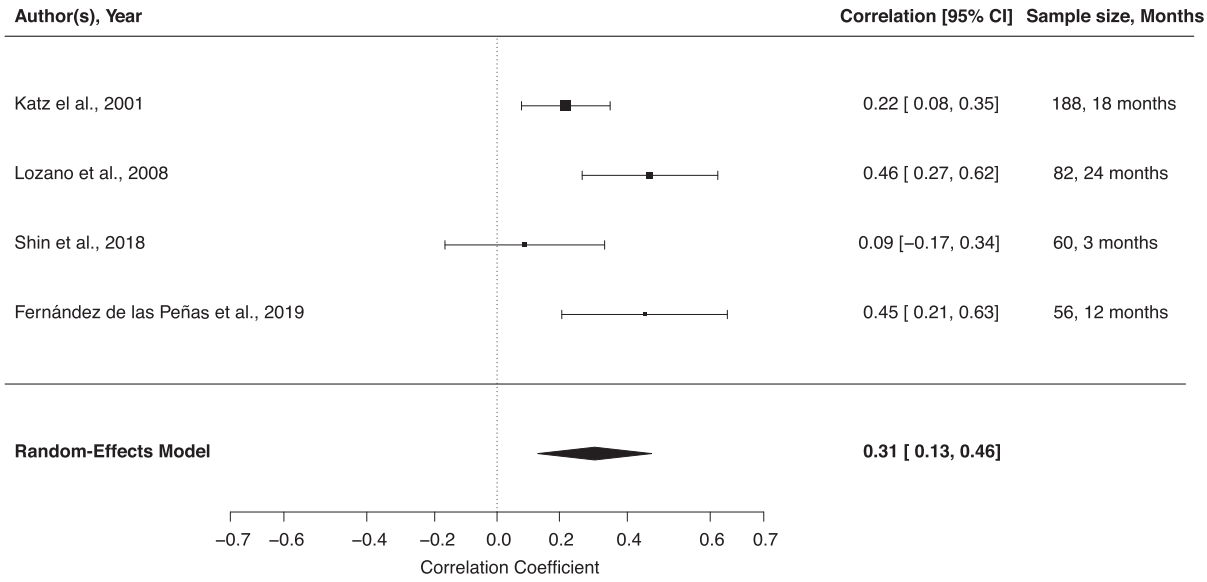


Fig 5 Forest plot of the relationship between symptoms of depression and function. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

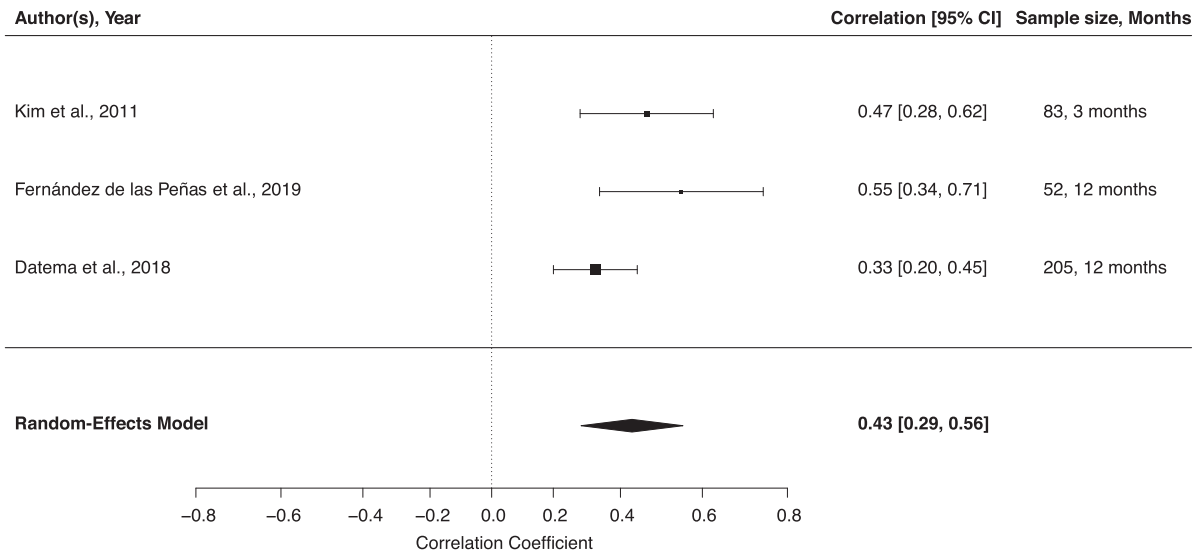


Fig 6 Forest plot of the relationship between symptoms of depression and pain. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

Symptoms of depression and satisfaction

Three studies reported estimates of the depressive symptoms on satisfaction (n=330). The overall result of the random-effects model was r=0.202 (95% CI, 0.096-0.305; P=.0002) (fig 7). Heterogeneity between studies was extremely low (I^2= 0.01%).

Discussion

This systematic review and meta-analysis provides updated evidence on the association between cognitive and mental health factors with self-reported outcomes in patients with CTS who undergo surgery. The majority of studies indicate a significant association between the cognitive or mental health factors and the outcomes after CTR. In general, the risk of bias in the included studies was low. Despite the heterogeneity of the available evidence, the results were consistent in the quantitative analysis regarding the effect of the symptoms of depression on symptom severity, function, and pain after CTR, 3 months after surgery, and beyond.

This evidence agrees with the other systematic reviews that emphasize the potential effect of the cognitive and mental

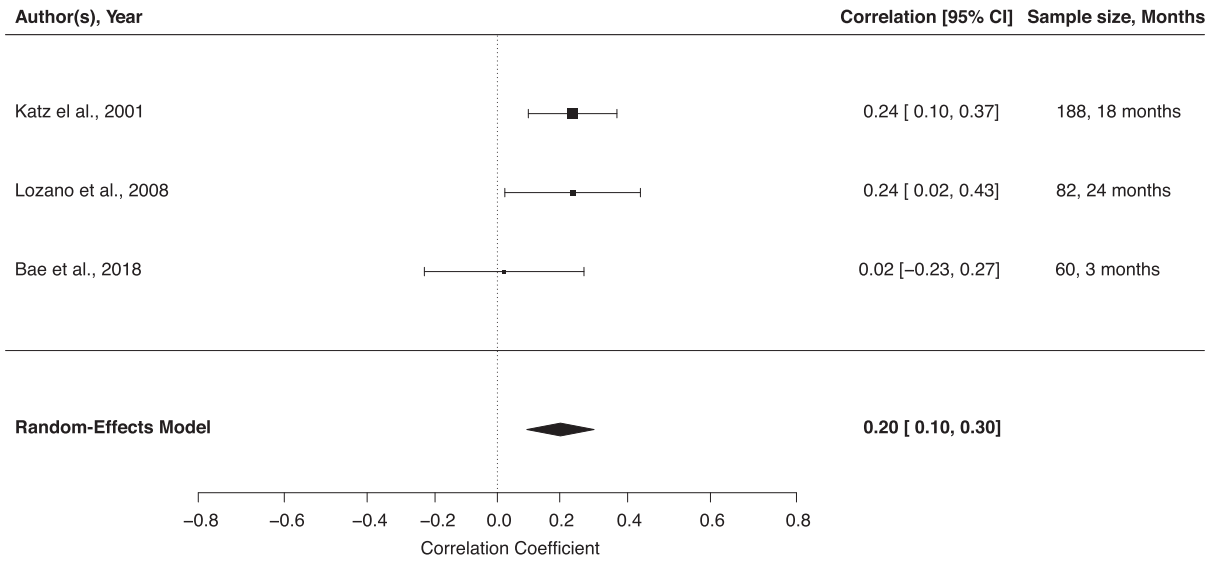


Fig 7 Forest plot of the relationship between symptoms of depression and dissatisfaction. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size than other studies.

health factors on postsurgical outcomes in individuals with chronic musculoskeletal pain.[66,67] For example, symptoms of depression, anxiety, and pain catastrophizing can predict poor outcomes in patients undergoing shoulder surgery,[18,20] spine surgery,[21,22] and knee replacement.[23,24] Therefore, physicians, physical therapists, and occupational therapists should consider evaluating the cognitive and mental health factors in patients undergoing hand surgery.

An interesting finding is that most of the studies found that the level of the symptoms of depression was associated more with the severity of the symptoms and postoperative pain than with functional impairment. This seems relevant because the severity of the symptoms is the most important reason for the patients undergoing surgery.[68] Postoperative pain control is an essential goal in rehabilitation because of the possibility of reducing the costs associated with the use of opioids.[9] On the other hand, although a quantitative analysis was not possible, the symptoms of depression with self-efficacy showed a significant association with a late return to work. The early identification of patients at a greater risk of a delayed return to work could prevent a prolonged absence from work or suboptimal performance at work.[69]

Study strengths and limitations

This systematic review has several strengths. We used the current guidelines to develop the systematic review.[33,34] We conducted a comprehensive search of 5 databases and additional sources to identify the relevant studies. Rigorous narrative approaches and a meta-analysis were considered to synthesize the available evidence. Most of the included studies were of high methodological quality and carried out a long-term follow-up (3-24 months). In contrast, a limitation of this review was the lack of measurement of the cognitive and mental health factors that may influence the CTR outcomes beyond those identified in the available studies. This limited the possibility of performing a quantitative synthesis of the data (meta-analysis) for all of the prognostic factors considered (ie, symptoms of anxiety, catastrophic thinking, self-efficacy). In addition, we did not find any studies that evaluated some of the psychosocial factors that we included in our search strategy (ie, fear avoidance or kinesiophobia). Although kinesiophobia, for example, has been shown to be an important predictor of upper extremity −specific disability in patients with CTS,[70] its prognostic value in postoperative outcomes has not yet been considered; therefore, future studies should evaluate this aspect. Another limitation was that we focused on evaluating the cognitive and mental health factors, while we know that many variables can modulate the symptoms in patients with CTS. For example, education level, intrinsic risk factors such as obesity, age, and sex, and occupational risk factors such as exposure to higher manual forces play a part.[32,71] In addition, peripheral nerve injury triggers changes in the central nervous system. These changes include central sensitization and changes in the cortical representation.[72] A comprehensive assessment that considers all of these aspects will allow clinicians to make more appropriate decisions and deliver greater benefits to their patients.

Directions for future studies

While some patients may experience an improvement in their depressive symptoms after CTR,[14,27] the effect of treating the depressive symptoms before surgery has been little studied. In other musculoskeletal pain conditions, it has been observed that depressed patients who received preoperative psychotherapy (eg, cognitive behavioral therapy) had fewer medical complications and less resource utilization than those who did not receive psychotherapy.[73] In addition, perioperative psychotherapy has been shown to be effective at reducing the level of postoperative pain and functional impairment in patients who undergo orthopedic surgery.[74] Future studies should therefore evaluate the efficacy of similar interventions in patients with CTS undergoing surgery, incorporating the approach to other aspects that negatively influence depressive symptoms, such as sleep quality.[75]

On the other hand, it is not just about identifying those at risk of a poor outcome but also providing evidence to support that having more positive emotional and cognitive responses can benefit the patient and their outcomes. For example, expectations and resilience measures (eg, optimism) have been shown to be strong predictors of postoperative functionality.[76] Therefore, implementing strategies early on that reinforce these more positive beliefs, attitudes, and behaviors could positively influence their current and future pain experience (eg, educational program).[77] In addition, educating patients on the expectations and beliefs that they hold before surgery may help them to increase their participation in the shared decision-making process while setting realistic expectations regarding the postoperative outcomes.[31] Similarly, the efficacy of treatments after CTR should focus on more favorable outcomes such as quality of life.[78] Future studies should consider this point to reframe the conversation about how more positive cognitive and emotional responses can lead to better rehabilitation outcomes. For this reason, addressing the patient's emotional state and coping strategies could be an essential treatment opportunity that results in the improvement of the health of patients undergoing CTR.

Conclusions

This systematic review and meta-analysis showed that symptoms of depression have a moderate association with symptom severity, function, and pain after CTR. Symptoms of anxiety, catastrophic thinking, and self-efficacy are also important indicators of poor postsurgery outcomes and should be considered. Therefore, a preoperative evaluation of this variable could help to identify patients at risk for unfavorable surgical outcomes and provide timely treatment. As more is learned about the role of the cognitive and mental health factors and their potential effect on CTR, clinicians will be able to use these findings to approach patients more effectively.

Keywords

Carpal tunnel syndrome; Psychology; Patient reported outcome measures; Pain, postoperative; Rehabilitation

Corresponding author

Sofía Pérez-Alenda, PT, PhD, Department of Physiotherapy, University of Valencia, C/ Gascó Oliag N 5, 46010 Valencia, Spain. *E-mail address:* sofia.perez-alenda@uv.es.

References

1. Nora DB, Becker J, Ehlers JA, Gomes I. What symptoms are truly caused by median nerve compression in carpal tunnel syndrome? Clin Neurophysiol 2005;116:275–83.
2. Keith MW, Masear V, Chung KC, et al. American Academy of Orthopaedic Surgeons Clinical Practice Guideline on diagnosis of carpal tunnel syndrome. J Bone Joint Surg Am 2009;91:2478–9.
3. Nazari G, Shah N, MacDermid JC, Woodhouse L. The impact of sensory, motor and pain impairments on patient-reported and performance based function in carpal tunnel syndrome. Open Orthop J 2017;11:1258–67.
4. Bickel KD. Carpal tunnel syndrome. J Hand Surg 2010;35:147–52.
5. Thiese MS, Gerr F, Hegmann KT, et al. Effects of varying case definition on carpal tunnel syndrome prevalence estimates in a pooled cohort. Arch Phys Med Rehabil 2014;95:2320–6.
6. Dale AM, Harris-Adamson C, Rempel D, et al. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. Scand J Work Environ Health 2013;39:495–505.
7. Tadjerbashi K, Åkesson A, Atroshi I. Incidence of referred carpal tunnel syndrome and carpal tunnel release surgery in the general population: increase over time and regional variations. J Orthop Surg 2019;27:2309499019825572.
8. Pourmemari MH, Heliövaara M, Viikari-Juntura E, Shiri R. Carpal tunnel release: lifetime prevalence, annual incidence, and risk factors. Muscle Nerve 2018;58:497–502.
9. Ingram J, Mauck BM, Thompson NB, Calandruccio JH. Cost, value, and patient satisfaction in carpal tunnel surgery. Orthop Clin North Am 2018;49:503–7.
10. Urits I, Gress K, Charipova K, Orhurhu V, Kaye AD, Viswanath O. Recent advances in the understanding and management of carpal tunnel syndrome: a comprehensive review. Curr Pain Headache Rep 2019;23:70.
11. Shi Q, Bobos P, Lalone EA, Warren L, MacDermid JC. Comparison of the short-term and long-term effects of surgery and nonsurgical intervention in treating carpal tunnel syndrome: a systematic review and meta-analysis. Hand 2020;15:13–22.
12. Wessel LE, Gu A, Asadourian PA, Stepan JG, Fufa DT, Osei DA. The epidemiology of carpal tunnel revision over a 1-year follow-up period. J Hand Surg 2021;46:758–64.
13. Kim JK, Kim YK. Predictors of scar pain after open carpal tunnel release. J Hand Surg Am 2011;36:1042–6.
14. Datema M, Tannemaat MR, Hoitsma E, et al. Outcome of carpal tunnel release and the relation with depression. J Hand Surg Am 2018;43:16–23.
15. Chester R, Jerosch-Herold C, Lewis J, Shepstone L. Psychological factors are associated with the outcome of physiotherapy for people with shoulder pain: a multicentre longitudinal cohort study. Br J Sports Med 2018;52:269–75.
16. Tseli E, Boersma K, Stålnacke BM, et al. Prognostic factors for physical functioning after multidisciplinary rehabilitation in patients with chronic musculoskeletal pain: a systematic review and meta-analysis. Clin J Pain 2019;35:148–73.
17. Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JWS. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. J Behav Med 2007;30:77–94.
18. Innocenti T, Ristori D, Galantini P, Testa M, Bari MD. The influence of central pain modulation on postoperative outcomes after shoulder surgery: a systematic review. Acta Orthop Traumatol Turc 2021;55:227–34.
19. Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis. Pain 2021;162:10–30.
20. Sheikhzadeh A, Wertli MM, Weiner SS, Rasmussen-Barr E, Weiser S. Do psychological factors affect outcomes in musculoskeletal shoulder disorders? A systematic review. BMC Musculoskelet Disord 2021;22:560.
21. Celestin J, Edwards RR, Jamison RN. Pretreatment psychosocial variables as predictors of outcomes following lumbar surgery and spinal cord stimulation: a systematic review and literature synthesis. Pain Med 2009;10:639–53.
22. Alodaibi FA, Minick KI, Fritz JM. Do preoperative fear avoidance model factors predict outcomes after lumbar disc herniation surgery? A systematic review. Chiropr Man Therap 2013;21:40.
23. Khatib Y, Madan A, Naylor JM, Harris IA. Do psychological factors predict poor outcome in patients undergoing TKA? A systematic review. Clin Orthop Relat Res 2015;473:2630–8.
24. Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. Br J Anaesth 2015;114:551–61.
25. Park JW, Gong HS, Rhee SH, Kim J, Lee YH, Baek GH. The effect of psychological factors on the outcomes of carpal tunnel release: a systematic review. J Hand Surg Asian Pac Vol 2017;22:131–7.
26. Bae JY, Kim JK, Yoon JO, Kim JH, Ho BC. Preoperative predictors of patient satisfaction after carpal tunnel release. Orthop Traumatol Surg Res 2018;104:907–9.
27. Shin YH, Yoon JO, Kim YK, Kim JK. Psychological status is associated with symptom severity in patients with carpal tunnel syndrome. J Hand Surg Am 2018;43:484.. e1-484.
28. Fernández-de-Las-Peñas C, de-la-Llave-Rincón AI, Cescon C, Barbero M, Arias-Buría JL, Falla D. Influence of clinical, psychological, and psychophysical variables on long-term treatment outcomes in carpal tunnel syndrome: evidence from a randomized clinical trial. Pain Pract 2019;19:644–55.
29. Jerosch-Herold C, Shepstone L, Houghton J, Wilson ECF, Blake J. Prognostic factors for response to treatment by corticosteroid injection or surgery in carpal tunnel syndrome (palms study): a prospective multicenter cohort study. Muscle Nerve 2019;60:32–40.
30. Mosegaard SB, Stilling M, Hansen TB. Higher preoperative pain catastrophizing increases the risk of low patient reported satisfaction after carpal tunnel release: a prospective study. BMC Musculoskelet. Disord 2020;21:42.
31. Sun PO, Walbeehm ET, Selles RW, et al. Patient mindset and the success of carpal tunnel release. Plast Reconstr Surg 2021;147:66e–75e.
32. Erickson M, Lawrence M, Jansen CWS, Coker D, Amadio P, Cleary C. Hand pain and sensory deficits: carpal tunnel syndrome. J Orthop Sports Phys Ther 2019;49:CPG1–85.
33. Moher D, Liberati A, Tetzlaff J, Altman DG, Group PRISMA. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. Int J Surg 2010;8:336–41.
34. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008–12.
35. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. Psychol Assess 1995;7:524–32.
36. Tkachuk GA, Harris CA. Psychometric properties of the Tampa Scale for Kinesiophobia-11 (TSK-11). J Pain 2012;13:970–7.
37. Keefe FJ, Lefebvre JC, Maixner W, Salley Jr AN, Caldwell DS. Self-efficacy for arthritis pain: relationship to perception of thermal laboratory pain stimuli. Arthritis Care Res 1997;10:177–84.
38. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157–68.
39. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–70.
40. Osman A, Barrios FX, Osman JR, Schneekloth R, Troutman JA. The Pain Anxiety Symptoms Scale: psychometric properties in a community sample. J Behav Med 1994;17:511–22.
41. Weissman MM, Sholomskas D, Pottenger M, Prusoff BA, Locke BZ. Assessing depressive symptoms in five psychiatric populations: a validation study. Am J Epidemiol 1977;106:203–14.
42. Wang YP, Gorenstein C. Assessment of depression in medical patients: a systematic review of the utility of the Beck Depression Inventory-II. Clinics 2013;68:1274–87.

43. McHorney C, Ware JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–63.
44. Kroenke K, Spitzer RL, Williams JBW, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics 2009;50:613–21.
45. Levine DW, Simmons BP, Koris MJ, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. J Bone Joint Surg Am 1993;75:1585–92.
46. Atroshi I, Lyrén PE, Gummesson C. The 6-item CTS symptoms scale: a brief outcomes measure for carpal tunnel syndrome. Qual Life Res 2009;18:347–58.
47. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). Am J Ind Med 1996;29:602–8.
48. Gummesson C, Ward MM, Atroshi I. The shortened Disabilities of the Arm, Shoulder and Hand questionnaire (QuickDASH): validity and reliability based on responses within the full-length DASH. BMC Musculoskelet Disord 2006;7:44.
49. Chung KC, Pillsbury MS, Walters MR, Hayward RA. Reliability and validity testing of the Michigan Hand Outcomes Questionnaire. J Hand Surg Am 1998;23:575–87.
50. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5:210.
51. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med 2013;158:280–6.
52. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods 2021;12:55–61.
53. R Core Team. 2017 R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2017.
54. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Chapter 7: converting among effect sizes. Introduction to meta-analysis. Chichester, England: John Wiley & Sons; 2009. p. 45–9.
55. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw 2010;36:1–48.
56. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods 2010;1:97–111.
57. Cohen J. A power primer. Psychol Bull 1992;112:155–9.
58. Higgins JPT, Thomas J. Cochrane handbook for systematic reviews of interventions. London: John Wiley & Sons; 2021.
59. Hobby JL, Venkatesh R, Motkur P. The effect of psychological disturbance on symptoms, self-reported disability and surgical outcome in carpal tunnel syndrome. J Bone Joint Surg Br 2005;87:196–200.
60. Lozano Calderón SA, Paiva A, Ring D. Patient satisfaction after open carpal tunnel release correlates with depression. J Hand Surg Am 2008;33:303–7.
61. Becker SJE, Makanji HS, Ring D. Expected and actual improvement of symptoms with carpal tunnel release. J Hand Surg Am 2012;37:1324–9.
62. Cowan J, Makanji H, Mudgal C, Jupiter J, Ring D. Determinants of return to work after carpal tunnel release. J Hand Surg Am 2012;37:18–27.
63. Katz JN, Losina E, Amick 3rd BC, Fossel AH, Bessette L, Keller RB. Predictors of outcomes of carpal tunnel release. Arthritis Rheum 2001;44:1184–93.
64. Amick 3rd BC, Habeck RV, Ossmann J, Fossel AH, Keller R, Katz JN. Predictors of successful work role functioning after carpal tunnel release surgery. J Occup Environ Med 2004;46:490–500.
65. Katz JN, Amick 3rd BC, Keller R, et al. Determinants of work absence following surgery for carpal tunnel syndrome. Am J Ind Med 2005;47:120–30.
66. Sobol-Kwapinska M, Bąbel P, Plotek W, Stelcer B. Psychological correlates of acute postsurgical pain: a systematic review and meta-analysis. Eur J Pain 2016;20:1573–86.
67. Theunissen M, Peters ML, Bruce J, Gramke HF, Marcus MA. Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with chronic postsurgical pain. Clin J Pain 2012;28:819–41.
68. Gong HS, Baek GH, Oh JH, Lee YH, Jeon SH, Chung MS. Factors affecting willingness to undergo carpal tunnel release. J Bone Joint Surg Am 2009;91:2130–6.
69. Loisel P, Durand MJ, Berthelette D, et al. Disability prevention. Dis Manag Health Outcomes 2001;9:351–60.
70. Das De S, Vranceanu AM, Ring DC. Contribution of kinesophobia and catastrophic thinking to upper-extremity-specific disability. J Bone Joint Surg Am 2013;95:76–81.
71. Núñez-Cortés R, Cruz-Montecinos C, Antúnez-Riveros MA, Pérez-Alenda S. Does the educational level of women influence hand grip and pinch strength in carpal tunnel syndrome? Med Hypotheses 2020;135:109474.
72. Schmid AB, Fundaun J, Tampin B. Entrapment neuropathies: a contemporary approach to pathophysiology, clinical assessment, and management. Pain Rep 2020;5:e829.
73. Schwartz AM, Wilson JM, Farley KX, Roberson JR, Guild GN, Bradbury TL. Modifiability of depression's impact on early revision, narcotic usage, and outcomes after total hip arthroplasty: the impact of psychotherapy. J Arthroplasty 2020;35:2904–10.
74. Wang L, Chang Y, Kennedy SA, et al. Perioperative psychotherapy for persistent post-surgical pain and physical impairment: a meta-analysis of randomised trials. Br J Anaesth 2018;120:1304–14.
75. Patel A, Culbertson MD, Patel A, et al. The negative effect of carpal tunnel syndrome on sleep quality. Sleep Disord 2014;2014 :962746.
76. Kadzielski J, Malhotra LR, Zurakowski D, Lee SGP, Jupiter JB, Ring D. Evaluation of preoperative expectations and patient satisfaction after carpal tunnel release. J Hand Surg Am 2008;33:1783–8.
77. Núñez-Cortés R, Espinoza-Ordóñez C, Pommer PP, Horment-Lara G, Pérez-Alenda S, Cruz-Montecinos C. A single preoperative pain neuroscience education: is it an effective strategy for patients with carpal tunnel syndrome? Med Hypotheses 2019;126:46–50.
78. Peters S, Page MJ, Coppieters MW, Ross M, Johnston V. Rehabilitation following carpal tunnel release. Cochrane Database Syst Rev 2016;2:CD004158.

Musculoskeletal Science and Practice 63 (2023) 102723

Contents lists available at ScienceDirect

Musculoskeletal Science and Practice

journal homepage: www.elsevier.com/locate/msksp

Original article

Social determinants of health and physical activity are related to pain intensity and mental health in patients with carpal tunnel syndrome

Rodrigo Núñez-Cortés [a,b,c], Carlos Cruz-Montecinos [a,b,d], Serghio Torreblanca-Vargas [e], Lars Louis Andersen [f], Claudio Tapia [b], Maritza Ortega-Palavecinos [c], Rubén López-Bueno [f,g,h], Joaquín Calatayud [f,g,*], Sofía Pérez-Alenda [a]

[a] Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), Department of Physiotherapy, University of Valencia, Valencia, Spain
[b] Department of Physical Therapy, Faculty of Medicine, University of Chile, Santiago, Chile
[c] Section of Clinical Research, Hospital Clínico La Florida, Santiago, Chile
[d] Section of Research, Innovation and Development in Kinesiology, Kinesiology Unit, San José Hospital, Santiago, Chile
[e] Service of Rehabilitation, Hospital Provincia Cordillera, Santiago, Chile
[f] National Research Centre for the Working Environment, Copenhagen, Denmark
[g] Exercise Intervention for Health Research Group (EXINH-RG), Department of Physiotherapy, University of Valencia, Spain
[h] Department of Physical Medicine and Nursing, University of Zaragoza, Zaragoza, Spain

ARTICLE INFO

Keywords:
Nerve compression syndromes
Educational level
Socioeconomic factors
Depression
Anxiety
Preoperative period

ABSTRACT

Background: Carpal tunnel syndrome (CTS) is the most common peripheral neuropathy of the upper limb and a frequent cause of disability.
Objective: To analyze the association between social determinants of health (SDH) and physical activity with pain intensity and mental health in patients with CTS.
Design: A cross-sectional study was conducted in patients with CTS awaiting surgery in two public hospitals in Chile.
Methods: The SDH collected included: employment status, educational level and monetary income. The level of physical activity was defined according to compliance with WHO recommendations. Outcome measures included: Pain intensity (Visual Analog Scale), Symptoms of anxiety and depression (Hospital Anxiety and Depression Scale), and catastrophic thinking (Pain Catastrophizing Scale). The adjusted regression coefficient (β) for the association between SDH and physical activity with each outcome was obtained using multivariable linear regression models controlling for age, sex, body mass index and symptom duration.
Results: Eighty-six participants were included (mean age 50.9 ± 10 years, 94% women). A high level of physical activity was associated with a 12.41 mm decrease in pain intensity (β = −12.41, 95%CI: −23.87 to −0.95) and a 3.29 point decrease in depressive symptoms (β = −3.29, 95%CI: −5.52 to −1.06). In addition, being employed was associated with a 2.30 point decrease in anxiety symptoms (β = −2.30; 95%CI: −4.41 to −0.19) and a high educational level was associated with a 7.71 point decrease in catastrophizing (β = −7.71; 95%CI: −14.06 to −1.36).
Conclusion: Multidisciplinary care teams should be aware of the association between SDH and physical activity with physical and mental health.

1. Introduction

Carpal tunnel syndrome (CTS) is a symptomatic condition caused by compression of the median nerve and is the most common peripheral neuropathy of the upper limb and a frequent cause of disability (Aroori and Spence, 2008; Nora et al., 2005; Núñez-Cortés et al., 2022). Population prevalence ranges from 6.3% to 11.7% and is more frequent in women (Dale et al., 2013; Thiese et al., 2014). Patients with CTS often present pain, paraesthesias and tingling sensations in the region of the median nerve, resulting in a significant impairment of quality of life and physical function (Bickel, 2010; Thiese et al., 2014). In severe cases with persistent hypoaesthesia and motor impairment, carpal tunnel release

* Corresponding author. C/ Gascó Oliag 5. PC, 46010, Valencia, Spain.
E-mail address: joaquin.calatayud@uv.es (J. Calatayud).

https://doi.org/10.1016/j.msksp.2023.102723
Received 26 October 2022; Received in revised form 24 January 2023; Accepted 30 January 2023
Available online 31 January 2023

(CTR) is usually indicated (Chandra et al., 2013). Literature has demonstrated that symptom severity and pain may be modulated by different social and mental health variables such as anxiety, depression and catastrophizing (De et al., 2013; Jerosch-Herold et al., 2017; Nunez et al., 2010). In addition, a recent meta-analysis concluded that depressive symptoms, anxiety, and catastrophic thinking were important indicators of poor postoperative outcomes in CTR (Núñez-Cortés et al., 2021). Likewise, it has been reported that social determinants of health (SDH) and physical activity may be related to mental health in several musculoskeletal and neurological diseases (Kim, 2014; Strube et al., 2019; Tan et al., 2014; Tawashy et al., 2009). However, little information exists about how the SDH and physical activity affects the mental health variables in CTS. Furthermore, a recent scoping review identified that physiotherapists lack the confidence and ability to identify psychosocial factors (Henning and Smith, 2022). Therefore, the approach to patients with CTS requires a broader understanding of how the SDH and physical activity may affect their health (physical and psychological), moving away from the biomedical bubble (The Lancet, 2018).

The SDH include the conditions in which people are born, grow, live, learn, work and age, as well as the social inequalities that are responsible for disparities in health outcomes (e.g., educational level, income and occupational status) (WHO Commission on Social Determinants of HealthWorld Health Organization, 2008). The literature has shown that SDH, such as low educational level, are related to negative beliefs associated with pain in women with CTS (i.e., catastrophizing) (Núñez-Cortés et al., 2020). Adults with pain who have a low level of education may also be less likely to exhibit good mental health (Axon and Chien, 2021). On the other hand, SDH such as low educational level and unemployment were associated with higher levels of pain in patients with musculoskeletal disorders in the shoulder and low back region (Fliesser et al., 2017; Karran et al., 2020; Strube et al., 2019). A recent meta-analysis found that low socio-economic status (in terms of educational level, income or occupational status) had a moderate association with increased risk of chronic pain, albeit none of the included studies focused on patients with painful hand conditions (Prego-Domínguez et al., 2021).

On the other hand, physical activity (as a lifestyle indicator) is an environmental health behavior that could also be influenced by SDH (Gidlow et al., 2006), such as having the financial means to sign up for an exercise class or having the appropriate education or health literacy to understand the benefits of physical activity. Physical activity has been shown to have a protective relationship for mental health among adults (Choi et al., 2019) and promotes positive coping strategies (e.g. self-efficacy) (Kandola et al., 2019). In addition, in other neurological conditions (e.g., spinal cord injury), whereas healthier lifestyles (e.g., higher physical activity) were associated with lower levels of pain and depressive symptoms (Tawashy et al., 2009).

Clinical assessment of more severe CTS cases (e.g. those awaiting surgery) should also take full account of social stressors, especially their impact on pain, depression, and anxiety. However, it is not fully known whether SDH and physical activity may be related to pain intensity, mental health and catastrophizing in CTS patients awaiting surgical intervention (i.e, CTR). Therefore, a preoperative assessment of these variables could be useful to identify the most vulnerable individuals and thus develop more specialized perioperative interventions to reduce pain and improve mental health. The aim of our study was to analyze the association between SDH and physical activity with pain intensity and mental health in patients with CTS awaiting surgery.

2. Methods

2.1. Study setting, design and participants

A cross-sectional study was conducted in patients with CTS who were awaiting surgery in two public hospitals in Chile (Hospital Clínico La Florida and Hospital Provincia Cordillera), between February and July 2022. Both institutions were located in an urban area composed mainly of families of middle socioeconomic status. Inclusion criteria were the following: over 18 years of age, medical diagnosis of moderate or severe CTS according to the clinical practice guideline of the Academy of Orthopaedic Physical Therapy and the Academy of Hand and Upper Extremity Physical Therapy (i.e. history, medical examination and tests/measurements) (Erickson et al., 2019), remain on the hospital's official waiting list for CTR for at least 3 months or more, and accept to participate in the study. Exclusion criteria were: inability to understand instructions (e.g. illiteracy), neurological conditions of the central nervous system (e.g. stroke, spinal cord injury), and previous surgery in the upper limb. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of the two participating hospitals. Written informed consent was obtained from all participants after explanation of the objectives of the study. This study was conducted in accordance with the guidelines "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) (von Elm et al., 2014).

2.2. Social determinants of health

Participants were interviewed face-to-face at each hospital. Data collected included: I) Employment status: employed versus unemployed (only for working-age participants); II) Educational level: participants were assigned to the lower educational level if they had not completed secondary education and to the higher educational level if they had completed secondary education or university studies; III) Monetary income was categorized according to individual monthly taxable income. The cut-off point was set at a value equal to or less than USD 320, which determines the degree of coverage provided by the Chilean public health system.

2.3. Physical activity

Participants reported the minutes and type of physical activities (moderate or vigorous) they performed as part of their daily life during the last seven days. Participants were classified according to the recommendations of the World Health Organization (WHO) 2020 guidelines on physical activity (Bull et al., 2020). Therefore, a level $\geq$150 min of moderate-intensity physical activity per week, or $\geq$75 min of vigorous-intensity physical activity per week, was used as the cutoff point (high vs. low level) (Bull et al., 2020).

2.4. Outcomes

Outcome measures included the following self-report assessments: I) Pain intensity, assessed using the Visual Analog Scale (VAS), a valid and reliable measure for pain assessment and widely used in patients with CTS (Ceceli et al., 2018; Kahl and Cleland, 2005). Participants were asked to rate their average pain during the seven days prior to assessment on a scale defined from 0 to 100 mm, where 0 is "no pain" and 100 is "the worst pain imaginable". II) Mental health, assessed with the Spanish version of the Hospital Anxiety and Depression Scale (HADS) (Herrero et al., 2003), which evaluates the level of anxiety and depression by means of two subscales of 0–21 points each. Higher values represent a worse outcome. In addition, catastrophic thinking in response to pain was assessed using the Spanish version of the Pain Catastrophizing Scale (PCS) (García Campayo et al., 2008). PCS has 13 items of four possible choices from 1 ″not at all" to 4 ″all the time," a higher score indicating greater catastrophic thinking, with a maximum score of 52 points (Sullivan et al., 1995).

2.5. Covariates

Data collected included: I) Sociodemographic variables (age and

sex); II) Body Mass Index was obtained from the ratio between weight and height squared (kg·m^2); III) Duration of symptoms associated with CTS (years).

2.6. Sample size

The sample size calculation was determined by considering a minimum of 10 participants for each independent variable entered in the multivariable linear regression. Considering a total of eight independent variables (four exposure factors and four covariates), the minimum sample size was set at 80 patients. Post-hoc power was calculated in the G*Power software, version 3.1.9.2 (Universität Düsseldorf, Germany) using the statistical test of multiple linear regression, one-tailed with an α err prob = 0.05. The post-hoc power was >80% for each of the models tested.

2.7. Statistical analyses

The normality of the data was tested using the Shapiro-Wilk test. Means and standard deviations (SD) were calculated for quantitative variables and percentages for categorical variables. For the employment status variable, only cases of working age (n = 75) were considered for the analysis. Considering the aim of our study, multivariable linear regression analysis was performed for each dependent variable (pain intensity, depressive symptoms, anxiety symptoms, catastrophizing). Dummy codes were used for the exposure factors, and unemployed, low educational level, low income and low physical activity were established as reference categories. Multivariable linear regression analysis examined the association of each of the exposure factors (educational level, employment status, monetary income, and physical activity) with each outcome (pain intensity, depressive symptoms, anxiety symptoms, catastrophizing), while controlling for each of the other exposure factors (i.e., mutually adjusted) and possible confounders (age, sex, body mass index, and symptom duration). For each analysis, the crude and adjusted regression coefficient (β) was obtained, with a 95% confidence interval (95% CI). All statistical analyses were performed in SPSS version 22.0 (IBM Corporation, Armonk, New York). Statistical significance was set at $p < 0.05$.

3. Results

A total of 92 patients were assessed for eligibility. Six participants were excluded for the following reasons: refusal to participate (n = 4), previous upper extremity surgery (n = 2). Finally, a total of 86 subjects were included in this study (Fig. 1). Ninety-four percent were women and the mean age was 50.9 ± 10 years. The mean duration of symptoms was 3.2 ± 2.5 years. The socio-demographic data, the SDH and the outcomes of the total sample are summarised in Table 1.

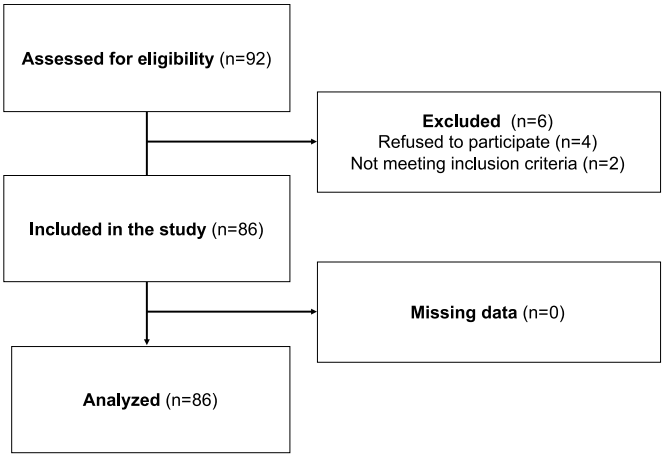


Fig. 1. Patient flow diagram.

Table 1
Characterization of patients (n = 86).

Characterics	Value
Age (years)	50.9 ± 10.0
Sex	
Male	5 (5.8%)
Female	81 (94.2%)
BMI (kg/m^2)	31.7 ± 6.2
Duration of CTS (years)	3.2 ± 2.5
Educational level	
Low level	43 (50%)
High level	43 (50%)
Employment status	
Unemployed	31 (36.0%)
Employed	44 (51.2%)
Non-working age	11 (12.8%)
Monetary Income	
≤320 USD	49 (57%)
>320 USD	37 (43%)
Physical Activity	
Low level	66 (76.7%)
High level	20 (23.3%)
VAS (0–100)	66.0 ± 20.8
HADS-D (0–21)	8.0 ± 4.5
HADS-A (0–21)	9.0 ± 4.2
PCS (0–52)	27.3 ± 13.0

Abbreviations: BMI, Body Mass Index; HADS, Hospital Anxiety and Depression Scale (D, depression; A, anxiety); PCS, Pain Catastrophizing Scale; USD, US dollar; VAS, Visual Analog Scale. Data are expressed as percentages or mean ± SD.

3.1. Pain intensity

Multivariable linear regression analysis for pain intensity showed that a high level of physical activity was significantly associated with a 12.41 mm decrease in VAS ($R^2 = 0.101$; β = −12.41; CI 95%: −23.87 to −0.95). No significant associations were found for the other exposure factors (Table 2).

3.2. Mental health

Depressive symptoms: Multivariable linear regression analysis for depressive symptoms showed that a high level of physical activity was significantly associated with a decrease of 3.29 points on the HADS (Depression subscale) ($R^2 = 0.264$; β = −3,29; CI: 95%: −5,52 to −1,06). No significant associations were found for the other exposure factors (Table 3).

Anxiety symptoms: Multivariable linear regression analysis for

Table 2
Multivariable associations for Pain Intensity (Visual Analog Scale 0–100).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	−3.41 [-12.94 to 6.12]	0.96 [-9.38 to 11.31]
Low education	ref.	ref.
High education	−7.21 [-16.05 to 1.63]	−2.83 [-13.31 to 7.64]
Low income	ref.	ref.
High income	−5.5 [-14.49 to 3.49]	−2.60 [-13.04 to 7.84]
Low physical activity	ref.	ref.
High physical activity	**−12.64 [-22.91 to -2.37]** *	**−12.41 [-23.87 to -0.95]** *

Data are shown as regression coefficient (β) and 95% confidence intervals (95% CI).
Notes: ref. = reference category.
Significant values are in bold; *Statistically-significant difference ($p < 0.05$).
[a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

Table 3
Multivariable associations for Depressive Symptoms (Hospital Anxiety and Depression Scale 0–21).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	0.15 [-1.9 to 2.21]	1.01 [-1.01 to 3.03]
Low education	ref.	ref.
High education	−1.16 [-3.07 to 0.74]	−0.51 [-2.56 to 1.53]
Low income	ref.	ref.
High income	−0.90 [-2.83 to 1.03]	−0.36 [-2.39 to 1.67]
Low physical activity	ref.	ref.
High physical activity	**−3.39 [-5.54 to -1.23]** **	**−3.29 [-5.52 to -1.06]** **

Data are shown as regression coefficient (β) and 95% confidence intervals (95% CI).
Notes: ref. = reference category.
Significant values are in bold; **Statistically-significant difference ($p < 0.01$).
[a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

Table 4
Multivariable associations for Anxiety Symptoms (Hospital Anxiety and Depression Scale 0–21).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	**−2.06 [-4.00 to -0.12]** *	**−2.30 [-4.41 to -0.19]** *
Low education	ref.	ref.
High education	−1.07 [-2.86 to 0.72]	0.14 [-1.99 to 2.28]
Low income	ref.	ref.
High income	0.09 [-1.74 to 1.91]	0.68 [-1.45 to 2.81]
Low physical activity	ref.	ref.
High physical activity	−0.95 [-3.08 to 1.18]	0.12 [-2.22 to 2.45]

Data are shown as regression coefficient (β) and 95% confidence intervals (95% CI).
Notes: ref. = reference category.
Significant values are in bold; *Statistically-significant difference ($p < 0.05$).
[a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

anxiety symptoms showed that being employed was significantly associated with a decrease of 2.30 points on the HADS (Anxiety subscale) ($R^2 = 0.142$; β = −2.30; 95% CI: −4.41 to −0.19). No significant associations were found for the other exposure factors (Table 4).

Catastrophizing: Multivariable linear regression analysis for catastrophizing showed that a high educational level was significantly associated with a decrease of 7.71 points on the PCS scale ($R^2 = 0.216$; β = −7.71; 95% CI: −14.06 to −1.36). No significant associations were found for the other exposure factors (Table 5).

Table 5
Multivariable associations for Catastrophizing (Pain Catastrophizing Scale 0–52).

Category	Crude β [95%CI]	Adjusted β [95%CI] [a]
Unemployment	ref.	ref.
Employment	0.55 [-5.66 to 6.75]	3.08 [-3.20 to 9.35]
Low education	1.0	ref.
High education	**−7.47 [-12.85 to -2.09]** **	**−7.71 [-14.06 to -1.36]** *
Low income	ref.	ref.
High income	−2.02 [-7.67 to 3.64]	−2.91 [-9.24 to 3.42]
Low physical activity	ref.	ref.
High physical activity	−4.67 [-11.25 to 1.89]	−3.92 [-10.86 to 3.03]

Data are shown as regression coefficient (β) and 95% confidence intervals (95% CI).
Notes: ref. = reference category.
Significant values are in bold; *Statistically-significant difference ($p < 0.05$).
[a] Mutually adjusted and controlling for age, sex, body mass index and duration of symptoms.

4. Discussion

This cross-sectional study aimed to analyze the association between SDH and physical activity with pain intensity and mental health in patients with CTS awaiting surgery. Although linear regression models explain only a small proportion of the variance of each outcome, a significant association of physical activity with pain intensity and depressive symptoms was identified. Likewise, a significant association was obtained between employment status and anxiety symptoms, and between low educational level and catastrophizing. Therefore, identifying SDH, such as employment status, educational level and physical activity level, could help clinicians develop more specialized perioperative interventions for pain and mental health management of patients with CTS.

4.1. Pain intensity

According to our results, a high level of physical activity was associated with a decrease in pain intensity. These results are consistent with the available literature in people with chronic pain. For example, Polaski et al. (2019) in a meta-analysis identified that physical activity and exercise (as a subset of physical activity) would be related to the analgesic effect in patients with chronic pain. Thus, one possible mechanism that could explain our results is the relationship between physical activity levels and descending pain modulatory function (Naugle and Riley, 2014). In fact, in healthy adults greater self-reported physical activity is associated with a greater pain inhibitory response through the conditioned modulatory pain response (Naugle and Riley, 2014).

On the other hand, our results disagree with the available literature on the association between educational level and income with pain intensity. In other conditions affecting the hand (e.g. rheumatoid arthritis), subjects with a high level of education, according to Swedish records, experience less pain than those with a low level of education (Jiang et al., 2015). In other surgical populations evaluated in North America (e.g. joint replacement), lack of university education was associated with higher pain scores before and after surgery (Goodman et al., 2018). The discrepancies found in our results could be explained in part by the differences in the educational systems and realities of each country. Therefore, multinational studies may be necessary to evaluate these associations in greater depth. Additionally, previous studies have identified that income (in terms of annual household income) is also related to pain and coping strategies in people with musculoskeletal pain (Palmlöf et al., 2012; Whitley et al., 2021). This could be explained by the fact that monetary income was classified according to individual monthly taxable income and there was no information on household income.

4.2. Mental health

Regarding depressive symptoms, it was observed that patients who met the WHO physical activity recommendations had lower levels of depressive symptoms. In fact, these patients had a reduction of up to 3.29 points in the depression subscales of the HADS (taking as a reference the patients with a low level of physical activity). This difference exceeds the minimal clinically important difference (MCID) of 1.7 points on the HADS, established for other health conditions (Lemay et al., 2019). These results are consistent with the available literature in the general population. For example, Choi et al. found a protective relationship between accelerometer-based activity and depression among adults (Choi et al., 2019). The antidepressant effects of physical activity could be explained by several neuroplastic processes related to depression (e.g., activation of the endocannabinoid system, optimisation of brain-derived neurotrophic factor) and by the ability to reduce inflammation and increase resistance to oxidative and physiological stress (Heyman et al., 2012; Kandola et al., 2019; Phillips, 2017). In addition, exercise promotes self-esteem, social support and self-efficacy (Kandola

et al., 2019). Therefore, our results reinforce the hypothesis that the promotion of physical activity (e.g., physical activity programs guided by WHO recommendations) could be a valuable strategy to reduce the risk of mental health issues (Mammen and Faulkner, 2013), which could be relevant for patients with CTS while awaiting surgery. Moreover, being employed was associated with a decrease of 2.30 points on the HADS anxiety subscale scores, which was also higher than the MCID reported in the literature of 1.7 points (Lemay et al., 2019). Previous research indicates that the negative effect of unemployment on mental health is mainly explained by distress (Paul and Moser, 2009). Our study also raises the need for policies to focus on the welfare of the unemployed, including support for re-employment.

On the other hand, according to our results, educational level was significantly associated with catastrophizing. In fact, having a high level of education was associated with a reduction of 7.71 points on the PCS, which was higher than the MCID of 6.71 points on the PCS for patients with chronic low back pain (Suzuki et al., 2020). Thus, for patients with CTS awaiting surgery, a comprehensive approach that takes into account both physical limitations due to pain and psychosocial challenges may be necessary.

We should be aware that the association between SDH and outcomes might be affected in our study, as patients were evaluated during the COVID-19 outbreak. The pandemic has highlighted pre-existing inequalities in terms of gender and socio-economic status (Bernardini et al., 2021). In this context, the SDH as mediators of the impact caused by the pandemic (e.g., job insecurity or economic concerns), amplified the consequences on the mental health of the most vulnerable populations (Bernardini et al., 2021; Campo-Arias and De Mendieta, 2021; Vindegaard and Benros, 2020; Wilson et al., 2020). Furthermore, although CTR is a common surgical procedure (Pourmemari et al., 2018), during the COVID-19 pandemic, hospitals around the world suspended elective or non-urgent hand surgeries to cope with the high demand for capacity caused by the health crisis (Picardo et al., 2021). The cancellation of elective surgeries and limited access to quality pain management care resulted in a greater focus on biomedical treatment (e.g., pharmacological management), with less consideration of psychological aspects (Karos et al., 2020). In this context, the implementation of physical activity programmes in the pre-surgical phase could help to reduce pain and improve mental health in this population.

4.3. Strengths and limitations

Our study has certain limitations. Firstly, these results should be interpreted with caution, as a cross-sectional design does not allow us to establish a cause-effect relationship between the variables studied. In addition SDH and physical activity were presented as dichotomous variables, which may lead to potential bias due to residual confounding. However, our study is consistent with the available literature on the importance of SDH in patients with CTS (Bernstein et al., 2022; Wright et al., 2019), and provides additional information in the context of non-North American/Western European countries. Furthermore, using these cutoff points could help clinicians to more clearly identify vulnerable groups that require further attention (e.g., unemployed, patients who have not completed secondary education). Therefore, our findings pave the way for future longitudinal investigations that may establish the directionality of the observed relationships. Second, we examined self-reported physical activity (i.e minute per week), and not based on an objective measure (e.g., accelerometer-based). However, the method used is valid and easy to apply at the clinical/hospital setting (Bull et al., 2020), and allows specific recommendations to be provided to healthcare teams (e.g., design physical activity programs guided by WHO criteria). Third, it is also important to mention that, although the results are in line with previous literature, our results only apply to the reality of one country. In addition, the high percentage of women in the sample is a limitation for the generalisability of the results. Future studies should include a larger population with follow-up over time to investigate how SDH might also affect clinical outcomes after surgery.

5. Conclusions

A high level of physical activity was associated with a decrease in pain intensity and depressive symptoms in patients with CTS awaiting surgery. In addition, being employed was associated with a decrease in anxiety symptoms and having a high educational level was associated with a decrease in catastrophizing. Multidisciplinary care teams should be aware of the association between SDH and physical activity with physical and mental health. Therefore, a comprehensive assessment of these variables may be relevant to identify cases of increased psychosocial risk and to plan strategies to reduce pain and improve the mental health of patients with CTS awaiting surgery, e.g., physical activity programs guided by WHO recommendations.

Ethics

All study procedures were approved by the Institutional Review Board of the Hospital Clínico la Florida and Hospital Provincia Cordillera (Santiago, Chile).

Declaration of competing interest

Rodrigo Núnez-Cortés is supported by a grant from the National Research and Development Agency of Chile (ANID/2020–72210026). Rubén López-Bueno is supported by European Union—NextGeneration-EU. The other authors have nothing to disclose.

References

Aroori, S., Spence, R.A.J., 2008. Carpal tunnel syndrome. Ulster Med. J. 77, 6–17.
Axon, D.R., Chien, J., 2021. Predictors of mental health status among older United States adults with pain. Behav. Sci. 11 https://doi.org/10.3390/bs11020023.
Bernardini, F., Attademo, L., Rotter, M., Compton, M.T., 2021. Social determinants of mental health as mediators and moderators of the mental health impacts of the COVID-19 pandemic. Psychiatr. Serv. 72, 598–601.
Bernstein, D.N., Kurucan, E., Fear, K., Hammert, W.C., 2022. Evaluating the impact of patient social deprivation on the level of symptom severity at carpal tunnel syndrome presentation. Hand 17, 339–345.
Bickel, K.D., 2010. Carpal tunnel syndrome. J. Hand Surg. https://doi.org/10.1016/j.jhsa.2009.11.003.
Bull, F.C., Al-Ansari, S.S., Biddle, S., Borodulin, K., Buman, M.P., Cardon, G., Carty, C., Chaput, J.-P., Chastin, S., Chou, R., Dempsey, P.C., DiPietro, L., Ekelund, U., Firth, J., Friedenreich, C.M., Garcia, L., Gichu, M., Jago, R., Katzmarzyk, P.T., Lambert, E., Leitzmann, M., Milton, K., Ortega, F.B., Ranasinghe, C., Stamatakis, E., Tiedemann, A., Troiano, R.P., van der Ploeg, H.P., Wari, V., Willumsen, J.F., 2020. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br. J. Sports Med. 54, 1451–1462.
Campo-Arias, A., De Mendieta, C.T., 2021. Social determinants of mental health and the COVID-19 pandemic in low-income and middle-income countries. Lancet Global Health 9 (8), e1029–e1030.
Ceceli, E., Gumruk, S., Okumus, M., Kocaoglu, S., Goksu, H., Karagoz, A., 2018. Comparison of 2 methods of neuropathic pain assessment in carpal tunnel syndrome and hand functions. Neurosciences 23, 23–28.
Chandra, P.S., Sarat Chandra, P., Singh, P.K., Goyal, V., Chauhan, A.K., Thakkur, N., Tripathi, M., 2013. Early versus Delayed Endoscopic Surgery for Carpal Tunnel Syndrome: Prospective Randomized Study. World Neurosurgery. https://doi.org/10.1016/j.wneu.2012.08.008.
Choi, K.W., Chen, C.-Y., Stein, M.B., Klimentidis, Y.C., Wang, M.-J., Koenen, K.C., Smoller, J.W., Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium, 2019. Assessment of bidirectional relationships between physical activity and depression among adults: a 2-sample mendelian randomization study. JAMA Psychiatr. 76, 399–408.
Dale, A.M., Harris-Adamson, C., Rempel, D., Gerr, F., Hegmann, K., Silverstein, B., Burt, S., Garg, A., Kapellusch, J., Merlino, L., Thiese, M.S., Eisen, E.A., Evanoff, B., 2013. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. Scandinavian Journal of Work. https://doi.org/10.5271/sjweh.3351. Environment & Health.
De, S.D., Vranceanu, A.-M., Ring, D.C., 2013. Contribution of kinesophobia and catastrophic thinking to upper-extremity-specific disability. J. Bone Joint Surg. https://doi.org/10.2106/jbjs.l.00064.
Erickson, M., Lawrence, M., Jansen, C.W.S., Coker, D., Amadio, P., Cleary, C., 2019. Hand pain and sensory deficits: carpal tunnel syndrome. J. Orthop. Sports Phys. Ther. 49. CPG1–CPG85.

Fliesser, M., De Witt Huberts, J., Wippert, P.-M., 2017. The choice that matters: the relative influence of socioeconomic status indicators on chronic back pain- a longitudinal study. BMC Health Serv. Res. 17, 800.
García Campayo, J., Rodero, B., Alda, M., Sobradiel, N., Montero, J., Moreno, S., 2008. [Validation of the Spanish version of the pain catastrophizing scale in fibromyalgia]. Med. Clin. 131, 487–492.
Gidlow, C., Johnston, L.H., Crone, D., Ellis, N., James, D., 2006. A systematic review of the relationship between socio-economic position and physical activity. Health Educ. J. https://doi.org/10.1177/0017896906069378.
Goodman, S.M., Mandl, L.A., Mehta, B., Navarro-Millan, I., Russell, L.A., Parks, M.L., Dey, S.A., Crego, D., Figgie, M.P., Nguyen, J.T., Szymonifka, J., Zhang, M., Bass, A. R., 2018. Does education level mitigate the effect of poverty on total knee arthroplasty outcomes? Arthritis Care Res. https://doi.org/10.1002/acr.23442.
Henning, M., Smith, M., 2022. The ability of physiotherapists to identify psychosocial factors in patients with musculoskeletal pain: a scoping review. Muscoskel. Care. https://doi.org/10.1002/msc.1725.
Herrero, M.J., Blanch, J., Peri, J.M., De Pablo, J., Pintor, L., Bulbena, A., 2003. A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. Gen. Hosp. Psychiatr. 25, 277–283.
Heyman, E., Gamelin, F.-X., Goekint, M., Piscitelli, F., Roelands, B., Leclair, E., Di Marzo, V., Meeusen, R., 2012. Intense exercise increases circulating endocannabinoid and BDNF levels in humans—possible implications for reward and depression. Psychoneuroendocrinology. https://doi.org/10.1016/j.psyneuen.2011.09.017.
Jerosch-Herold, C., Houghton, J., Blake, J., Shaikh, A., Wilson, E.C., Shepstone, L., 2017. Association of psychological distress, quality of life and costs with carpal tunnel syndrome severity: a cross-sectional analysis of the PALMS cohort. BMJ Open 7, e017732.
Jiang, X., Sandberg, M.E.C., Saevarsdottir, S., Klareskog, L., Alfredsson, L., Bengtsson, C., 2015. Higher education is associated with a better rheumatoid arthritis outcome concerning for pain and function but not disease activity: results from the EIRA cohort and Swedish rheumatology register. Arthritis Res. Ther. https://doi.org/10.1186/s13075-015-0836-6.
Kahl, C., Cleland, J.A., 2005. Visual analogue scale, numeric pain rating scale and the McGill pain Questionnaire: an overview of psychometric properties. Phys. Ther. Rev. https://doi.org/10.1179/108331905x55776.
Kandola, A., Ashdown-Franks, G., Hendrikse, J., Sabiston, C.M., Stubbs, B., 2019. Physical activity and depression: towards understanding the antidepressant mechanisms of physical activity. Neurosci. Biobehav. Rev. 107, 525–539.
Karos, K., McParland, J.L., Bunzli, S., Devan, H., Hirsh, A., Kapos, F.P., Keogh, E., Moore, D., Tracy, L.M., Ashton-James, C.E., 2020. The social threats of COVID-19 for people with chronic pain. Pain 161, 2229–2235.
Karran, E.L., Grant, A.R., Moseley, G.L., 2020. Low back pain and the social determinants of health: a systematic review and narrative synthesis. Pain 161, 2476–2493.
Kim, H.-J., 2014. Influence of educational attainment on pain intensity and disability in patients with lumbar spinal stenosis: mediation effect of pain catastrophizing. Spine J. https://doi.org/10.1016/j.spinee.2014.08.360.
Lemay, K.R., Tulloch, H.E., Pipe, A.L., Reed, J.L., 2019. Establishing the minimal clinically important difference for the hospital anxiety and depression scale in patients with cardiovascular disease. J. Cardiopulm. Rehabil. Prev. 39, E6–E11.
Mammen, G., Faulkner, G., 2013. Physical activity and the prevention of depression: a systematic review of prospective studies. Am. J. Prev. Med. 45, 649–657.
Naugle, K.M., Riley 3rd, J.L., 2014. Self-reported physical activity predicts pain inhibitory and facilitatory function. Med. Sci. Sports Exerc. 46, 622–629.
Nora, D.B., Becker, J., Ehlers, J.A., Gomes, I., 2005. What symptoms are truly caused by median nerve compression in carpal tunnel syndrome? Clin. Neurophysiol. 116, 275–283.
Núñez-Cortés, R., Cruz-Montecinos, C., Antúnez-Riveros, M.A., Pérez-Alenda, S., 2020. Does the educational level of women influence hand grip and pinch strength in carpal tunnel syndrome? Med. Hypotheses. https://doi.org/10.1016/j.mehy.2019.109474.
Núñez-Cortés, R., Cruz-Montecinos, C., Tapia, C., Pommer, P.P., Pérez-Alenda, S., 2022. Carpal tunnel syndrome and pain. Features and Assessments of Pain, Anaesthesia, and Analgesia. https://doi.org/10.1016/b978-0-12-818988-7.00031-5.
Núñez-Cortés, R., Cruz-Montecinos, C., Torres-Castro, R., Tapia, C., Püschel, T.A., Pérez-Alenda, S., 2021. Effects of cognitive and mental health factors on the outcomes following carpal tunnel release: a systematic review and meta-analysis. Arch. Phys. Med. Rehabil. https://doi.org/10.1016/j.apmr.2021.10.026.
Nunez, F., Vranceanu, A.-M., Ring, D., 2010. Determinants of pain in patients with carpal tunnel syndrome. Clin. Orthop. Relat. Res. 468, 3328–3332.
Palmlöf, L., Skillgate, E., Alfredsson, L., Vingård, E., Magnusson, C., Lundberg, M., Holm, L.W., 2012. Does income matter for troublesome neck pain? A population-based study on risk and prognosis. J. Epidemiol. Community Health 66, 1063–1070.
Paul, K.I., Moser, K., 2009. Unemployment impairs mental health: meta-analyses. J. Vocat. Behav. https://doi.org/10.1016/j.jvb.2009.01.001.
Phillips, C., 2017. Brain-derived neurotrophic factor, depression, and physical activity: making the neuroplastic connection, 2017 Neural Plast., 7260130
Picardo, N.E., Walker, H., Vanat, Q., Nizar, B., Madura, T., Jose, R., 2021. Service reconfiguration in the department of hand surgery during the UK COVID-19 lockdown: birmingham experience. Postgrad. Med. https://doi.org/10.1136/postgradmedj-2020-139280.
Polaski, A.M., Phelps, A.L., Kostek, M.C., Szucs, K.A., Kolber, B.J., 2019. Exercise-induced hypoalgesia: a meta-analysis of exercise dosing for the treatment of chronic pain. PLoS One 14, e0210418.
Pourmemari, M.-H., Heliövaara, M., Viikari-Juntura, E., Shiri, R., 2018. Carpal tunnel release: lifetime prevalence, annual incidence, and risk factors. Muscle Nerve 58, 497–502.
Prego-Domínguez, J., Khazaeipour, Z., Mallah, N., Takkouche, B., 2021. Socioeconomic status and occurrence of chronic pain: a meta-analysis. Rheumatology 60, 1091–1105.
Strube, P., Schöpe, T., Hölzl, A., Brodt, S., Matziolis, G., Zippelius, T.K., 2019. Influence of anxiety and depression, self-rated return-to-work problems, and unemployment on the outcome of outpatient rehabilitation after shoulder arthroscopy. Am. J. Phys. Med. Rehabil. 98, 1118–1124.
Sullivan, M.J.L., Bishop, S.R., Pivik, J., 1995. The Pain Catastrophizing Scale: Development and Validation. Psychological Assessment. https://doi.org/10.1037/1040-3590.7.4.524.
Suzuki, H., Aono, S., Inoue, S., Imajo, Y., Nishida, N., Funaba, M., Harada, H., Mori, A., Matsumoto, M., Higuchi, F., Nakagawa, S., Tahara, S., Ikeda, S., Izumi, H., Taguchi, T., Ushida, T., Sakai, T., 2020. Clinically significant changes in pain along the Pain Intensity Numerical Rating Scale in patients with chronic low back pain. PLoS One 15, e0229228.
Tan, B.-K., Smith, A.J., O'Sullivan, P.B., Chen, G., Burnett, A.F., Briggs, A.M., 2014. Low back pain beliefs are associated to age, location of work, education and pain-related disability in Chinese healthcare professionals working in China: a cross sectional survey. BMC Muscoskel. Disord. https://doi.org/10.1186/1471-2474-15-255.
Tawashy, A.E., Eng, J.J., Lin, K.H., Tang, P.F., Hung, C., 2009. Physical activity is related to lower levels of pain, fatigue and depression in individuals with spinal-cord injury: a correlational study. Spinal Cord 47, 301–306.
The Lancet, 2018. UK life science research: time to burst the biomedical bubble. Lancet 392, 187.
Thiese, M.S., Gerr, F., Hegmann, K.T., Harris-Adamson, C., Dale, A.M., Evanoff, B., Eisen, E.A., Kapellusch, J., Garg, A., Burt, S., Bao, S., Silverstein, B., Merlino, L., Rempel, D., 2014. Effects of varying case definition on carpal tunnel syndrome prevalence estimates in a pooled cohort. Arch. Phys. Med. Rehabil. https://doi.org/10.1016/j.apmr.2014.08.004.
Vindegaard, N., Benros, M.E., 2020. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. Brain Behav. Immun. 89, 531–542.
von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P., Strobe Initiative, 2014. The strengthening the reporting of observational studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Int. J. Surg. 12, 1495–1499.
Whitley, M.D., Herman, P.M., Aliyev, G.R., Sherbourne, C.D., Ryan, G.W., Coulter, I.D., 2021. Income as a predictor of self-efficacy for managing pain and for coping with symptoms among patients with chronic low back pain. J. Manip. Physiol. Ther. 44, 433–444.
WHO Commission on Social Determinants of Health, World Health Organization, 2008. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health : Commission on Social Determinants of Health Final Report. World Health Organization.
Wilson, J.M., Lee, J., Fitzgerald, H.N., Oosterhoff, B., Sevi, B., Shook, N.J., 2020. Job insecurity and financial concern during the COVID-19 pandemic are associated with worse mental health. J. Occup. Environ. Med. 62, 686–691.
Wright, M.A., Beleckas, C.M., Calfee, R.P., 2019. Mental and physical health disparities in patients with carpal tunnel syndrome living with high levels of social deprivation. J. Hand Surg. Am. 44, 335 e1–335.e9.

Musculoskeletal Science and Practice 67 (2023) 102835

Contents lists available at ScienceDirect

Musculoskeletal Science and Practice

journal homepage: www.elsevier.com/locate/msksp

Original article

Effectiveness of adding pain neuroscience education to telerehabilitation in patients with carpal tunnel syndrome: A randomized controlled trial

Rodrigo Núñez-Cortés [a,b,c], Carlos Cruz-Montecinos [b,d], Serghio Torreblanca-Vargas [e], Claudio Tapia [b,f], Miguel Gutiérrez-Jiménez [e], Pablo Torres-Gangas [c], Joaquín Calatayud [g,h,*], Sofía Pérez-Alenda [a]

[a] Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), Department of Physiotherapy, University of Valencia, Valencia, Spain
[b] Departament of Physical Therapy, Faculty of Medicine, University of Chile, Santiago, Chile
[c] Section of Clinical Research, Hospital Clínico La Florida, Santiago, Chile
[d] Section of Research, Innovation and Development in Kinesiology, Kinesiology Unit, San José Hospital, Santiago, Chile
[e] Service of Rehabilitation, Hospital Provincia Cordillera, Santiago, Chile
[f] Department of Physical Therapy, Catholic University of Maule, Talca, Chile
[g] National Research Centre for the Working Environment, Copenhagen, Denmark
[h] Exercise Intervention for Health Research Group (EXINH-RG), Department of Physiotherapy, University of Valencia, Spain

ARTICLE INFO

Keywords:
Nerve compression syndromes
Telemedicine
Health education
Exercise therapy
Preoperative period

ABSTRACT

Background: Previous studies have shown positive results of pain neuroscience education (PNE) combined with exercise in patients with chronic musculoskeletal disorders. However, the effects of this intervention in patients with carpal tunnel syndrome (CTS) admitted to a telerehabilitation program remain unexplored.
Objective: To compare the effectiveness of a 6-week telerehabilitation program based on PNE + exercise versus exercise alone on patient-reported outcomes after treatment and at 6-weeks post-treatment follow-up in patients with CTS awaiting surgery.
Design: Randomized controlled trial.
Methods: Thirty participants were randomly assigned to the PNE + exercise or exercise-only group. Outcome measures included pain intensity, pain catastrophizing, kinesiophobia, symptom severity, function, symptoms of anxiety and depression, quality of life, self-perception of improvement. Inferential analyses of the data were performed using a two-factor mixed analysis of variance.
Results: Twenty-five participants completed the study. A significant time × group interaction with a large effect size was observed for kinesiophobia ($F = 6.67$, $p = 0.005$, $\eta p^2 = 0.225$) and symptom severity ($F = 4.82$, $p = 0.013$, $\eta p^2 = 0.173$). No significant interaction was observed for the other variables ($p > 0.05$). A significant difference in self-perceived improvement was observed in favor of the PNE + exercise group after treatment ($p < 0.05$). Although there were significant and clinically relevant improvements within the PNE + exercise group in pain intensity and catastrophizing, there were no significant differences between the groups.
Conclusions: The addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity and greater self-perceived improvement in patients with CTS awaiting surgery. This study highlighted the benefits of including PNE in telerehabilitation interventions for patients with CTS.

1. Introduction

Carpal tunnel syndrome (CTS) is a frequent cause of disability that occurs when the median nerve is compressed by inflammation or narrowing at the level of the carpal tunnel (Núñez-Cortés et al., 2022). The most common symptoms of CTS are the gradual onset of tingling or numbness in the region of the median nerve and weakness of the thumb (Erickson et al., 2019; Thiese et al., 2014). The severity of symptoms and pain in CTS may be modulated by different psychosocial variables (e.g. catastrophizing, depression and anxiety) (De et al., 2013; Jerosch-Herold

* Corresponding author. Department of Physiotherapy, University of Valencia, C/ Gascó Oliag 5. PC, 46010, Valencia, Spain.
E-mail address: joaquin.calatayud@uv.es (J. Calatayud).

https://doi.org/10.1016/j.msksp.2023.102835
Received 25 May 2023; Received in revised form 4 July 2023; Accepted 26 July 2023
Available online 28 July 2023

et al., 2017; Nunez et al., 2010).

Carpal tunnel release is usually indicated in cases where symptoms do not improve after six weeks of non-surgical treatment or for those who have ongoing symptoms or atrophy of the thumb musculature (Chandra et al., 2013; Erickson et al., 2019). Nevertheless, the literature suggests that conservative treatment should be considered as a first-line option before surgery, even in severe cases of CTS (Fernández-de-Las Peñas et al., 2015). Nerve and tendon gliding exercises are often included as part of multimodal treatment to improve function and reduce pain and symptom severity (Fernández-de-Las Peñas et al., 2015; Hamzeh et al., 2021; Horng et al., 2011). In fact, exercise-based physical therapy can produce similar results to surgery in terms of pain and function (Fernández-de-Las Peñas et al., 2015). In addition, encouraging physical activity may be a valuable strategy for reducing pain intensity and depressive symptoms in patients with CTS awaiting surgery (Núñez-Cortés et al., 2023).

The high healthcare demand caused by the COVID-19 pandemic forced many hospitals around the world to suspend elective or non-urgent hand surgeries (Picardo et al., 2021; Toia et al., 2021). Importantly, this situation may lead to increased attention to pharmaceutical alternatives for pain management, particularly opioid treatments (Choe et al., 2023; Karos et al., 2020). In this scenario, the use of telerehabilitation allowed to improve the accessibility of rehabilitation care, offering physiotherapists an accessible and low-cost opportunity to educate patients, improve compliance with therapeutic exercise and monitor patients' progress through remote consultations in musculoskeletal conditions (Turolla et al., 2020; Zhang et al., 2022). Indeed, telerehabilitation has demonstrated some clinical and functional outcomes as effective as face-to-face interventions, making it a good alternative to improve accessibility to rehabilitation care in a context of social distancing (Cifu and Eapen, 2021). However, to our knowledge, telerehabilitation in patients with CTS remains unexplored.

A recent meta-analysis identified depressive symptoms, anxiety and catastrophizing as important predictors of poor postoperative outcomes in patients with CTS (Núñez-Cortés et al., 2021), therefore, these variables should be addressed by clinicians at the preoperative level. In addition, some patients with CTS awaiting surgery during the COVID-19 pandemic may present with high levels of pain, catastrophizing and depressive symptoms, which may be related to a low level of physical activity and a low educational level (Núñez-Cortés et al., 2023). In this context, it is necessary to evaluate the efficacy of preoperative telerehabilitation programs with biopsychosocial approaches aimed at both increasing physical activity levels and providing the knowledge and skills needed to understand pain, in the short term, so that patients can better cope with surgery. Considering that the symptoms of CTS may be modulated by different psychosocial variables (De et al., 2013; Jerosch-Herold et al., 2017; Nunez et al., 2010), the treatment approaches, including telerehabilitation, need to move away from the biomedical bubble (The Lancet, 2018). In this regard, pain neuroscience education (PNE), which aims to facilitate individuals to change their negative beliefs related to pain, could be a promising alternative (Louw et al., 2016; Moseley and Butler, 2015). Recent meta-analyses have concluded that PNE has positive short-term effects in achieving improvements in pain, disability, kinesiophobia, and pain catastrophizing in patients with chronic musculoskeletal disorders, especially when combined with exercise (Siddall et al. (2022); Watson et al. (2019)). Although international clinical guidelines recommend exercise as a key element in the management of chronic musculoskeletal pain (Daenen et al., 2015), exercise combined with PNE in telerehabilitation programs is scarce.

The addition of PNE to an exercise-based telerehabilitation program may be an innovative alternative to reduce kinesiophobia and negative beliefs related to pain (Taulaniemi et al., 2020), improving the physical and mental health of patients with CTS who have not been able to access face-to-face treatment. Therefore, the aim of this study was to compare the effectiveness of a 6-week telerehabilitation program based on PNE plus exercise versus exercise alone on patient-reported outcomes after treatment (week 6) and at six weeks post-treatment follow-up (week 12) in patients with CTS awaiting surgery.

2. Methods

2.1. Participants and design

A randomized controlled trial (RCT) with two parallel groups was performed. Participants with a diagnosis of CTS awaiting surgery in two hospitals of the Chilean public health system (Hospital Clínico la Florida and Hospital Provincia Cordillera), who were invited to participate between January and June 2022, were candidates for the present study. The inclusion criteria were: i) age between 18 and 60 years; ii) medical diagnosis of moderate or severe CTS in accordance with the clinical practice guidelines of the Academy of Orthopaedic Physical Therapy and the Academy of Hand and Upper Extremities Physical Therapy (i.e. history, physical examination and tests/measurements) (Erickson et al., 2019); iii) symptoms of at least three months duration, iv) unilateral or bilateral symptoms; v) availability of a smartphone with Internet access, and agreement to participate in the study. Exclusion criteria were: inability to understand instructions, neurological conditions of the central nervous system (e.g. stroke, spinal cord injury), patients on treatment with alternative therapies, previous participation in a telerehabilitation program, and previous surgery on the affected upper limb. All participants were informed about the objective and procedures of the research and gave written informed consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the South East Metropolitan Health Service (ID: CEC-08-04/RAD-03), Santiago de Chile. The study was registered on ClinicalTrials.gov (NCT05184413) and adheres to the CONSORT Statement (Moher et al., 2012).

2.2. Randomization and allocation

After receiving the surgical waiting list from a physician not involved in the study in each hospital, the investigator involved in the recruitment process randomly contacted potential participants by telephone. The first 30 participants who agreed to participate and met the selection criteria were randomized following a simple randomization procedure using the Randomization software (www.randomization.com). A 1:1 allocation ratio to a PNE + exercise group or to an exercise-only group was considered. The randomization sequence was determined prior to the start of the baseline assessments and was known only to an external research assistant who had no access to participant characteristics and was not involved in the assessment or study intervention. Allocation remained concealed and stored in the cloud until the end of the intervention and collection of all study data. When a participant was enrolled in the study, the external research assistant informed the therapist of the assigned intervention group.

2.3. Telerehabilitation program

The telerehabilitation program was conducted using a smartphone videoconferencing method via WhatsApp™ and lasted 6 weeks. Both groups received three telerehabilitation sessions supervised by physiotherapists every 15 days. In the first session, all participants received an individual self-managed exercise program (see below). The PNE + exercise group also received three individual PNE sessions before each exercise session (on the same day). Participants in the study did not have to stop taking any pain medication at the time of the study.

2.4. Exercise program

The type and amount of exercises were the same for both groups. The exercise was multicomponent and included aerobic exercise (Hoffman and Hoffman, 2007), digital flexor tendon gliding (Horng et al., 2011),

neurodynamic home exercises (Hamzeh et al., 2021), and self-stretching (Shem et al., 2020). Each participant received printed material with the different types of exercises and videos of the execution of each exercise as reinforcement. The exercise program and the characteristics of each exercise are shown in Fig. 1 and Table 1, respectively. In the first videoconference, the physiotherapist demonstrated the exercises and corrected each participant to ensure correct technique and to check that the participants were confident to perform the exercises independently at home. Each participant received on the day of the initial assessment a folder with printed material with the different types of exercises and a sheet to record compliance and prescription of each exercise. Participants were instructed to perform each exercise three days a week for 6 weeks, with a 48-h interval between each session. Each exercise session lasted approximately 30 min. A total of 18 exercise sessions were performed (15 self-managed and 3 supervised). Supervization of the exercises was performed every 15 days. In case of bilateral symptoms, participants were instructed to perform the exercises with both upper extremities.

2.5. Pain neuroscience education

The PNE + exercise group additionally received three individual 40-min PNE sessions every 15 days for 6 weeks, via WhatsApp™ video conferencing. The intervention was performed by a physiotherapist with seven years of clinical experience and training in PNE (Butler and Lorimer Moseley, 2013). Participants were instructed to be in a room with no distractions for the videoconferencing session. In addition, audiovisual material was sent between each session (i.e., two videos with examples and metaphors, 6 min each) to reinforce the key contents of the PNE. The total duration of the intervention was 132 min (120 min of synchronous pain education and 12 min of asynchronous material). The key concepts addressed during the online sessions are presented in Table 1. At the end of the last session, as feedback, a multiple-choice and true/false questionnaire was used to assess perceived knowledge and self-management skills. This assessment has not yet been validated and was suggested by Ziegler et al. (available in the Supplementary Material) to motivate patients/participants to learn (Ziegler et al., 2022). For evaluation purposes in our study, the percentage of correct answers was reported.

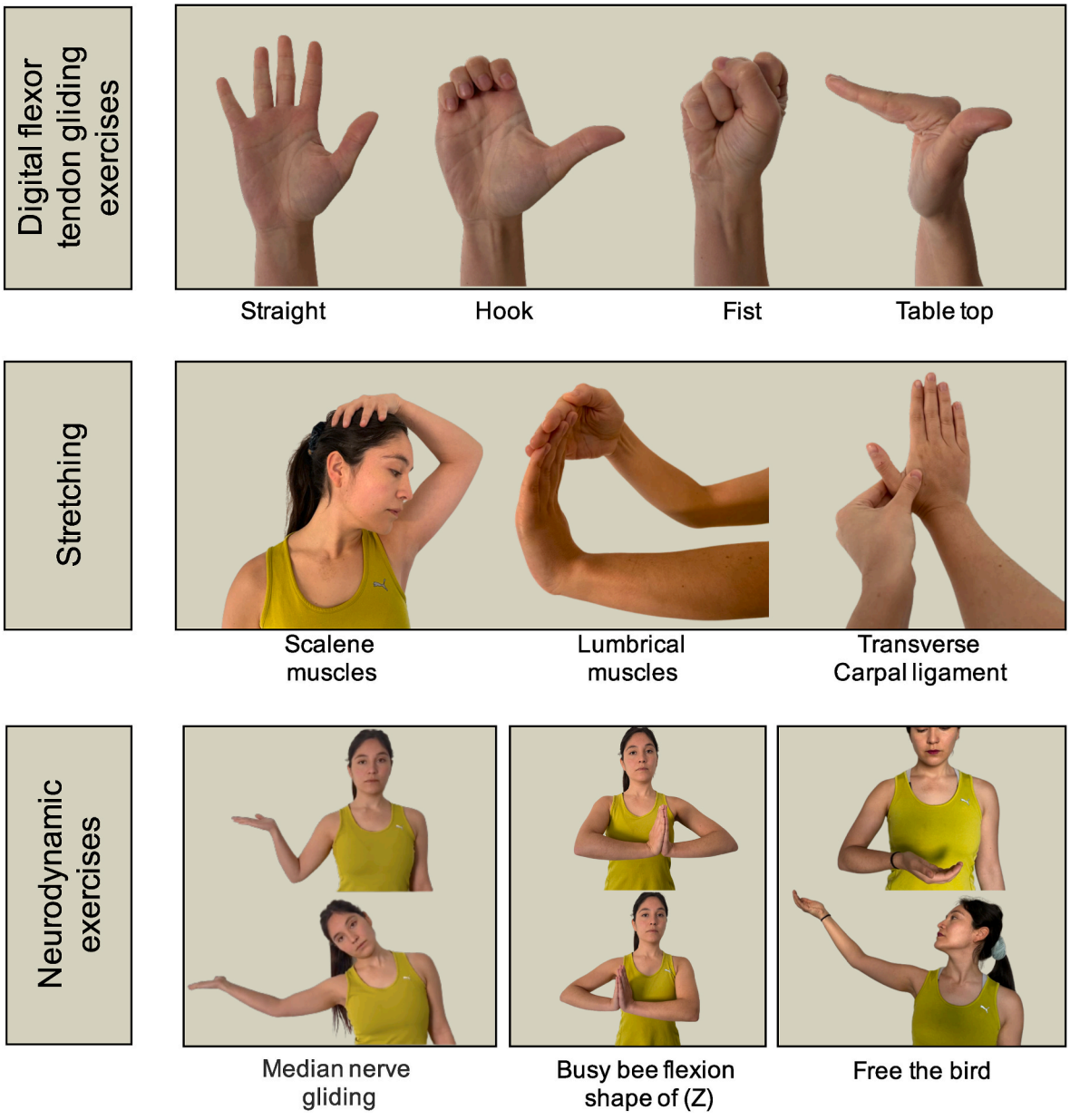


Fig. 1. Exercises included in the telerehabilitation program.

Table 1
Intervention characteristics.

INTERVENTIONS	WEEKS						CHARACTERISTICS
	1	2	3	4	5	6	
Brisk walking (all patients) [a]							
15 min at moderate intensity	●	●					Moderate intensity was determined by the Talk test (i.e. can hold a conversation but not sing).
20 min at moderate intensity			●	●			
25 min at moderate intensity					●	●	
Digital flexor tendon gliding exercises (all patients) [a]							
Straight	●	●	●	●	●	●	Maximum number of repetitions up to a perceived exertion on the Borg CR10 scale of 4/10 (week 1–2), 5/10 (week 3–4) and 6/10 (week 5–6).
Hook	●	●	●	●	●	●	
Fist	●	●	●	●	●	●	
Table top	●	●	●	●	●	●	
Stretching (all patients) [a]							
Scalene muscles	●	●					45 s 2 times
Transverse carpal ligament			●	●	●	●	30 s 4 times
Lumbrical muscles			●	●	●	●	45 s 2 times
Neurodynamic exercise (all patients) [a]							
Median nerve gliding exercise	●	●					Each exercise included 3 sets of 10 repetitions.
Busy bee flexion shape of (Z) exercise			●	●			
Free the bird exercise					●	●	
Pain Neuroscience Education (only in experimental group)							
Neurobiology concepts: pain pathways; the synapse; the neuron; pain is a function of the body's alert system.	●						Three synchronous individual sessions of 40 min by interactive videoconference plus asynchronous reinforcement videos between each session (two 6-min videos). Theoretical information was illustrated with images, examples and metaphors (visual support)
Examples on "Pain does not always equate to tissue injury".	●						
Pain is a nerve sensitivity: concept of central sensitization and pain modulation, i.e., descending nociceptive inhibition and facilitation.	●						
Reinforcement videos (asynchronous).		●					
Review of content covered in previous sessions; Dispelling common misconceptions about pain.			●				
Influencing/sustaining factors: Pain can be positively and negatively influenced by many factors, e.g., influence of stress, emotions, thoughts, quality of sleep and expectations.			●				
Examples of neuroplastic changes due to experience and learning.			●				
Reinforcement videos (asynchronous).				●			
Review of content covered in previous sessions.					●		
Concepts related to self-management perception: strategies to help manage pain, e.g., importance of movement and relaxation/breathing techniques.					●		
Learning assessment [b]					●		

[a] Three days a week (self-managed), each session was separated by 48 h. Supervision for reinforcement and adjustment of progressions every 15 days by interactive videoconference via WhatsApp™. Restriction: Pain intensity >4 during exercise, on a numerical pain rating scale (0–10).

[b] A multiple-choice and true/false questionnaire to assess knowledge and perceived self-management skills was used as feedback at the end of the intervention (Available in the previous study by Ziegler et al., 2022).

2.6. Usability

At the end of each treatment, all participants completed the System Usability Scale (SUS) to assess their experience with the telerehabilitation system (Jordan et al., 1996), to ensure that both groups perceived the same subjective usability of telerehabilitation. The SUS is a simple 10-item scale that provides an overview of subjective usability evaluations (range, 0–100). Scores between 68 and 80 suggest a "good" useable interactive system and scores above 80 can be considered "excellent" (Bangor et al., 2008).

2.7. Clinical outcome measures

The evaluations of the participants were performed by an evaluator from each hospital who was unaware of the group allocation. The physiotherapist who performed the interventions was not involved in the evaluation process. In the first interview, participants completed self-reported information regarding age, sex, duration of CTS (months), educational level (primary, secondary or higher), analgesic intake and minutes of moderate physical activity per week. Participants were assessed before starting treatment (baseline) and reassessed after treatment (week 6) and at six weeks post-treatment follow-up (week 12). If there were symptoms in both hands, the hand with the more severe symptoms was evaluated because it was the hand that was to be operated on. Compliance with the exercise program was assessed by means of a record sheet to be filled out by the patient at home. To define 100% adherence to the exercise program, both the number of sessions completed (out of a total of 18 sessions) and the number of exercises completed within each session were considered.

2.8. Pain intensity

The primary outcome measure was pain intensity assessed using the numeric pain rating scale (NPRS) (Dworkin et al., 2005). Participants were asked to rate the average pain intensity during the seven days prior to the assessment on a defined 0 to 10-point scale, where 0 represents "no pain" and 10 is "worst pain imaginable." The minimum clinically important difference (MCID) for this scale is 2 points (Dworkin et al., 2008).

2.9. Pain catastrophizing

The Pain Catastrophizing Scale (PCS) was used to measure catastrophic thinking in response to pain through 13 statements with four possible options, from 1 "not at all" to 4 "all the time" (Sullivan et al., 1995). Higher scores (range, 0–52) indicate greater pain catastrophizing. The Spanish version of the PCS has shown adequate internal consistency and test-retest reliability (García Campayo et al., 2008). The minimum detectable change (MDC) of the PCS is 10.45 points (García

Campayo et al., 2008).

2.10. Kinesiophobia

The Spanish version of the Tampa Scale for Kinesiophobia-11 (TSK-11) was used to measure fear of movement (Gómez-Pérez et al., 2011). The TSK-11 has demonstrated acceptable consistency and validity (Gómez-Pérez et al., 2011). Total scores range from 11 to 44, with higher values representing worse outcome (i.e. greater interference of pain with fear avoidance behavior). The MDC for the TSK-11 is 5.6 points in people with chronic pain(Hapidou et al., 2012).

2.11. Severity of symptoms and function

The Boston Carpal Tunnel Questionnaire (BCTQ) measures self-reported functional status (BCTQ-FS) and severity of symptoms (BCTQ-SSS) (Levine et al., 1993). The BCTQ-SSS consists of 11 questions, each question provides 5 response choices, from 1 (no symptoms) to 5 (most severe/often). The BCTQ-FS includes 8 questions assessing difficulty with daily tasks. These responses are also scored on a 5-point scale (1–5). The MCID has been determined to be 0.74 points for the function subscale and 1.14 points for the symptom severity subscale (Kim and Jeon, 2013).

2.12. Mental health

The Hospital Anxiety and Depression Scale (HADS) was used to assess mental health using two 0–21 point subscales (anxiety and depression) (Zigmond and Snaith, 1983). The score is obtained by summing the items of each subscale, with higher values representing a worse outcome. A score of 0–7 is considered normal, 8–10 is considered a possible case and ≥11 indicates a probable clinical case of anxiety or depression (Zigmond and Snaith, 1983). The MCID is 1.67 points for the anxiety subscale and 1.85 for the depression subscale (Lemay et al., 2019).

2.13. Quality of life

The EuroQol5-dimensions (EQ-5D) was used as a self-assessed health-related quality of life questionnaire (EuroQol Group, 1990). The EQ-5D essentially consists of two pages: First, the EQ-5D description system, which provides a single index value for health status where a score of 1 represents "perfect health", 0 is a health state equivalent to death and values below 0 represent "worse than death" states. Second, a visual analogue scale (EQ-VAS) numbered from 0 "the worst health you can imagine" to 100 "the best health you can imagine".

2.14. Self-perception of improvement

The Patient Global Impression of Change Scale (PGICS) consists of two subscales, one categorical and one quantitative (Perrot and Lantéri-Minet, 2019). The categorical scale is a 7-point verbal scale with the following options: i) "very much improved", ii) "much improved", ii) "minimally improved", iv) "no change", v) "worse", vi) "much worse", and vii) "very much worse". The categories "very much improved" and "much improved" are considered a clinically significant improvement (Perrot and Lantéri-Minet, 2019). The quantitative scale consists of a line from 0 to 10, where 0 = much better and 10 = much worse.

2.15. Sample size calculation

An a priori sample size calculation was performed in G*Power software (version 3.1, Universität Düsseldorf, Germany) using the fixed effects ANOVA statistical test. An effect size of f = 0.685 was estimated based on a previous study on the effectiveness of PNE, which found a between-group difference greater than the MCID of 2 points on the NPRS with a large effect size (d = 1.37) (Bodes Pardo et al., 2018). The effect size transformation was performed with an online calculator (Lenhard and Lenhard, 2017). With α err prob = 0.05 and power (β-1 err prob) = 0.8, a total of 24 patients were required. The sample size was increased by 20% to account for potential dropouts during the follow-up period. The resulting sample size was 30 participants.

2.16. Statistical methods

Statistical analysis was performed with SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The normality of the data was tested using the Shapiro-Wilk test. Mean ± standard deviation (SD) or median and interquartile range (IQR) values were calculated for continuous data according to parametric or nonparametric distribution, respectively. The significance level was set at 0.05 for all statistical analyses.

Baseline differences between groups were compared using the Chi-square test for distributions of categorical variables and the independent *t*-test for continuous variables. If the data did not have a normal distribution, the Mann Whitney *U* test was used. The mean difference (MD) between groups was calculated with a 95% confidence interval (95% CI). Inferential analyses of the data were performed using a two-factor mixed analysis of variance (ANOVA): i) a between-subjects factor with two categories (two treatment groups); ii) a within-subject factor with three categories (three measures of time). When a significant interaction between factors was found, the simple mean effect (one-way ANOVA for each group) and simple pairwise comparisons (unpaired *t*-test between the two groups) were used. The chi-square test and independent *t*-test were used to explore differences between groups for the categorical and continuous PGICS, respectively, at each time measurement. Differences between usability and adherence at the end of treatment were tested with the independent *t*-test or Mann Whitney *U* test according to the distribution. The partial eta squared (ηp^2) values were calculated as a measure of the effect size and the results were interpreted as small (>0.01), medium (>0.06) and large (>0.14) (Cohen, 2013).

3. Results

Twenty-five participants completed the study and their data were used in the final analyses (Fig. 2). No significant differences were observed between the PNE + exercise group and the exercise group before starting the intervention (Table 2). The mean usability of the interaction system for telerehabilitation was "excellent" in both groups (SUS score >80). No significant differences were observed between groups ($p > 0.05$) (Table 3). Compliance with the telerehabilitation program was over 80% in both groups, with no significant differences ($p > 0.05$) (Table 3). In the PNE + exercise group, the assessment of learning after pain education was 88% (IQR = 19) for the assessment of knowledge of key concepts and 100% (IQR = 17) for perceived self-management (Table S1).

3.1. Pain intensity

The ANOVA model indicated a significant main effect of the time factor ($F = 3.52$, $p = 0.038$, $\eta p^2 = 0.133$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 1.81$, $p = 0.174$, $\eta p^2 = 0.073$). Significant and clinically relevant differences in NPRS were observed at week 6 in the PNE + exercise group (MD: 2.0 points, 95% CI: 3.8 to −0.2). The exercise group showed no improvement at any time point (Table 4).

3.2. Pain catastrophizing

The ANOVA model indicated a significant main effect of the time factor ($F = 9.43$, $p < 0.001$, $\eta p^2 = 0.291$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 2.27$, $p = 0.115$, $\eta p^2 = 0.090$). Significant and clinically relevant differences from baseline were observed in PCS at week 6 (MD: 13.2 points 95%CI: 21.4

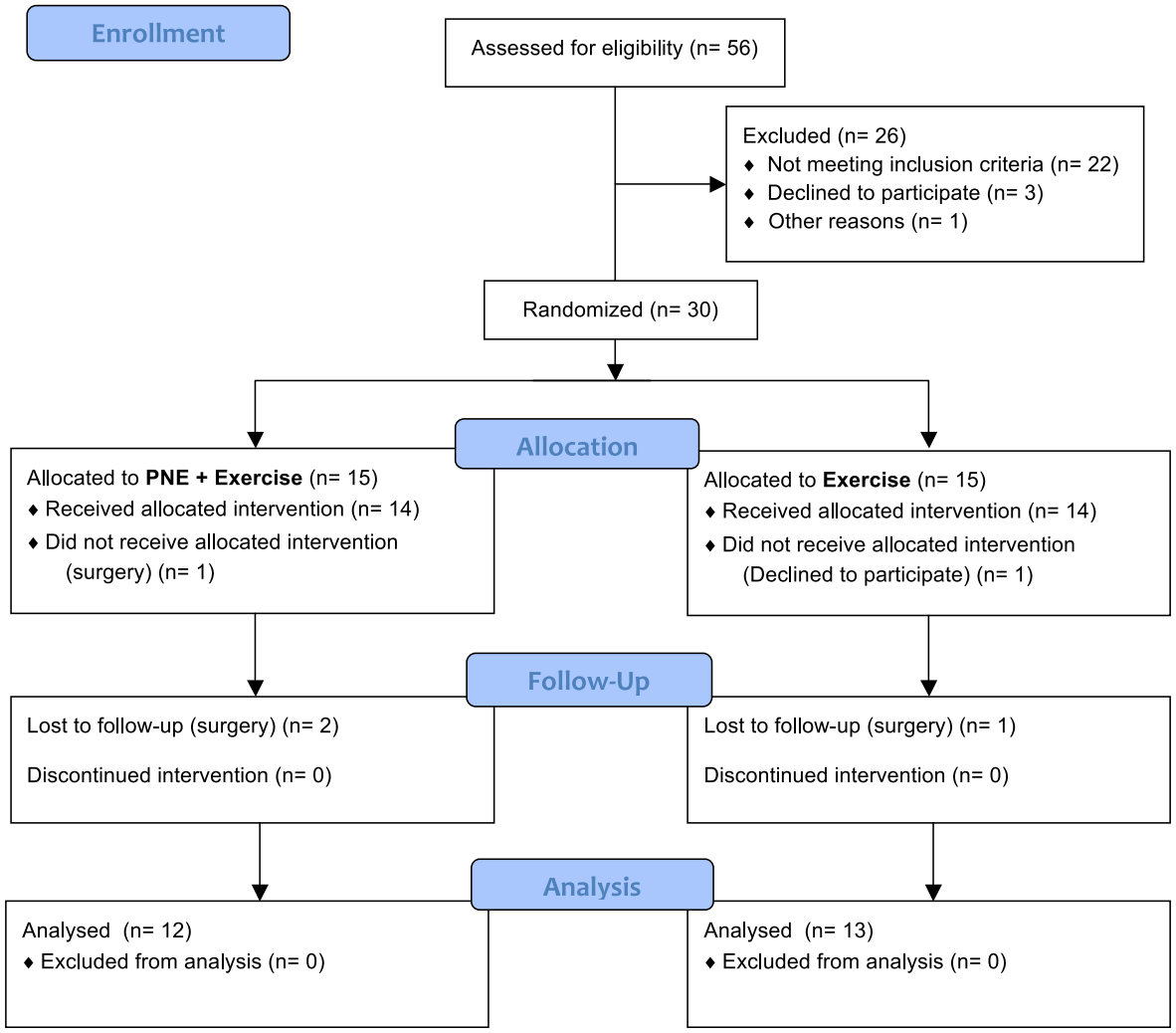


Fig. 2. CONSORT flowchart for the selection of participants.
Note: PNE, Pain Neuroscience Education.

to −4.9) and week 12 (MD: 8.8 points, 95%CI: 17.1 to −0.4) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4).

3.3. Kinesiophobia

The ANOVA model indicated a significant main effect of the time factor ($F = 6.65$, $p = 0.003$, $\eta p^2 = 0.221$) and on the group factor ($F = 5.41$, $p = 0.022$, $\eta p^2 = 0.074$). Additionally, a significant time × group interaction with a large effect size was observed ($F = 6.67$, $p = 0.005$, $\eta p^2 = 0.225$). Significant and clinically relevant differences from baseline were observed in TSK-11 at week 6 (MD: 6.1 points 95%CI: 10.3 to −1.8) and week 12 (MD: 7.7 points, 95%CI: 12.8 to −2.4) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4). At weeks 6 and 12, the mean between-group difference in TSK-11 was −5.2 points [95% CI: 9.7 to −0.6; $p = 0.028$] and −5.7 points [95% CI: 10.8 to −0.5; $p = 0.034$], respectively.

3.4. Function

The ANOVA model indicated a significant main effect of the time factor ($F = 5.02$, $p = 0.014$, $\eta p^2 = 0.179$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 1.25$, $p = 0.296$, $\eta p^2 = 0.051$). Significant differences from baseline were observed in BCTQ-FS at week 6 in the PNE + exercise group (MD: 0.7 points, 95% CI: 1.2 to −0.1) but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 4).

3.5. Severity of symptoms

The ANOVA model indicated a significant main effect of the time factor ($F = 11.32$, $p = 0.003$, $\eta p^2 = 0.330$). In addition, a significant time × group interaction with a large effect size was observed ($F = 4.82$, $p = 0.013$, $\eta p^2 = 0.173$). Significant differences from baseline were observed in BCTQ-SSS at week 6 (MD: 0.9 points 95%CI: 1.4 to −0.4) and week 12 (MD: 0.6 points, 95%CI: 1.0 to −0.2) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4).

3.6. Mental health

The ANOVA model indicated a non-significant main effect of the time factor and group factor in both subscales ($p > 0.05$). Additionally, a non-significant time × group interaction was observed for both subscales (anxiety: $F = 1.50$, $p = 0.235$, $\eta p^2 = 0.061$; depression: $F = 1.29$, $p = 0.286$, $\eta p^2 = 0.053$). Clinically relevant improvements in both subscales of the HADS were observed at week 6 in the PNE + exercise group, but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 4).

Table 2
Baseline comparison between groups.

Characteristics	PNE + Exercise (n = 12)	Exercise (n = 13)	Valor-p
Age (years)	45.9 ± 7.5	43.6 ± 8.1	0.469
Female gender (%)	91.7%	92.3%	0.740
BMI (kg/m^2)	29.7 ± 5.2	33.3 ± 7.3	0.177
Duration of CTS (months)	36 (51)	43 (45)	0.810
Symptom distribution			
Bilateral symptoms	33.3%	30.8%	0.891
Unilateral symptoms	66.7%	69.2%	
Educational level (%)			
Primary	41.7%	53.8%	0.418
Secondary/Higher	58.3%	46.2%	
Physical Activity (minutes)	37.5 (150)	45 (165)	0.810
Patients taking analgesics (%)	50%	69%	0.327
NPRS (0–10)	6.8 ± 1.9	5.8 ± 2.1	0.234
PCS (0–52)	25.5 ± 11.8	26.4 ± 15.9	0.866
TSK-11 (0–44)	31.1 ± 5.6	29.4 ± 4.3	0.404
BCTQ-FS (0–5)	3.0 ± 0.6	3.1 ± 0.5	0.769
BCTQ-SSS (0–5)	3.4 ± 0.7	3.0 ± 0.5	0.059
HADS-A (0–21)	10.4 ± 4.2	9.5 ± 4.3	0.580
HADS-D (0–21)	7.5 ± 4.4	5.7 ± 3.9	0.284
EQ5D (0–1)	0.5 ± 0.2	0.6 ± 0.2	0.424
EQVAS (0–100)	56.3 ± 13.9	57.2 ± 16.4	0.883

Data are expressed as mean ± SD or median (interquartile range).
Abbreviations: BMI, Body Mass Index; BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11,Tampa Scale for.

Table 3
Comparison between groups for impression of change, usability and adherence.

Outcome	PNE + TE (n = 12)	TE (n = 13)	Valor-p	Effect size
Week 6 (after treatment)				
PGIC (0–10)	3.1 ± 1.6	4.3 ± 1.1	**0.037***	0.893
PGIC (% "very much improved" or "much improved")	66.7	23.1	**0.028***	1.050
SUS (0–100)	83.8 ± 10.7	81.2 ± 8.6	0.508	0.270
Adherence (%)	84.0 (7.5)	92.0 (27.5)	0.406	0.153
Week 12 (follow-up)				
PGIC (0–10)	3.7 ± 2.7	3.8 ± 2.2	0.857	0.073
PGIC (% "very much improved" or "much improved")	50	38.5	0.561	0.259

Data are expressed as mean ± SD or median (interquartile range).
Abbreviation: SUS, System Usability Scale; PNE, Pain Neuroscience Education; PGIC, Patients' Global Impression of Chang scale; TE, Therapeutic Exercise. The parametric (d) and nonparametric (r) effect size of d and r can be interpreted as follows: d = 0.2 and r = 0.1, small; d = 0.5 and r = 0.3, medium; d = 0.8 and r = 0.5, large, respectively. Bold type denotes statistically significant differences.

3.7. Quality of life

The ANOVA model indicated a non-significant main effect of the time factor in both subscales ($p > 0.05$). Only a significant main effect of the group factor on the EQ-VAS was observed ($F = 5.56$, $p = 0.021$, $\eta p^2 = 0.075$), but a non-significant time × group interaction was observed for both EQ-5D ($F = 1.47$, $p = 0.240$, $\eta p^2 = 0.060$) and EQ-VAS ($F = 2.93$, $p = 0.063$, $\eta p^2 = 0.113$) (Table 4). At week 12, a mean difference between groups of 15.7 points [95% CI: 3.57 to 27.85, $p = 0.013$] was obtained on the EQ-VAS.

3.8. Self-perception of improvement

Significant differences were observed in favor of the PNE + exercise group after treatment on the continuous subscale (0–10) of the PGICS (3.1 ± 1.6 vs 4.3 ± 1.1, $p = 0.037$, ES = 0.893). Furthermore, on the categorical subscale, 66.7% of patients in the PNE + exercise group reported clinically significant improvement (i.e. categories "very much improved" and "much improved"), compared to 23.1% in the exercise group (chi-square = 4.812, $p = 0.023$). No significant differences were observed between groups at week 12 ($p > 0.05$) (Table 3).

4. Discussion

This RCT compared two telerehabilitation programs, combined treatment with PNE + exercise versus isolated exercise in patients with CTS awaiting surgery in two hospitals of the Chilean public health system. Overall, the proposed interactive system for telerehabilitation had excellent usability and adherence was over 80% in both groups. Our results showed that a combined PNE + exercise program was more effective than exercise alone in reducing kinesiophobia and symptom severity. In addition, self-perceived improvement was greater in the PNE + exercise group compared to that of the exercise-only group at the end of treatment. In the last decade there have been an increasing number of systematic reviews and meta-analyses on telerehabilitation. To date, the available systematic reviews on the effects of PNE have not included RCTs in patients with CTS in a telerehabilitation setting (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). This study is therefore a novelty in this field.

Several studies have reported positive effects of PNE on pain, function, and some psychosocial variables in patients with musculoskeletal conditions (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). Some of our results are consistent with the available evidence. For example, Watson et al., 2019 found in their meta-analysis that the effect of PNE treatment for kinesiophobia in adults with chronic musculoskeletal pain was clinically relevant in the short term. Siddall et al., 2022 also found in their meta-analysis that the combination of PNE and exercise resulted in greater improvements in kinesiophobia than exercise

Table 4
Outcome measures during the follow-up period and results of the time x group comparative analysis.

Outcome	Follow-up	PNE + Exercise (n = 12)		Exercise (n = 13)		ANOVA Interaction Effect		
		Mean ± SD	Mean within-group difference [95% CI]	Mean ± SD	Mean within-group difference [95% CI]	F	p-value	η^2p
NPRS (0–10)	Baseline	6.8 ± 1.9		5.8 ± 2.1		1.81	0.174	0.073
	Week 6	4.8 ± 1.7	−2.0 [-3.8 to −0.2]	5.5 ± 1.4	−0.2 [-1.9 to 1.5]			
	Week 12	5.4 ± 2.0	−1.3 [-3.4 to 0.8]	4.9 ± 2.5	−0.9 [-2.8 to 1.2]			
PCS (0–52)	Baseline	25.5 ± 11.8		26.4 ± 15.9		2.27	0.115	0.090
	Week 6	12.3 ± 6.8	−13.2 [-21.4 to −4.9]	22.2 ± 13.8	−4.2 [-12.2 to 3.6]			
	Week 12	16.8 ± 11.5	−8.8 [-17.1 to −0.4]	19.8 ± 15.7	−6.6 [-14.6 to 1.4]			
TSK-11 (0–44)	Baseline	31.1 ± 5.6		29.4 ± 4.3		6.67	**0.005****	0.225
	Week 6	25.0 ± 5.3	−6.1 [-10.3 to −1.8]	30.2 ± 5.7	0.8 [-3.3 to 4.8]			
	Week 12	23.4 ± 5.9	−7.7 [-12.8 to-2.4]	29.1 ± 6.6	−0.3 [-5.2 to 4.6]			
BCTQ-FS (0–5)	Baseline	3.0 ± 0.6		3.1 ± 0.5		1.25	0.296	0.051
	Week 6	2.3 ± 0.5	−0.7 [-1.2 to −0.1]	2.7 ± 0.7	−0.4 [-0.8 to 0.2]			
	Week 12	2.7 ± 0.8	−0.3 [-0.9 to 0.3]	2.5 ± 0.9	−0.5 [-1.1 to 0.1]			
BCTQ-SSS (0–5)	Baseline	3.4 ± 0.7		3.0 ± 0.5		4.82	**0.013***	0.173
	Week 6	2.5 ± 0.5	−0.9 [-1.4 to −0.4]	2.8 ± 0.7	−0.2 [-0.6 to 0.3]			
	Week 12	2.8 ± 0.8	−0.6 [-1.0 to −0.2]	2.6 ± 0.8	−0.4 [-0.8 to 0.0]			
HADS-A (0–21)	Baseline	10.4 ± 4.2		9.5 ± 4.3		1.50	0.235	0.061
	Week 6	8.1 ± 3.8	−2.3 [-4.5 to −0.2]	9.2 ± 4.1	−0.3 [-2.4 to 1.7]			
	Week 12	8.8 ± 5.1	−1.6 [-3.8 to 0.6]	8.5 ± 4.8	−0.9 [-3.0 to 1.2]			
HADS-D (0–21)	Baseline	7.5 ± 4.4		5.7 ± 3.9		1.29	0.286	0.053
	Week 6	5.2 ± 3.9	−2.3 [-5.4 to 0.7]	5.4 ± 3.6	−0.3 [-3.2 to 2.6]			
	Week 12	6.1 ± 4.5	−1.4 [-3.7 to 0.8]	4.5 ± 4.1	−1.2 [-3.4 to 1.0]			
EQ5D (0–1)	Baseline	0.51 ± 0.2		0.57 ± 0.2		1.47	0.240	0.060
	Week 6	0.62 ± 0.2	0.11 [-0.1 to 0.3]	0.55 ± 0.2	−0.02 [-0.2 to 0.2]			
	Week 12	0.61 ± 0.2	0.10 [0.0 to 0.2]	0.56 ± 0.2	−0.01 [-0.2 to 0.1]			
EQVAS (0–100)	Baseline	56.3 ± 13.9		57.2 ± 16.4		2.93	0.063	0.113
	Week 6	69.0 ± 10.3	13.7 [0.2 to 27.1]	60.8 ± 16.8	3.6 [-9.3 to 16.5]			
	Week 12	70.5 ± 14.8	14.3 [0.8 to 27.7]	55.6 ± 15.9	−1.5 [-14.1 to 11.3]			

Abbreviations: BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11, Tampa Scale for Kinesiophobia-11; 95%CI, 95% confidence interval. *Statistically-significant difference ($p < 0.05$); **Statistically-significant difference ($p < 0.01$); Bold type denotes statistically significant differences.

alone in the same population. Based on our results, we confirm that PNE + exercise as a telerehabilitation modality is a useful intervention to reduce fear of movement in patients with CTS. This could be explained by the fact that the aim of a combined therapy is to reconceptualize pain, reducing the threat value and promoting gradual and safe exercise (Louw et al., 2021). On the other hand, there was a significant improvement in symptom severity reduction in favor of the PNE + exercise group compared to exercise alone. However, the intra-group difference in the BCTQ-SSS was not superior to the MCID (Kim and Jeon, 2013). In relation to self-perception of improvement after treatment, 66.7% of participants in the PNE + exercise group considered that they had much improved or very much improved after treatment. In addition, half of the participants maintained this improvement at the 6-week follow-up, which is considered a clinically significant improvement for this variable (Perrot and Lantéri-Minet, 2019).

In contrast to these findings, most systematic reviews report improvements in pain or function with PNE in patients with chronic musculoskeletal pain (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). For example, Malfliet et al. (2018) conclude in a multicenter RCT that combined treatment including PNE appears to be more effective than conventional physical therapy in improving pain and disability, among other outcomes. In fibromyalgia patients, Amer-Cuenca et al. (2020) found that higher doses of PNE (270 min) produced greater improvements in pain intensity than lower doses of PNE (90 min). In our study, 120 min of PNE were delivered by videoconference plus 12 min of reinforcement videos. With this in mind, higher doses of PNE may have improved the results of our study. Additionally, our sample included patients with severe CTS awaiting surgical intervention, most of whom had been symptomatic for longer than 30 months (Table 1). Because of COVID-19, most patients did not have access to timely treatment with a biopsychosocial approach, which may have increased uncertainty and sources of pain-related threat (Karos et al., 2020). In addition, patients in the PNE + exercise group had a mean HADS score above the cutoff point on both subscales (ie, ≥8 points), indicating high levels of anxiety or depression in our sample (Table 1) (Zigmond and Snaith, 1983). Both of these factors may negatively influence the prognosis of physical functioning after rehabilitation (Tseli et al., 2019). All of these factors suggest that our study population may be a group with higher levels of vulnerability in various domains. This may also explain why the exercise-only group did not achieve positive results, despite the literature claiming that exercise-based physical therapy produces improvements in symptoms and function in patients with CTS (Fernández-de-Las Peñas et al., 2015; Hamzeh et al., 2021; Horng et al., 2011). Therefore, future studies should investigate the efficacy of telerehabilitation combined with the support of an interdisciplinary team (i.e., psychologist, occupational therapist, and social worker).

On the other hand, our study showed no significant improvement in the levels of catastrophizing in the PNE + exercise group compared to the exercise group. Nevertheless, it is relevant to mention that in the PNE + exercise group an improvement above the MCD (i.e. above 10.45) was obtained on the PCS at week 6 (García Campayo et al., 2008). This improvement was not sustained at the 12-week assessment, indicating that a greater number of sessions may be necessary to demonstrate stronger results. In terms of symptoms of depression and anxiety, our study also showed no significant differences when comparing the two treatments. Although the MCID of 1.85 and 1.67 points for the depression and anxiety subscales of the HADS were exceeded in the PNE + exercise group (Lemay et al., 2019), this improvement was also not sustained at the week 12 follow-up. In contrast to our results, Chimenti et al. (2023) and Barrenengoa-Cuadra et al. (2021), who also considered higher doses of pain education in the treatment of patients with chronic pain, found greater benefits for catastrophizing and mental health, respectively. Future research should explore the dose-response of PNE to guide clinicians in developing telerehabilitation interventions to find the optimal duration of intervention.

4.1. Implications for clinical practice

This study highlights that in this new era of telemedicine, researchers and clinicians should explore biopsychosocial treatment approaches, including PNE, to improve telerehabilitation interventions. The reduction of kinesiophobia following pain education combined with exercise may be a key factor in determining changes in disability and analgesic use in the medium to long term (Murillo et al., 2023). Additionally, clinically relevant improvements in catastrophizing and anxiety symptoms immediately after PNE should also be considered by surgeons, as both variables are important predictors of poor outcomes after surgery (Núñez-Cortés et al., 2021). Therefore, it would be interesting to coordinate surgery in patients with CTS immediately after completion of the 6-week pain education combined with exercise and to evaluate the long-term efficacy of the intervention. Future studies should also consider combining PNE with interdisciplinary and multimodal treatments (e.g. cognitive behavioral therapy and mindfulness), which have shown promise for these variables in other painful conditions such as fibromyalgia (Serrat et al., 2021). Furthermore, these interventions should be tailored to account for social determinants of health (e.g., education level) (Núñez-Cortés et al., 2023) and the diverse cultural backgrounds of patients (Reis et al., 2022).

4.2. Strengths and limitations

The novel and useful guidance on how telerehabilitation can improve its effectiveness when combined with PNE is the main strength of our study. In addition, our research provides additional information in the context of non-North American/Western European countries on digital support for patients with persistent pain, specifically on the effectiveness of a low-cost telerehabilitation programme focusing on biopsychosocial aspects. On the other hand, our results should be interpreted taking into account the following limitations. 1) The absence of a control group that did not receive any intervention did not allow the results of the two groups to be compared with the natural history of CTS. Ethical considerations make it difficult to allocate patients with persistent symptoms to a non-intervention group; 2) The effect of the intervention was only assessed preoperatively. Therefore, future RCTs are needed to know both the postoperative and long-term effects of the intervention; 3) Due to the nature of the intervention, it was not possible to blind the patients about PNE. Also, the influence of treatment expectations was not assessed, which may be relevant as patients were candidates for surgery to resolve their symptoms; 4) Although the sample size was calculated, a larger sample could increase the precision, generalizability, and statistical power of their study. Future multicenter studies are needed to corroborate these findings and to address the cultural aspects of pain (Reis et al., 2022).

5. Conclusions

The addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity and greater self-perceived improvement in patients with CTS awaiting surgery. Although there were significant and clinically relevant improvements within the PNE + exercise group in pain intensity and catastrophizing, there were no significant differences between the groups. This study highlighted the benefits of including PNE in telerehabilitation interventions.

Ethics

All study procedures were approved by the Ethics Committee of the South East Metropolitan Health Service (ID: CEC-08-04/RAD-03).

Protocol register

ClinicalTrials.gov (NCT05184413).

Declarations of competing interest

Rodrigo Núñez-Cortés is supported by a grant from the National Research and Development Agency of Chile (ANID/2020–72210026). The other authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2023.102835.

References

Amer-Cuenca, J.J., Pecos-Martín, D., Martínez-Merinero, P., Lluch Girbés, E., Nijs, J., Meeus, M., Ferrer Peña, R., Fernández-Carnero, J., 2020. How much is needed? Comparison of the effectiveness of different pain education dosages in patients with fibromyalgia. Pain Med. 21, 782–793.

Bangor, A., Kortum, P.T., Miller, J.T., 2008. An empirical evaluation of the system usability scale. In: International Journal of Human-Computer Interaction. https://doi.org/10.1080/10447310802205776.

Barrenengoa-Cuadra, M.J., Muñoa-Capron-Manieux, M., Fernández-Luco, M., Angón-Puras, L.Á., Romón-Gómez, A.J., Azkuenaga, M., Etxebarria, A., Orrantia, G., Pikaza, A., Uribe-Etxebarria, L., Zorrilla, A., Larrinaga, G., Arana-Arri, E., Gracia-Ballarín, R., FIMIDOC Working Group researchers, 2021. Effectiveness of a structured group intervention based on pain neuroscience education for patients with fibromyalgia in primary care: a multicentre randomized open-label controlled trial. Eur. J. Pain 25, 1137–1149.

Bodes Pardo, G, Lluch Girbés, E, Roussel, NA, Gallego Izquierdo, T, Jiménez Penick, V, Pecos Martín, D, 2018. Pain Neurophysiology Education and Therapeutic Exercise for Patients With Chronic Low Back Pain: A Single-Blind Randomized Controlled Trial. Arch. Phys. Med. Rehabil. 99 (2), 338–347. https://doi.org/10.1016/j.apmr.2017.10.016.

Bülow, K., Lindberg, K., Vaegter, H.B., Juhl, C.B., 2021. Effectiveness of pain neurophysiology education on musculoskeletal pain: a systematic review and meta-analysis. Pain Med. 22, 891–904.

Butler, D.S., Lorimer Moseley, G., 2013. Explain Pain, second ed. Noigroup Publications.

Chandra, P.S., Sarat Chandra, P., Singh, P.K., Goyal, V., Chauhan, A.K., Thakkur, N., Tripathi, M., 2013. Early versus Delayed Endoscopic Surgery for Carpal Tunnel Syndrome: Prospective Randomized Study. World Neurosurgery. https://doi.org/10.1016/j.wneu.2012.08.008.

Chimenti, R.L., Post, A.A., Rio, E.K., Moseley, G.L., Dao, M., Mosby, H., Hall, M., de Cesar Netto, C., Wilken, J.M., Danielson, J., Bayman, E.O., Sluka, K.A., 2023. The effects of pain science education plus exercise on pain and function in chronic Achilles tendinopathy: a blinded, placebo-controlled, explanatory, randomized trial. Pain 164, e47–e65.

Choe, K., Zinn, E., Lu, K., Hoang, D., Yang, L.H., 2023. Impact of COVID-19 pandemic on chronic pain and opioid use in marginalized populations: a scoping review. Front. Public Health 11, 1046683.

Cifu, D.X., Eapen, B., 2021. Telerehabilitation, an Issue of Physical Medicine and Rehabilitation Clinics of North America. Elsevier Health Sciences.

Cohen, J., 2013. Statistical Power Analysis for the Behavioral Sciences. Routledge.

Daenen, L., Varkey, E., Kellmann, M., Nijs, J., 2015. Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice. Clin. J. Pain 31, 108–114.

De, S.D., Vranceanu, A.-M., Ring, D.C., 2013. Contribution of kinesophobia and catastrophic thinking to upper-extremity-specific disability. J. Bone Joint Surg. https://doi.org/10.2106/jbjs.l.00064.

Dworkin, R.H., Turk, D.C., Farrar, J.T., Haythornthwaite, J.A., Jensen, M.P., Katz, N.P., Kerns, R.D., Stucki, G., Allen, R.R., Bellamy, N., Carr, D.B., Chandler, J., Cowan, P., Dionne, R., Galer, B.S., Hertz, S., Jadad, A.R., Kramer, L.D., Manning, D.C., Martin, S., McCormick, C.G., McDermott, M.P., McGrath, P., Quessy, S., Rappaport, B.A., Robbins, W., Robinson, J.P., Rothman, M., Royal, M.A., Simon, L., Stauffer, J.W., Stein, W., Tollett, J., Wernicke, J., Witter, J., Immpact, 2005. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 113, 9–19.

Dworkin, R.H., Turk, D.C., Wyrwich, K.W., Beaton, D., Cleeland, C.S., Farrar, J.T., Haythornthwaite, J.A., Jensen, M.P., Kerns, R.D., Ader, D.N., Brandenburg, N., Burke, L.B., Cella, D., Chandler, J., Cowan, P., Dimitrova, R., Dionne, R., Hertz, S., Jadad, A.R., Katz, N.P., Kehlet, H., Kramer, L.D., Manning, D.C., McCormick, C., McDermott, M.P., McQuay, H.J., Patel, S., Porter, L., Quessy, S., Rappaport, B.A., Rauschkolb, C., Revicki, D.A., Rothman, M., Schmader, K.E., Stacey, B.R., Stauffer, J. W., von Stein, T., White, R.E., Witter, J., Zavisic, S., 2008. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J. Pain 9, 105–121.

Erickson, M., Lawrence, M., Jansen, C.W.S., Coker, D., Amadio, P., Cleary, C., 2019. Hand pain and sensory deficits: carpal tunnel syndrome. J. Orthop. Sports Phys. Ther. 49, CPG1–CPG85.

EuroQol Group, 1990. EuroQol–a new facility for the measurement of health-related quality of life. Health Pol. 16, 199–208.
Fernández-de-Las Peñas, C., Ortega-Santiago, R., de la Llave-Rincón, A.I., Martínez-Perez, A., Fahandezh-Saddi Díaz, H., Martínez-Martín, J., Pareja, J.A., Cuadrado-Pérez, M.L., 2015. Manual physical therapy versus surgery for carpal tunnel syndrome: a randomized parallel-group trial. J. Pain 16, 1087–1094.
García Campayo, J., Rodero, B., Alda, M., Sobradiel, N., Montero, J., Moreno, S., 2008. [Validation of the Spanish version of the pain catastrophizing scale in fibromyalgia]. Med. Clin. 131, 487–492.
Gómez-Pérez, L., López-Martínez, A.E., Ruiz-Párraga, G.T., 2011. Psychometric properties of the Spanish version of the Tampa scale for kinesiophobia (TSK). J. Pain 12, 425–435.
Hamzeh, H., Madi, M., Alghwiri, A.A., Hawamdeh, Z., 2021. The long-term effect of neurodynamics vs exercise therapy on pain and function in people with carpal tunnel syndrome: a randomized parallel-group clinical trial. J. Hand Ther. 34, 521–530.
Hapidou, E.G., O'Brien, M.A., Pierrynowski, M.R., de Las Heras, E., Patel, M., Patla, T., 2012. Fear and avoidance of movement in people with chronic pain: psychometric properties of the 11-item Tampa scale for kinesiophobia (TSK-11). Physiother. Can. 64, 235–241.
Hoffman, M.D., Hoffman, D.R., 2007. Does aerobic exercise improve pain perception and mood? A review of the evidence related to healthy and chronic pain subjects. Curr. Pain Headache Rep. https://doi.org/10.1007/s11916-007-0004-z.
Horng, Y.-S., Hsieh, S.-F., Tu, Y.-K., Lin, M.-C., Horng, Y.-S., Wang, J.-D., 2011. The comparative effectiveness of tendon and nerve gliding exercises in patients with carpal tunnel syndrome: a randomized trial. Am. J. Phys. Med. Rehabil. 90, 435–442.
Jerosch-Herold, C., Houghton, J., Blake, J., Shaikh, A., Wilson, E.C., Shepstone, L., 2017. Association of psychological distress, quality of life and costs with carpal tunnel syndrome severity: a cross-sectional analysis of the PALMS cohort. BMJ Open 7, e017732.
Jordan, P.W., Thomas, B., McClelland, I.L., Weerdmeester, B., 1996. Usability Evaluation in Industry. CRC Press.
Karos, K., McParland, J.L., Bunzli, S., Devan, H., Hirsh, A., Kapos, F.P., Keogh, E., Moore, D., Tracy, L.M., Ashton-James, C.E., 2020. The social threats of COVID-19 for people with chronic pain. Pain 161, 2229–2235.
Kim, J.K., Jeon, S.H., 2013. Minimal clinically important differences in the Carpal Tunnel Questionnaire after carpal tunnel release. J. Hand Surg. Eur. 38, 75–79.
Lemay, K.R., Tulloch, H.E., Pipe, A.L., Reed, J.L., 2019. Establishing the minimal clinically important difference for the hospital anxiety and depression scale in patients with cardiovascular disease. J. Cardiopulm. Rehabil. Prev. 39, E6–E11.
Lenhard, W., Lenhard, A., 2017. Computation of effect sizes. https://doi.org/10.13140/RG.2.2.17823.92329.
Levine, D.W., Simmons, B.P., Koris, M.J., Daltroy, L.H., Hohl, G.G., Fossel, A.H., Katz, J. N., 1993. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. J. Bone Joint Surg. https://doi.org/10.2106/00004623-199311000-00002.
Louw, A., Sluka, K.A., Nijs, J., Courtney, C.A., Zimney, K., 2021. Revisiting the provision of pain neuroscience education: an adjunct intervention for patients but a primary focus of clinician education. J. Orthop. Sports Phys. Ther. 51, 57–59.
Louw, A., Zimney, K., Puentedura, E.J., Diener, I., 2016. The efficacy of pain neuroscience education on musculoskeletal pain: a systematic review of the literature. Physiother. Theory Pract. 32, 332–355.
Malfliet, A., Kregel, J., Coppieters, I., De Pauw, R., Meeus, M., Roussel, N., Cagnie, B., Danneels, L., Nijs, J., 2018. Effect of pain neuroscience education combined with cognition-targeted motor control training on chronic spinal pain: a randomized clinical trial. JAMA Neurol. 75, 808–817.
Moher, D., Hopewell, S., Schulz, K.F., Montori, V., Gøtzsche, P.C., Devereaux, P.J., Elbourne, D., Egger, M., Altman, D.G., Consort, 2012. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int. J. Surg. 10, 28–55.
Moseley, G.L., Butler, D.S., 2015. Fifteen years of explaining pain: the past, present, and future. J. Pain 16, 807–813.
Murillo, C., Galán-Martín, M.Á., Montero-Cuadrado, F., Lluch, E., Meeus, M., Loh, W.W., 2023. Reductions in kinesiophobia and distress after pain neuroscience education and exercise lead to favourable outcomes: a secondary mediation analysis of a randomized controlled trial in primary care. Pain. https://doi.org/10.1097/j.pain.0000000000002929.
Núñez-Cortés, R., Cruz-Montecinos, C., Tapia, C., Pommer, P.P., Pérez-Alenda, S., 2022. Carpal tunnel syndrome and pain. Feat. Assess. Pain, Anaesthesia,Analgesia. https://doi.org/10.1016/b978-0-12-818988-7.00031-5.
Núñez-Cortés, R., Cruz-Montecinos, C., Torreblanca-Vargas, S., Andersen, L.L., Tapia, C., Ortega-Palavecinos, M., López-Bueno, R., Calatayud, J., Pérez-Alenda, S., 2023. Social determinants of health and physical activity are related to pain intensity and mental health in patients with carpal tunnel syndrome. Musculoskelet Sci. Pract. 63, 102723.
Núñez-Cortés, R., Cruz-Montecinos, C., Torres-Castro, R., Tapia, C., Püschel, T.A., Pérez-Alenda, S., 2021. Effects of cognitive and mental health factors on the outcomes following carpal tunnel release: a systematic review and meta-analysis. Arch. Phys. Med. Rehabil. https://doi.org/10.1016/j.apmr.2021.10.026.
Nunez, F., Vranceanu, A.-M., Ring, D., 2010. Determinants of pain in patients with carpal tunnel syndrome. Clin. Orthop. Relat. Res. 468, 3328–3332.
Perrot, S., Lantéri-Minet, M., 2019. Patients' Global Impression of Change in the management of peripheral neuropathic pain: clinical relevance and correlations in daily practice. Eur. J. Pain 23, 1117–1128.
Picardo, N.E., Walker, H., Vanat, Q., Nizar, B., Madura, T., Jose, R., 2021. Service reconfiguration in the department of hand surgery during the UK COVID-19 lockdown: birmingham experience. Postgrad. Med. https://doi.org/10.1136/postgradmedj-2020-139280.
Reis, F.J.J., Nijs, J., Parker, R., Sharma, S., Wideman, T.H., 2022. Culture and musculoskeletal pain: strategies, challenges, and future directions to develop culturally sensitive physical therapy care. Braz. J. Phys. Ther. 26, 100442.
Serrat, M., Sanabria-Mazo, J.P., Almirall, M., Musté, M., Feliu-Soler, A., Méndez-Ulrich, J.L., Sanz, A., Luciano, J.V., 2021. Effectiveness of a multicomponent treatment based on pain neuroscience education, therapeutic exercise, cognitive behavioral therapy, and mindfulness in patients with fibromyalgia (FIBROWALK study): a randomized controlled trial. Phys. Ther. 101 https://doi.org/10.1093/ptj/pzab200.
Shem, K., Wong, J., Dirlikov, B., 2020. Effective self-stretching of carpal ligament for the treatment of carpal tunnel syndrome: a double-blinded randomized controlled study. J. Hand Ther. 33, 272–280.
Siddall, B., Ram, A., Jones, M.D., Booth, J., Perriman, D., Summers, S.J., 2022. Short-term impact of combining pain neuroscience education with exercise for chronic musculoskeletal pain: a systematic review and meta-analysis. Pain 163, e20–e30.
Sullivan, M.J.L., Bishop, S.R., Pivik, J., 1995. The pain catastrophizing scale: development and validation. Psychol. Assess. 7, 524–532.
Taulaniemi, A., Kankaanpää, M., Rinne, M., Tokola, K., Parkkari, J., Suni, J.H., 2020. Fear-avoidance beliefs are associated with exercise adherence: secondary analysis of a randomised controlled trial (RCT) among female healthcare workers with recurrent low back pain. BMC Sports Sci. Med. Rehabil. 12, 28.
Tegner, H., Frederiksen, P., Esbensen, B.A., Juhl, C., 2018. Neurophysiological pain education for patients with chronic low back pain: a systematic review and meta-analysis. Clin. J. Pain 34, 778–786.
The Lancet, 2018. UK life science research: time to burst the biomedical bubble. Lancet 392, 187.
Thiese, M.S., Gerr, F., Hegmann, K.T., Harris-Adamson, C., Dale, A.M., Evanoff, B., Eisen, E.A., Kapellusch, J., Garg, A., Burt, S., Bao, S., Silverstein, B., Merlino, L., Rempel, D., 2014. Effects of varying case definition on carpal tunnel syndrome prevalence estimates in a pooled cohort. Arch. Phys. Med. Rehabil. https://doi.org/10.1016/j.apmr.2014.08.004.
Toia, F., 2021. Impact of COVID-19 on hand surgery in Italy: a comparison between the Northern and the Southern regions. Hand Surg. Rehabil. 40, 139–144.
Tseli, E., Boersma, K., Stålnacke, B.-M., Enthoven, P., Gerdle, B., Äng, B.O., Grooten, W.J. A., 2019. Prognostic factors for physical functioning after multidisciplinary rehabilitation in patients with chronic musculoskeletal pain: a systematic review and meta-analysis. Clin. J. Pain 35, 148–173.
Turolla, A., Rossettini, G., Viceconti, A., Palese, A., Geri, T., 2020. Musculoskeletal physical therapy during the COVID-19 pandemic: is telerehabilitation the answer? Phys. Ther. 100, 1260–1264.
Watson, J.A., Ryan, C.G., Cooper, L., Ellington, D., Whittle, R., Lavender, M., Dixon, J., Atkinson, G., Cooper, K., Martin, D.J., 2019. Pain neuroscience education for adults with chronic musculoskeletal pain: a mixed-methods systematic review and meta-analysis. J. Pain 20 (1140), e1–e1140.e22.
Wood, L., Hendrick, P.A., 2019. A systematic review and meta-analysis of pain neuroscience education for chronic low back pain: short-and long-term outcomes of pain and disability. Eur. J. Pain 23, 234–249.
Zhang, Z.-Y., Tian, L., He, K., Xu, L., Wang, X.-Q., Huang, L., Yi, J., Liu, Z.-L., 2022. Digital rehabilitation programs improve therapeutic exercise adherence for patients with musculoskeletal conditions: a systematic review with meta-analysis. J. Orthop. Sports Phys. Ther. 1–36.
Ziegler, A.-M., Minkalis, A.L., Langdon, E.R., Vining, R., 2022. Learning the neurobiology of pain: a scoping review of pain education from an instructional design perspective. Patient Educ. Counsel. 105, 1379–1401.
Zigmond, A.S., Snaith, R.P., 1983. The hospital anxiety and depression scale. Acta Psychiatr. Scand. 67, 361–370.

Appendix 4. Ethics Committee Approval

SERVICIO DE SALUD METROPOLITANO SUR ORIENTE
COMITE ETICO-CIENTIFICO

ACTA DE APROBACIÓN

Miembros del Comité de Evaluación Ético Científico que participaron en la sesión del
10 de marzo del 2022.

Comité constituido en conformidad a la resolución exenta N°2886 del Servicio de Salud Metropolitano Sur Oriente de fecha de fecha 06 de julio 2009.
Acreditado por SEREMI de Salud 019892 de fecha 14 Abril 2014.

Dr. Patricio Michaud Ch, S.S.M.S.O.
Sra. Verónica Cantuarias B. Enfermera matrona. Hospital Padre Hurtado
Sra. Andrea Mesina A. Fonoaudióloga, Hospital Sótero del Río, Presidenta del Comité.
Dra. Lorna Luco C. Miembro Externo, Vice presidenta
Sr. Hernán Pardo Roche. Abogado S.S.M.S.O.
Dr. Rafael Téllez T. Hospital Sótero del Río
Sra. Elizabeth Valenzuela. Miembro de la Comunidad

Protocolo: Evaluación de factores psicosociales en pacientes con síndrome del túnel carpiano. Estudio Multicéntrico.
Investigador Responsable: Dr. Rodrigo Núñez.
Centro: CRS Hospital Provincia Cordillera.
Fecha Aprobación: 10 de marzo del 2022.

Este informe se refiere a la revisión que el Comité hizo de los siguientes documentos:

- Proyecto.
- Consentimiento Informado.
- Carta Autorización, Director CRS Hospital Provincia Cordillera, Dr. Luis Arteaga J.
- Curriculum Vitae

Evaluación Ética.

El propósito de este estudio es determinar los componentes psicosociales que influyen en los síntomas y funcionalidad de las personas con Síndrome del túnel carpiano en espera de cirugía, Hospital Provincia Cordillera, comuna Puente Alto.

Realizando para esto cuestionario a pacientes que se encuentren en lista espera quirúrgica para cirugía de liberación del túnel carpiano, encuestas para perfil sociodemográfico, se realizarán categorizaciones de pacientes según variables cognitivas, emocionales, categorizaciones demográficos o psicosociales.

De esto se desprenden objetivos que se dirigen a determinar los componentes psicosociales que influyen en los síntomas y funcionalidad de las personas con Síndrome túnel carpiano, estimando diferencias respecto a la percepción del dolor y la funcionalidad.

Valor Social, proyecto de gran valor social , ya que , es importante conocer perfil y variables del paciente que pueden afectar favorable o desfavorablemente de diferente forma evolución cuadro clínico.

Valor científico, el conocimiento que de este estudio emane es de gran valor científico , permitirá saber acerca de datos relevantes a considerar sobre este tipo de paciente.

EVALUACIÓN ÉTICA

Referente a la metodología de este estudio, es un estudio multicéntrico de diseño observacional de corte transversal, los pacientes serán seleccionados de la lista de espera quirúrgica de liberación del túnel carpiano, en Hospital Cordillera, con claros criterios de inclusión y exclusión.

Se ha determinado un tamaño muestra de 45 pacientes.

Los costos asociados a los recursos humanos y los tiempos destinados para la ejecución se realizarán dentro de la jornada laboral del investigador, esto avalado por carta director institución.

Relación riesgo/ beneficio, es favorable para el paciente.

En lo que respecta al Consentimiento Informado, cumple con los requisitos éticos, respetando la voluntariedad y autonomía de los pacientes., entregando información explicita clara y oportuna.

Se mantendrá confidencialidad de los datos, resguardando documentación.

CONCLUSIÓN: Teniendo presente, que: Este protocolo cumple con los requisitos éticos de una investigación; con la legislación nacional vigente, con relación a las Leyes: 19628, 20120 y 20584 y que no implica costos materiales adicionales, ni en recurso humano para la Institución; Este Comité considera que no hay inconvenientes, para solicitar a la Dirección del, CRS Hospital Provincia Cordillera., la **autorización para la realizar esta Investigación.**

Le solicitamos:

1. **Le solicitamos *antes* de iniciar el estudio obtener la aprobación de él, por la autoridad administrativa correspondiente de la Institución, (Director de Hospital, CESFAM, o quien corresponda) y hacernos llegar una copia de dicha a probación. El no cumplimiento de esta obligación lo expone a sanciones administrativas de acuerdo a la legislación vigente.**
2. **Conservar toda la documentación en su poder por lo menos hasta tres años cerrado el estudio.**
3. **Usar los consentimientos informados validados por este Comité.**
4. **Informar cada 6 meses o lo menos una vez al año de su marcha, como También de cualquier publicación o presentación a congresos que dé él se generen.**
5. **La validez de esta aprobación es por un año al cabo del cual con el Informe Correspondiente debe solicitarse su renovación.**
6. **Solicitamos al Investigador Responsable informar sobre la marcha del estudio y solicitar la renovación anual de la presente aprobación ética con al menos 45 días de anticipación si desea continuar con el estudio. Si no ha recibido la respuesta oficial a su solicitud, el investigador deberá detener las actividades del proyecto, no podrá enrolar a ningún nuevo participante y no podrá proceder con el análisis de los datos.**

Andrea Mesina Araos.
Fonoaudióloga.
Magíster en Bioética.
Presidenta
Comité de Evaluación Etico Científico
S.S.M.S.O.

Cc Dirección, CRS Hospital Provincia Cordillera.

Nº PACIENTES A CONSIDERAR EN EL ESTUDIO: 34 pacientes con Dg. de STC en espera de cirugía

TIPO DE ESTUDIO (observación, intervención, multicentrico): Prospectivo, controlado, multicentrico

FUENTE DE FINANCIAMIENTO Y COSTO DEL PROYECTO: no aplica

TIEMPO ESTIMADO DE DURACIÓN DEL PROYECTO: 6 meses

TIPO DE REQUERIMIENTOS AL HOSPITAL: Acceso a la lista de espera quirúrgica de los pacientes con STC

Nombre, Firma y timbre de Jefe Unidad que autoriza la investigación.	Héctor Lara E. HOSPITAL CLÍNICO METROPOLITANO LA FLORIDA TRAUMATOLOGIA
Fecha de recepción de Proyecto en el CEC-HLF	22-04-2024
Fecha de Envío a Dirección.	

SOLICITUD PATROCINIO PARA INVESTIGACIONES

Uso información Hospital

Aprobación Comité Ético Científico (CEC-HLF) **Presidente**	**Dra. Yasna Moreno Yáñez** COMITÉ ÉTICO CIENTÍFICO CEC - HLF HOSPITAL CLÍNICO LA FLORIDA
Firma y Timbre de Patrocinio Institucional **Director**	**Dr. Rubén Gennero** HOSPITAL LA FLORIDA DIRECCIÓN
Firma del Investigador de Recepción conforme de Patrocinio Institucional.	

ACTA DE APROBACIÓN

Miembros del Comité de Evaluación Ético Científico que participaron en la sesión del 26 de agosto del 2021.

Comité constituido en conformidad a la resolución exenta N°2886 del Servicio de Salud Metropolitano Sur Oriente de fecha de fecha 06 de julio 2009.
Acreditado por SEREMI de Salud 019892 de fecha 14 Abril 2014.

Sra. Verónica Cantuarias B. Enfermera matrona. Hospital Padre Hurtado
Sra. Andrea Mesina A. Fonoaudióloga, Hospital Sótero del Río
Dr. Robert Davis C. Hospital Sótero del Río
Dra. María Inés Gómez. Medico Externo.
Dra. Lorna Luco C. Miembro Externo
Sra. Edith Mora San M. Asistente Social, Hospital Sótero del Río.
Dr. Rafael Téllez T. Secretario. Hospital Sótero del Río
Sra. Elizabeth Valenzuela. Miembro de la Comunidad
Dr. Juan Carlos Flores. Medico Hospital Sotero del Río.

Protocolo: Intervención multimodal por telerehabilitación para pacientes con Síndrome del Túnel Carpiano.
Investigador Responsable: Klgo. Rodrigo Núñez Cortés
Centro: Hospital Clínico la Florida
Fecha Aprobación: 26 de agosto 2021.

Este informe se refiere a la revisión que el Comité hizo de los siguientes documentos:

- Proyecto
- Consentimiento Informado
- Patrocinio CEC Hospital Clínico la Florida
- Compromiso Investigador

Evaluación Ética.

El síndrome del túnel carpiano (STC) es una neuropatía periférica compresiva, caracterizada por dolor, sensación de hormigueo y parestesia en el territorio del nervio mediano.

Estos síntomas provocan un deterioro funcional significativo que afecta la calidad de vida de los pacientes. La tele rehabilitación ha demostrado resultados clínicos y funcionales.

tan efectivos como las intervenciones cara a cara, siendo una buena alternativa para mejorar la accesibilidad a la atención de rehabilitación en un contexto de pandemia y distanciamiento social.

El objetivo de este estudio es proporcionar atención coordinada y centrada en el paciente mediante la implementación de un modelo de Telerehabilitación para pacientes con STC en espera de cirugía.

Se realizará un estudio prospectivo, controlado, aleatorizado, doble ciego. Los sujetos incluidos serán todos los pacientes con diagnóstico médico de STC en espera de cirugía del Hospital Clínico de Florida y Hospital San José, mayores de 18 años.

El estudio no implica mayores riesgos y su beneficio puede ser importante.

El Consentimiento Informado cumple con los requisitos éticos de este documento de respeto a autonomía voluntariedad y confidencialidad

CONCLUSIÓN: Teniendo presente, que: Este protocolo cumple con los requisitos éticos de una investigación; con la legislación nacional vigente, con relación a las Leyes: 19628, 20120 y 20584 y que no implica costos materiales adicionales, ni en recurso humano para la Institución; Este Comité considera que no hay inconvenientes, para solicitar a la Dirección del Hospital Clínico la Florida, la autorización para la realizar esta Investigación.

Le solicitamos:

1. **Le solicitamos *antes* de iniciar el estudio obtener la aprobación de él, por la autoridad administrativa correspondiente de la Institución, (Director de Hospital, CESFAM, o quien corresponda) y hacernos llegar una copia de dicha a probación. El no cumplimiento de esta obligación lo expone a sanciones administrativas de acuerdo a la legislación vigente.**
2. **Conservar toda la documentación en su poder por lo menos hasta tres años cerrado el estudio.**
3. **Usar los consentimientos informados validados por este Comité.**
4. **Informar cada 6 meses o lo menos una vez al año de su marcha, como También de cualquier publicación o presentación a congresos que dé él se generen.**
5. **La validez de esta aprobación es por un año al cabo del cual con el Informe Correspondiente debe solicitarse su renovación.**
6. **Solicitamos al Investigador Responsable informar sobre la marcha del estudio y solicitar la renovación anual de la presente aprobación ética con al menos 45 días de anticipación si desea continuar con el estudio. Si no ha recibido la respuesta oficial a su solicitud, el investigador deberá detener las actividades del proyecto, no podrá enrolar a ningún nuevo participante y no podrá proceder con el análisis de los datos.**

SERVICIO DE SALUD METROPOLITANO SUR ORIENTE
COMITÉ DE EVALUACION ETICO-CIENTIFICO

Dr. Patricio Michaud Ch
Presidente
Comité de Evaluación Etico científico
S.S.M.S.O.

Cc Dirección, Hospital Clínico la Florida.

SERVICIO DE SALUD METROPOLITANO SUR ORIENTE
COMITE ETICO-CIENTIFICO

ACTA DE APROBACION EXPEDITA

Santiago, Chile 18 de enero del 2022

El Klgo. **Rodrigo Núñez Cortés**., Investigador para los Centros, Hospital Clínico la Florida y Hospital Provincia Cordillera, nos ha hecho llegar, nueva enmienda, para el Protocolo: "Intervención multimodal por telerehabilitación para pacientes con Síndrome del Túnel Carpiano. **Estudio Multicéntrico**"

Ha hecho llegar a este Comité los siguientes documentos:

- Enmienda presentada al CEC-SSMSO
- Aceptación de enmienda por el Hospital Clínico la Florida
- Carta de autorización del director CRS-Hospital Provincia Cordillera
- Consentimiento informado para CRS-Hospital Provincia Cordillera

Revisada la documentación enviada y teniendo en consideración que los cambios no alteran la validez del estudio, ni implican riesgos a los pacientes, se le otorga **APROBACIÓN EXPEDITA.**

Se adjunta C.I. Validado

Agradeciendo su información, Saluda Atentamente a Ud.

Andrea Mesina Araos.
Fonoaudióloga.
Magíster en Bioética.
Presidenta
Comité de Evaluación Etico Científico S.S.M.S.O.

Cc: Archivo.

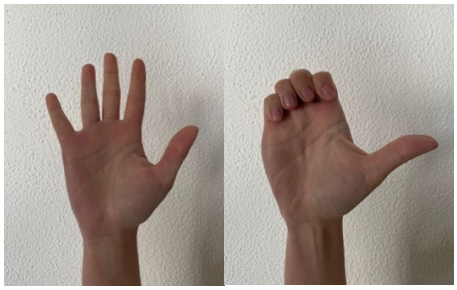
Appendix 5. Exercise Programme

WEEK 1-2

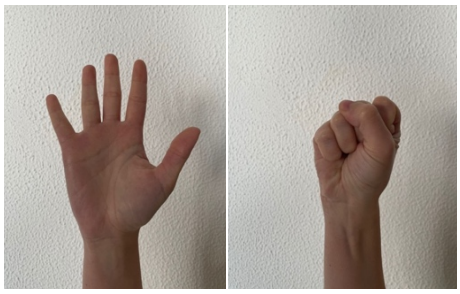
Brisk Walking

Brisk walking for **15 minutes** three days a week with **moderate intensity** (you can talk during the exercise but with difficulty, e.g. you would not be able to sing). Walking days should be every other day (not consecutive days).

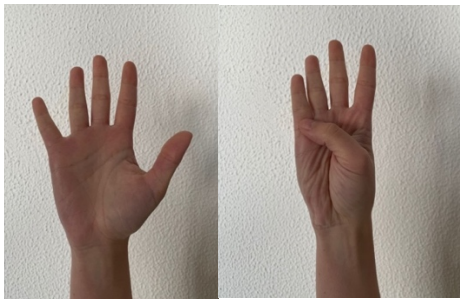
Hand Exercises



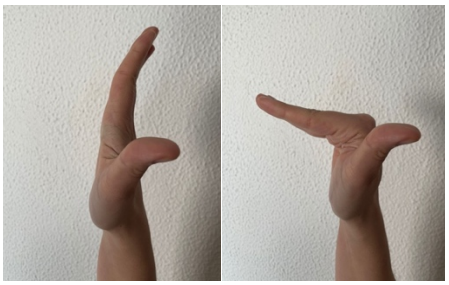
Move from **position 1** (open hand) to **position 2** (hook).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 4/10



Move from **position 1** (open hand) to **position 2** (fist).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 4/10



Move from **position 1** (open hand) to **position 2** (thumb opposition).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 4/10



Move from **position 1** (straight) to **position 2** (table top).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 4/10

Stretching

Sitting in a relaxed position. With the opposite hand bring the head to tilt and rotate, while the other hand holds on to the chair to avoid raising the shoulder. The stretching position is held for **45 seconds 2 times.**

Neural Mobilisation

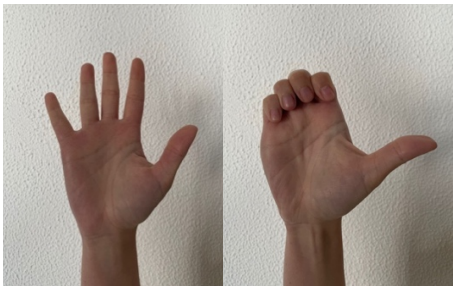
Move from **position 1** (head neutral, shoulder neutral, elbow flexed, wrist flexed) to **position 2** (head bent, shoulder separated, elbow extended, wrist neutral).
Repeat the movement extending in 2 seconds and returning in 2 seconds.
Sets: 3 cycles of 10 repetitions
Rest: 30 seconds between cycles.

WEEK 3-4

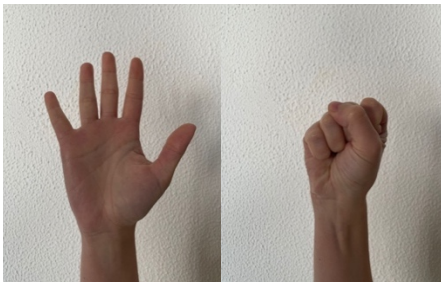
Brisk Walking

Brisk walking for **20 minutes** three days a week with **moderate intensity** (you can talk during the exercise but with difficulty, e.g. you would not be able to sing). Walking days should be every other day (not consecutive days).

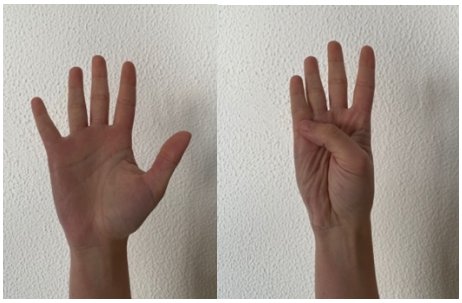
Hand Exercises



Move from **position 1** (open hand) to **position 2** (hook).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 5/10



Move from **position 1** (open hand) to **position 2** (fist).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 5/10



Move from **position 1** (open hand) to **position 2** (thumb opposition).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 5/10

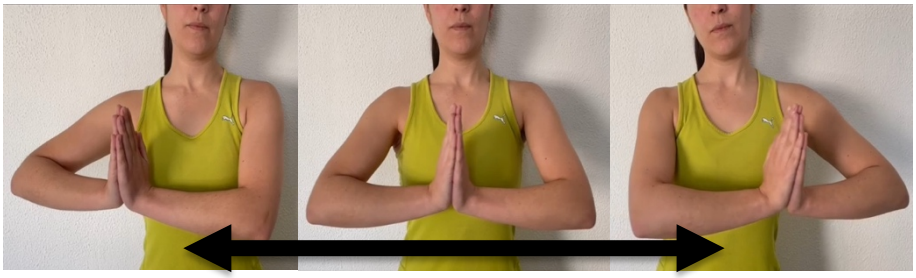
Stretching

Stretch finger joints to maximum extension with opposite hand (lumbrical muscles). Keep the elbow of the symptomatic arm flexed.

Stretch position is held for **45 seconds and repeat 2 times.**

Extend your wrist at 90 degrees against a wall and grasp the nearby eminence with the opposite hand to stretch the palm of your symptomatic hand (transverse carpal ligament).
Hold for 30 seconds and repeat 4 times.

Neural Mobilisation



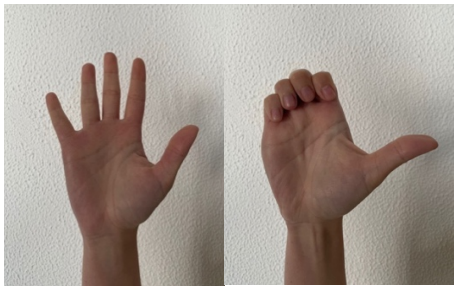
Move from the neutral position (hands on the vertical) sliding right and left in a horizontal line. Repeat the cycle from one side to the other, performing each movement in series of 2 sec.
4 cycles of 15 repetitions. Rest: 30 sec. between cycles.

WEEK 5-6

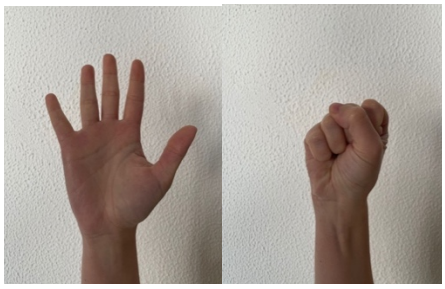
Brisk Walking

Brisk walking for **25 minutes** three days a week with **moderate intensity** (you can talk during the exercise but with difficulty, e.g. you would not be able to sing). Walking days should be every other day (not consecutive days).

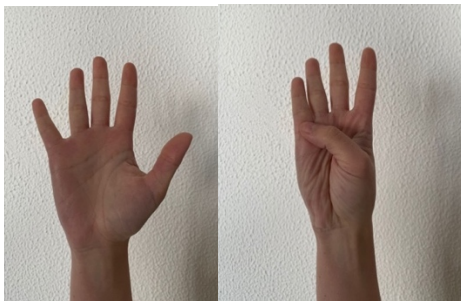
Hand Exercises



Move from **position 1** (open hand) to **position 2** (hook).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 6/10



Move from **position 1** (open hand) to **position 2** (fist).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 6/10



Move from **position 1** (open hand) to **position 2** (thumb opposition).
Sets: _____
Repetitions: _____
Rest: _____
Effort: 6/10

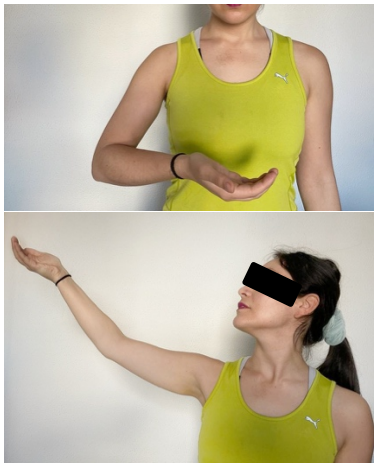
Stretching

Stretch finger joints to maximum extension with opposite hand (lumbrical muscles). Keep the elbow of the symptomatic arm flexed.

Stretch position is held for **45 seconds and repeat 2 times.**

Extend your wrist at 90 degrees against a wall and grasp the nearby eminence with the opposite hand to stretch the palm of your symptomatic hand (transverse carpal ligament).
Hold for 30 seconds and repeat 4 times.

Neural Mobilisation



Move from **position 1** (Protected bird) to **position 2** (Free the bird).

Repeat the movement extending in 2 seconds and returning in 2 seconds.
Sets: 3 cycles of 10 repetitions
Rest: 30 seconds between cycles.

Appendix 6. Visual Support for Educational Sessions
(Translated into English for the purposes of this thesis.
Own material based on previous literature.)

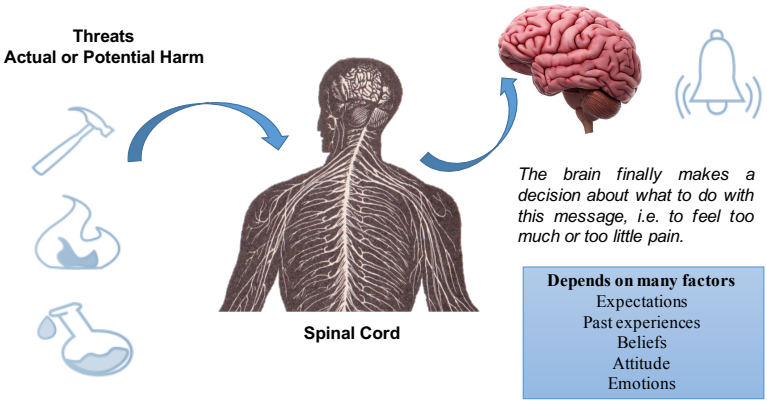
Why do we feel pain?

Learning about pain helps to change the way you think about your problem and can help you begin to plan your own personal recovery strategies.

Pain System

Special nerves alert us to messages in our body.

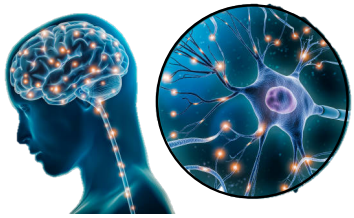
The brain analyses the information and based on many factors can create the sensation of little pain or a lot of pain.



The brain finally makes a decision about what to do with this message, i.e. to feel too much or too little pain.

Depends on many factors
Expectations
Past experiences
Beliefs
Attitude
Emotions

Excessive Pain = Very Sensitive Nerves



Excessive pain can be explained by the fact that the nerves are very sensitive and easily activated.

Excessive Pain = Very Sensitive Nerves

The brain releases chemicals that make nerves more sensitive to protect us.

Pain is an Internal Alarm

Although unpleasant, a fire alarm can warn us and save our lives.

But what would happen if a fire alarm was too sensitive?
It would interrupt even a birthday party

Pain is NOT proportional to damage

Small injuries, such as baby bites, can cause a lot of pain.

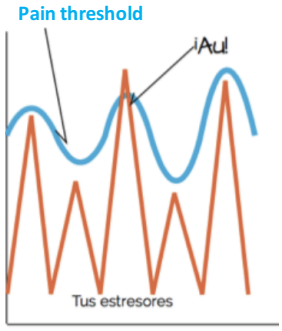
While in 2003, Bethany Hamilton went surfing and was attacked by a shark. Later in an interview for CNN she said: "I didn't feel any pain, I was in shock... I'm very lucky".

Why is this happening?

Dopamine
Serotonin
Endorphin
Noradrenaline
Endocannabinoids

The brain can also activate chemicals that turn off the messages sent by the nerves. For example, if you want to run away from a lion and you prick your foot

Pain fluctuates depending on many factors



- Too much work
- Poor sleep
- Anger
- Fear of movement
- Stress
- Frustration
- Lack of support
- False beliefs
- Anxiety

Therefore
Many options to reduce our pain!

Life's stressors apply to our protection

It is not the bee sting that is dangerous. It is our response to that bee sting. Pain can be viewed in a similar way. This overprotective pain response is influenced by a number of different factors

The pain system becomes hyper-reactive and overprotective, like someone who is allergic to a bee sting.

"Like a habit, pain can be activated"

Have you ever felt a smell that suddenly triggered a memory or an emotion?

We must create new memories and associations.

Seek more positive associations with movements or activities that generate concern.

We focus on the things that might be sensitising you, but what about the positive?

Things that help →

This can cause the brain to release chemicals that decrease the sensitivity of the nerves. It can also relieve stressors

- General exercise or physical activity
- Resuming meaningful hobbies or activities
- Starting a consistent sleep schedule
- Giving your body permission to move and explore any movement
- Almost anything that makes you happier
- Focus on your successes!