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ORIGINAL ARTICLE

Effects of exercise programs on physical function and activity levels in patients undergoing hemodialysis: a randomized controlled trial

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ABSTRACT

BACKGROUND: There are still many barriers when implementing exercise routines within daily dialysis care, even though benefits are well-known. Developing cost-effective strategies is necessary to overcome these barriers and include exercise as a complementary therapy in dialysis.
AIM: To compare several exercise programs on hemodialysis patient's functional capacity and health-related quality of life.
DESIGN: This study was a 16-week follow-up, two-parallel group trial with balanced randomization.
SETTING: Participants in this study belonged to a private hospitalized care center.
POPULATION: Referred sample of 71 patients that suffered end-stage chronic kidney disease who underwent hemodialysis for at least 3 months and had a medical stable condition.
METHODS: Thirty-six participants performed for 16 weeks an intradialytic exercise program lead by the nursing staff of the hemodialysis unit and 35 a home-based program supervised by physical therapists of the hospital.
RESULTS: The main researcher and the data analyst were both blinded to participant allocation. There was a significant effect in time for both groups. Participants improved significantly in the Short Performance Physical Battery (SPPB), One-Leg Heel-Rise (OLHR) and 6 Minute-Walk Test (6MWT), and in the Physical Activity Scale for the Elderly (PASE) and Short Survey Form 36 (SF-36) questionnaires.
CONCLUSIONS: Nurse-led and home-based exercise interventions produce beneficial effects involving physical function, activity levels and health-related quality of life in patients undergoing hemodialysis.
CLINICAL REHABILITATION IMPACT: The study emphasizes the importance of exercise rehabilitation routines in fragile populations such as dialysis patients, and the potential to overcome barriers for its daily implementation.

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Key words: Dialysis; Exercise; Rehabilitation.

Chronic kidney disease (CKD) is an exponentially growing disease that accounts for a world prevalence of 9.1%[1] and shows even bigger numbers in countries such as Spain, that has a prevalence of 15.1%.[2] Patients with CKD on maintenance hemodialysis (HD) suffer from a progressive and gradual deterioration of impaired physical function.[3, 4] This, associates with a higher risk of mortality and morbidity,[5] and leads to decreased physical activity and health related quality of life (HRQOL) levels.[4]

Existing guidelines[6, 7] address this issue and encourage patients to engage in physical activities. Several systematic reviews and meta-analyses[3, 5] have proven that exercise is an effective strategy in improving physical function, psychological issues and HRQOL levels in patients with CKD.

Despite this, exercise programs are not commonly implemented on dialytic routines in many countries[8] due to a myriad of existing barriers that health-care professionals have to face when trying to propose an exercise intervention during dialysis. These barriers include lack of knowledge, fear of injury or medical complications, fatigue or just simply a lack of motivation by both the patient and the healthcare professional.[8]

Many studies focus on overcoming these barriers. For example, nurse-led exercise interventions have been previously proven to be efficient in physically impaired populations, such as the elderly,[9] complex ambulatory[10] or diabetic patients.[11] In studies involving patients with CKD, these types of interventions have also improved clinical outcomes and reduced hospitalization rates.[10]

Also, home-based exercise programs enhance schedule flexibility and empower patients to have an active role in their treatment. Several studies[12, 13] even defend their sustainability amongst other interventions, while allude to higher compliance rates in order to defend intradialytic interventions.[14]

More so, the multidisciplinary approach healthcare is experimenting in recent years is leading towards a collaborative model where patient's well-being is predominant over professional disputes. Therefore, many interventions, such as exercise, are no longer a single professional domain, but rather a responsibility for the whole medical team.

Regarding this matter, the aim of this study was to compare different interventions by assessing their effect on patient's functional capacity. Secondary assessments include patient's physical condition, activity levels and health-related quality of life.

Materials and methods

Study design

This study was a two-parallel group trial with balanced randomization (1:1). Data were collected at baseline and after 16 weeks of intervention. Participants were allocated using simple randomization with a computer-generated randomization list. Outcome assessors and data analysts were kept blinded to the allocation.

Participants

Patients that suffered end-stage CKD who underwent hemodialysis were enrolled. Participants in this study belonged to a private hospitalized care center. Every participant was assessed for eligibility by their medical record and were granted permission by the head nephrologist of the HD unit. Every participant was given verbal and written information regarding the procedure and objective of the study and were also required to give written consent in order to enroll. All of the participants were informed, and it was made clear that their participation was voluntary, and withdrawal could be done at any time. The study was registered at Clinical Trials (NCT04051515).

Inclusion criteria were for the participant to have been treated with hemodialysis for at least 3 months and having a stable medical condition to participate in physical activity. Exclusion criteria included: 1) myocardial infarction 6 weeks prior to the intervention; 2) unstable cardiovascular disease that might worsen with exercise; 3) above-knee lower limb amputation; 4) ischemic brain disease; 5) muscle-skeletal or respiratory condition that could worsen with exercise; or 6) inability to perform functional tests for several reasons, such as language barrier.

Description of the exercise programs

The intervention for this study was performed by a main researcher and the hospital's nursing and physical therapy staff members. The main researcher was blinded to participant allocation and staff members served as intermediaries for daily data collection and exercise guidance.

Nursing staff delivered trial exercise sessions during 2 weeks with the assistance of the main researcher, a physical therapist specialized in exercise interventions, in order to familiarize with the procedure and the equipment. Then, participants were randomly allocated to an intradialytic (ID) or home-based (HB) exercise program groups and the main researcher became blinded to the intervention. This intervention lasted for 16 weeks, were participants performed 1-hour exercise sessions 3 times a week for a total of 48 exercise sessions. Exercise progression was discussed by both the nursing staff and the main researcher based on Borg's perceived exertion scale, that was routinely passed to the participant. Participants were asked to perceive around 12 points on this scale, equivalent to a "somehow hard" effort.

Intradialytic exercise program

A combined generic strengthening and aerobic resistance training program. Group sessions began with a 5-minute warm-up consisting of active joint mobilizations, followed by a strengthening section that combined isometric and isotonic exercises for the lower limb and non-dialyzed upper limb muscles using different level resistance elastic bands, and concluded with a 30-minute aerobic resistance training with the use of a cycloergometer that could be easily adapted to the dialyzing chair. When finished, participants were instructed to "cool down" with active joint mobilizations and stretching exercises.

Home-based exercise program

Participants allocated in this group were instructed 3-weekly exercise sessions in days of their own choice. They were given an exercise diary where they could keep track of their progress and an exercise aid guide, with pictures and explanations they were asked to do. Exercises in this program were similar to those in the ID group but adapted so every participant could exercise without requiring expensive material, substituting the cycloergometer endurance training with walking for total of 30 minutes per session. Each participant performed the exercise session individually. In order to control supervision over this group, weekly meetings were arranged between participants and Physical therapy staff members, so the main researcher could maintain blindness. Meetings were scheduled 15 minutes prior to the first weekly dialysis session.

Outcomes

Clinical and anthropometric data were collected for every patient, including age, gender, dry weight, Body Mass Index (BMI), albumin, creatinine and hemoglobin values, renal disease etiology, if the participant was diabetic or a smoker, type of dialyzer used and Charlson's Comorbidity Index.

Every test was performed an hour prior to the dialytic treatment in the same order for every participant at baseline and after 16 weeks of intervention. Both assessments were administered by the same researcher, blinded to allocation, for every participant in order to avoid possible interrater bias. Tests were administered following specific scripted instructions.

Primary outcome measures

Outcome measures assessed change from baseline at 16 weeks for the following:

- short physical performance battery (SPPB): a combination of physical tests that assess balance, gait speed and lower limb functional strength that scored over a total of 12 points;[15]
- gait speed: Assessment of the speed to cover 4 meters in meters/second from an initial standing position.[15]

Secondary outcome measures

Outcome measures assessed change from baseline at 16 weeks for the following:

- sit-to stand-to sit 10 and 60 tests (STS): used for resistance and strength assessment, respectively, of the lower limbs.[16] STS-10 is calculated as the total time needed to complete 10 repetitions of standing up and sitting down again, and the STS-60 registers the repetitions performed in 60 seconds;
- 6 Minute Walk Test (6MWT) as an indicator of the participant's functional capacity.[16] It registers the maximal number of meters the participant is able to walk in a 30-m distance corridor;
- handheld dynamometry for grip strength,[16] a value proven to have a correlation with health status in patients undergoing HD;
- one-leg heel rise (OLHR) in order to assess the strength and resistance of the triceps surae muscles.[16] This test assesses by counting the number of lifts the participant could do with one leg, paced by a metronome up to a maximum of 25 repetitions;
- one-leg standing test (OLST): Performed in order to assess single leg balance;[16]
- timed-up and go test (TUG): A mobility test.[17] It assesses the time needed to stand up, walk around a mark placed 3 meters from the starting point, come back and sit down again;
- physical activity scale for the elderly (PASE), that addressed the participant's physical activity level of the previous week;[18]
- Medical Outcomes Survey Short Form 36 (SF-36), that analyzes the participant's HRQOL.[19]

Statistical analysis

The researcher responsible for statistical analysis was blinded to which group each participant belonged. To perform statistical calculations, SPSS© version 23.0 (IBM; Armonk, NY, USA) was used. OpenEpi© version 3 (https://www.openepi.com/Menu/OE_Menu.htm) was used to assess sample size estimation basing its calculations on previous studies,[16] establishing that to reach an $\alpha=0.05$ with a power of 80% and a confidence interval of 95, 25 participants should be in each group. In this study, 36 participants were allocated in each group.

Trial hypothesis was intended to test for superiority of the ID program against the HB program, first comparing differences between interventions using an interparticipant factor (exercise groups) that could differentiate between ID and HB. To compare different groups within each intervention, a combined ANOVA model was used, with an intraparticipant factor (time) that could differentiate two values (baseline and after 16 weeks). Minimal detectable change (MDC) was established based on previous studies.[16]

Potential bias

Excluding participants due to medical reasons and asking for their voluntary participation may lead to a sample that could be non-representative. Also, not having a control group for either exercise intervention makes it challenging to fully understand their real effect.

Results

Results from the intervention are reported in Table I, II, III. A total of 71 participants were included in this study. 36 were randomly allocated in the ID exercise group and 35 in the HB exercise group. After 16 weeks of the exercise program,

TABLE II.—*Outcome measures between-group differences: ID* vs. *HB groups.*

Variable	Variance analysis (between-group) F	P value	Size effect
SPPB	2.223	0.142	0.038
OLST	0.039	0.844	0.001
TUG	0.381	0.540	0.007
STS-10	0.273	0.603	0.005
STS-60	0.055	0.816	0.001
Handgrip R	1.482	0.229	0.027
Handgrip L	0.341	0.562	0.006
OLHR R	1.936	0.173	0.055
OLHR L	0.274	0.605	0.009
6MWT	0.781	0.381	0.015

HB: home based; ID: intradialysis; L: left; OLHR: one leg heel rise; R: right; STS: sit to stand to sit; TUG: timed up and go; 6MWT: 6 Minute Walk Test; OLST: One Leg Standing Test.

TABLE I.— *Participant baseline demographic and clinical characteristics.*

Value	Intradialysis exercise group (N.=36)	Home-based exercise group (N.=34)	P value
Age, median (SD) (years)	67.2 (13.3)	67.2 (15.9)	0.991
Gender, N. (%)			0.863
Male	24 (67)	22 (65)	
Female	12 (33)	12 (35)	
Weight, median (SD) (kg)	73.4 (14.1)	76.4 (17.1)	0.423
Height, median (SD) (cm)	162.6 (8.9)	163.7 (11.0)	0.642
Body Mass Index, median (SD) (kg/m²)	27.5 (4.8)	28.7 (6.9)	0.418
Albumin, median (SD) (mg/dL)	3.9 (0.3)	3.8 (0.3)	0.204
Creatine, media (SD) (mg/dL)	7.0 (2.0)	6.5 (2.2)	0.277
Glycolyzed hemoglobin, median (SD) (g/dL)	6.1 (0.9)	5.8 (1.7)	0.403
CKD Diagnosis			0.219
Diabetes mellitus	4	5	
Glomerular nephritis	3	5	
Lupus	1	0	
Pyelonephritis	0	3	
Polycystosis	1	2	
Other	26	16	
Hypertension	1	3	
Diabetes			0.877
No	19	20	
Diabetes Type I	5	4	
Diabetes Type II	12	10	
Smoker			0.183
No	26	29	
Yes	10	5	
Dialyzer			0.461
FX100	5	11	
FX80	17	12	
FX60 Classix	10	8	
F70S	2	1	
FX10	2	2	
Charlson's Index			0.962
2	4	5	
3	1	1	
4	3	1	
5	4	5	
6	6	4	
7	7	6	
8	6	7	
9	3	3	
10	2	1	
11	0	1	

TABLE III.—*ANOVA significance for primary outcome measures: ID* vs. *HB groups.*

Assessment	Group	Median (SD)		Variance analysis (group time), P value	Size effect	Variance analysis (time), P value	Size effect
		Pre	Post				
SPPB (points)	ID	9.7 (2.4)	10.5 (2.1)	F=0.065, P=0.799	0.001	F=14.126, P<0.001	0.201
Median (SD)	HB	8.9 (2.4)	9.6 (2.8)				
Gait speed (seconds)	ID	4.1 (1.7)	3.7 (1.1)	F=0.087, P=0.769	0.002	F=3.954, P=0.052	0.066
Median (SD)	HB	4.7 (2.2)	4.3 (2.8)				

HB: home based; ID: intradialysis; SD: standard deviation SPPB: short performance physical batterY.

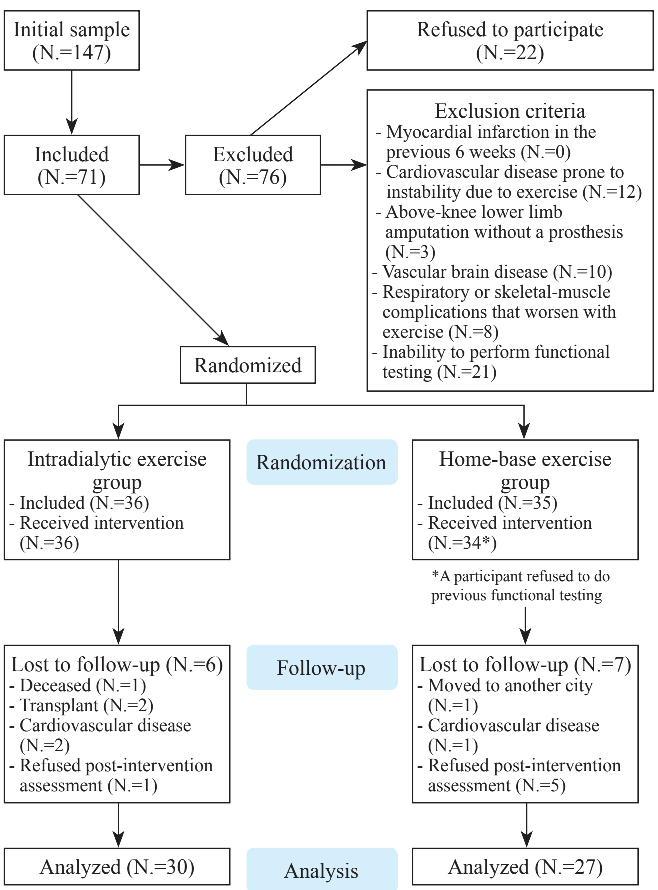

Figure 1.—Participant flow diagram.

a total of 57 participants were finally analyzed (Figure 1) and 13 were lost to follow-up (1 passed away, 1 moved to a different city, 3 developed cardiovascular complications, 2 had a transplant and 6 refused to postintervention assessment). Baseline clinical characteristics of the sample are summarized in Table I. Results in Table II show there were no significant differences involving factors "group" and "time" for any outcome, so both interventions showed significant improvements without a significant difference between them.

Primary results

There were no differences between groups at the beginning of the study in any of the functional tests. There were significant improvements in the SPPB and gait speed assessments, so both groups improved their general physical function at the end of 16 weeks, as seen in Table III.

Secondary results

Regarding physical functioning tests, there was a significant improvement in the OLHR and 6MWT for both groups and in the STS-10 test for the ID group. There was also an improvement in the OLST and STS-10 for the HB group and in the TUG and handheld dynamometry for the ID group. Questionnaires showed a significant improvement in the PASE for both groups, and regarding health-related quality of life, the SF-36 showed a significant improvement in all of its subscales except for the Social Functioning subscale. Results are shown in Table IV, V.

Discussion

The results of this study showed that after 16 weeks of intervention, even though any significant differences were found between groups, both a nurse-led intradialytic exercise program and a home-based exercise program supervised by physical therapists improved patient's functional capacity and HRQOL. This study highlighted the effectiveness of a multidisciplinary approach to exercise and indicated that trained nurses are capable of implementing exercise interventions along with their daily regular job responsibilities.

Several studies had previously proven the beneficial effects of an exercise intervention in this population,[20, 21] but in most of them the intervention used aerobic training. Other studies[22-24] used strength training as well, and our study combined aerobic and strength training for both exercise programs. The combination of both exercise modalities could have developed a more complete exercise training program, leading to the enhancement of the benefits.

TABLE IV.—*ANOVA significance for secondary outcome measures: ID* vs. *HB groups.*

Assessment	Group	Median (SD)		Variance analysis (group-time), P value	Size effect	Variance analysis (time), P value	Size effect
		Pre	Post				
STS-10 (seconds)	ID	28.4 (11.2)	25.2 (12.3)	F=1.056, P=0.309	0.020	F=7.764, P=0.007	0.128
Median (SD)	HB	26.2 (8.1)	24.7 (8.3)				
STS-60 (repetitions)	ID	21.1 (9.7)	24.1 (10.4)	F=3.149, P=0.082	0.056	F=1.991, P=0.164	0.036
Median (SD)	HB	23.3 (8.5)	23.0 (9.0)				
6MWT (meters)	ID	360.3 (109.5)	398.1 (98.6)	F=1.103, P=0.299	0.021	F=8.362, P=0.006	0.139
Median (SD)	HB	342.7 (123.9)	360.4 (146.0)				
Handgrip R (kg)	ID	25.3 (10.5)	26.5 (10.6)	F=1.335, P=0.253	0.024	F=0.093, P=0.762	0.002
Median (SD)	HB	29.6 (11.1)	28.9 (11.0)				
Handgrip L (kg)	ID	24.6 (9.7)	23.6 (9.1)	F=0.131, P=0.719	0.002	F=0.963, P=0.331	0.018
Median (SD)	HB	25.8 (8.9)	25.4 (10.7)				
OLHR R (repetitions)	ID	14.6 (10.1)	18.3 (7.4)	F=0.530, P=0.472	0.016	F=5.724, P=0.023	0.148
Median (SD)	HB	19.0 (8.6)	21.0 (6.3)				
OLHR L (repetitions)	ID	16.5 (8.7)	17.0 (7.3)	F=3.261, P=0.081	0.098	F=4.828, P=0.036	0.139
Median (SD)	HB	15.4 (9.2)	20.8 (6.7)				
OLST (seconds)	ID	15.9 (17.0)	14.1 (15.1)	F=1.953, P=0.169	0.041	F=0.049, P=0.826	0.001
Median (SD)	HB	14.7 (16.3)	17.2 (17.8)				
TUG (seconds)	ID	9.3 (5.5)	9.0 (4.0)	F=1.332, P=0.253	0.023	F=0.712, P=0.402	0.013
Median (SD)	HB	8.9 (5.2)	10.9 (7.9)				
PASE (points)	ID	85.6 (75.9)	74.8 (47.4)	F=0.231, P=0.633	0.004	F=0.748, P=0.390	0.012
Median (SD)	HB	65.3 (55.3)	62.2 (43.1)				

HB: home based; ID: intradialysis; L: left; OLHR: one leg heel rise; PASE: Physical Activity Scale for the elderly; R: right; SD: standard deviation; STS: sit to stand to sit; TUG: timed up and go; 6MWT: 6 Minute Walk Test; OLST: One Leg Standing Test.

TABLE V.—*ANOVA significance involving health-related quality of life: ID* vs. *HB group.*

Assessment	Group	Median (SD)		Variance analysis (group-time), P value	Size effect	Variance analysis (time), P value	Size effect
		Pre	Post				
SF36. Physical functioning	ID	62.5 (25.5)	74.7 (23.0)	F=0.464, P=0.498	0.007	F=15.517, P<0.001	0.200
Median (SD)	HB	62.7 (26.3)	71.3 (17.6)				
SF36 Role physical functioning	ID	56.3 (47.5)	80.5 (38.5)	F=0.888, P=0.767	0.001	F=15.844, P<0.001	0.204
Median (SD)	HB	59.4 (46.1)	87.5 (28.4)				
SF36 Bodily pain	ID	75.3 (28.6)	84.1 (25.2)	F=0.005, P=0.942	0.000	F=5.420, P=0.023	0.080
Median (SD)	HB	67.7 (30.5)	75.9 (25.9)				
SF36 General health	ID	38.7 (19.3)	54.6 (21.8)	F=2.739, P=0.103	0.042	F=18,474, P<0.001	0.230
Median (SD)	HB	45.2 (21.3)	52.3 (20.2)				
SF36 Vitality	ID	53.9 (18.7)	57.2 (15.0)	F=1.287, P=0.261	0.020	F=5.869, P=0.018	0.086
Median (SD)	HB	52.8 (23.9)	61.9 (15.2)				
SF36 Social functioning	ID	89.8 (21.9)	87.1 (25.1)	F=2.921, P=0.092	0.045	F=0.447, P=0.506	0.007
Median (SD)	HB	90.6 (17.4)	96.9 (11.9)				
SF36 Role emotional	ID	61.5 (48.7)	85.4 (34.8)	F=0.455, P=0.503	0.007	F=26.079, P<0.001	0.296
Median (SD)	HB	61.5 (45.7)	92.7 (20.3)				
SF36 Mental health	ID	63.9 (19.7)	68.1 (16.7)	F=0.277, P=0.601	0.004	F=5.356, P=0.024	0.080
Median (SD)	HB	67.1 (20.3)	73.9 (15.4)				
Physical component scale	ID	42.2 (10.8)	47.5 (7.8)	F=0.732, P=0.396	0.012	F=12.131, P=0.001	0.164
Median (SD)	HB	42.1 (10.0)	45.3 (7.0)				
Mental component scale	ID	45.8 (13.3)	47.9 (10.3)	F=2.140, P=0.149	0.033	F=8.806, P=0.004	0.124
Median (SD)	HB	46.7 (12.2)	52.8 (7.1)				

HB: home based; ID: intradialysis; SF36: Short Form Survey 36; SD: Standard deviation.

Our study shows a significant improvement in the SPPB for both groups, similar to what Chen *et al.*[25] found in their study. This occurred even though our sample had high baseline values for this test, so there is an encouraging range of improvement for future studies. Similar results were found in the 6MWT, a test widely used for functional capacity that also showed improvements in previous studies[26-30] with different exercise interventions, so we can understand that diverse exercise interventions have positive effects in the functional capacity of these patients. Significant improvements were also found in the OLHR for both groups and STS-10 test for the intradialytic exercise group. To our knowledge, only one study had previously assessed OLHR in hemodialysis patients,[31] and other studies used the STS-10[30-32] as well, finding improvements in their results.

Tao *et al.*[32] showed significant between-group changes with a nurse-lead intervention. They had a bigger sample and follow-up rates were also high, but the nurse-lead supervision was for a home-based intervention, they did not have an intradialytic group to compare results to and their follow-up timeline was inferior to ours, so these significant changes need to be interpreted.

Physical activity levels and HRQOL were assessed with the PASE and the SF-36 questionnaires, respectively. Significant improvements for both groups were found, so we can say that both our exercise interventions improved physical activity levels in patients in HD, as found in other studies.[32] In the SF-36 significant and non-significant improvements were found except for one of its subscales, and these results are similar to those who assessed quality of life in these patients in other studies.[30, 32]

The sample in this study was relatively small, and due to exclusion criteria and participation willingness, results could only be interpreted in patients with high motivation. Analyses of missing data were handled as per protocol, due to the refusal of the drop-out participants to even perform preintervention primary outcome assessments. Neither exercise programs were compared to a control group, and the intervention was short, so no long-term effects could be observed.

Limitations of the study

The sample might not be representative since their initial motivation was high. Participant willingness might have excluded other participants that could have shown even greater improvements. None of the interventions were compared to a control group, and both exercise interventions were relatively short and are unable to show long-term exercise effects.

Conclusions

Exercise interventions showed promising results involving functional capacity, physical condition, HRQOL and activity levels. Results were unable to show an intradialytic intervention was more efficient than a home-based one but demonstrate that both interventions are efficient. These results support the idea that performing exercise is more important than exercise modality by itself, so we encourage therapists to implement exercise on their daily dialysis routine no matter the resources they can count on.

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