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ORIGINAL ARTICLE

Rehabilitation, Exercise

Effectiveness of a resistance exercise program for lower limbs in chronic renal patients on hemodialysis: A randomized controlled trial

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Abstract

Introduction: Physical inactivity in hemodialysis patients is associated with increased mortality. The objective of this study was evaluated the effect of an intradialytic resistance exercise program on chronic kidney disease (CKD) patients on hemodialysis.

Methods: One hundred seven patients were included in the study. They were aged 18–60 years, of both sexes, had undergone hemodialysis treatment for at least 1 year, sedentary. Patients were randomly divided into two groups: stretching (STG) and resistance exercise (REG). Intervention programs were performed for 8 weeks, three times a week. The evaluations were performed before and after the training programs. The primary outcome was functional capacity using the 6-minute walk test (6MWT). Secondary outcomes were peripheral muscle strength, respiratory muscle strength, spirometric respiratory function, and laboratory data.

Findings: Comparisons between groups revealed the following clinically relevant results in favor of REG: lower limb muscle strength (mean difference [MD] = −1.99, 95% confidence interval [CI] = −2.77 to −1.21; d = −0.53), distance walked in the 6MWT (MD = −26.27, 95% CI = −45.40 to −7.14; d = −0.46), creatinine (MD = −1.52, 95% CI = −2.49 to −0.54; d = −0.66), and calcium (MD = −0.44, 95% CI = −0.78 to −0.10; d = −0.49).

Discussion: CKD patients on hemodialysis have reduced functional capacity compared to healthy sedentary individuals. In turn, this reduction appears to be associated with a lower survival rate and affects the performance of their daily living activities. Thus, resistance exercise performed in the intradialytic phase is an effective therapeutic strategy for CKD patients, mainly because it increases functional capacity and lower limb muscle strength.

KEYWORDS
exercise, physical therapy, strength

INTRODUCTION

Chronic kidney disease (CKD) is considered a worldwide public health problem; it affects more than 300 million people worldwide.[1] CKD is characterized by slow, progressive, and irreversible loss of kidney regulatory functions, which can be identified by the presence of a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 that persists for at least three consecutive months, regardless of the cause.[2] Diabetes and high blood pressure are the most common causes of CKD. Furthermore, CKD is associated with morbidity/mortality and a high proportion in health care spending.[3]

End-stage renal disease (ESRD) is a severe, irreversible kidney damage that is measured by the proteinuria level and a reduction in the glomerular filtration rate to <15 ml/min/1.73 m^2. Affected patients require dialysis or a kidney transplant.[4,5] ESRD patients need a renal replacement therapy (RRT), among which hemodialysis (HD) is the most prevalent.[6] Due to the inherent conditions of hemodialysis, these patients have reduced aerobic capacity,[7] which is associated with increased incidence of anemia,[8] peripheral vascular disease, coronary disease,[9] hypertension,[10] and electrolyte imbalances.[11] These changes contribute to the presence/increase of weakness, muscle fatigue, and pain mainly in the spine, hips, knees, and lower extremities.[12] These conditions are known to cause a progressive reduction in functionality and fitness, which negatively influences the quality of life.[13]

Physical inactivity in HD patients is associated with increased mortality. Therefore, measures to stimulate regular exercise should be proposed,[14] including in the context of public health policies. In particular, exercise has been considered one of the pillars for reversing or delaying the negative effects on functional capacity and quality of life.[15] Additionally, when performed during the intradialytic period, it appears to provide greater adherence to treatment and a reduction in the monotony of HD sessions.[16]

Although the literature is robust regarding the benefits of resistance training in patients on HD, it is consensus that clinical practice guidelines should be updated to improve the benefits of resistance training.[17] Besides, resistance training implementation is still low compared with aerobic training protocols.[18] Therefore, resistance exercise protocols and routines during HD sessions must be investigated further for future implementations of these services to ultimately achieve better results. Additionally, clinical trials that evaluate respiratory muscle strength, functional capacity, and biochemical outcomes were conducted with a small number of patients.[19,20] This fact justifies conducting clinical trials addressed to answer such questions.

The effectiveness of intradialytic exercise has not yet reached a consensus for HD patients. Therefore, intradialytic exercise—especially resistance exercise—is still not a routine treatment for HD patients. Given the above information, the aim of this study was to verify the efficacy of an intradialytic resistance training program in ESRD patients maintained on HD. We hypothesized that a resistance exercise program will increase peripheral and respiratory muscle strength, functional capacity, and biochemical aspects of these patients.

METHODS

Trial design, recruitment process, and participants

The study was a single-center, randomized, and sham-controlled crossover study. All subjects were fasted overnight, and blood was subsequently collected. All tests were performed between August 2013 and February 2016.

The study followed the Declaration of Helsinki guidelines and was approved by the Human Research Ethics Committee of our institution (protocol number 15159213.6.0000.5013). The procedure was explained and all subjects were informed of the risks and benefits of the study before any data collection and the subjects subsequently confirmed their participation in the study by written informed consent. Participants also consented to the publication of this original manuscript and any accompanying images. The study was registered in Brazilian Clinical Trials Registry (RBR-4xqq6n).

The following inclusion criteria were considered for this study: aged 18–60 years of both sexes; in HD treatment for at least 1 year via arteriovenous fistulas; sedentary; nonsmoker. Participants with the following characteristics were excluded from the study: patients with infectious disease; history of severe heart disease; and patients with motor or cognitive deficits that made it difficult to perform study evaluations.

Randomization, blinding, and concealed allocation

On the first day, to characterize the samples, an initial evaluation and screening were performed to select the study sample according to the inclusion and exclusion criteria. On the same day, an independent staff member randomly assigned participants to the resistance exercise group (REG) or stretching group (STG) using the website randomization.com. Concealed allocation of subjects was performed using opaque envelopes. Randomization and concealed allocation were performed by an independent researcher who was not involved in the recruitment, evaluation, or intervention processes. The envelopes were opened only at the time of intervention by the researcher responsible for applying the treatment programs.

The study blinded the examiners, that is, recruitment to fit the eligibility criteria was performed by one researcher, functional and biochemical assessments were performed by another examiner, and the intervention was performed by a third researcher.

Assessments of functional capacity and respiratory function were performed before and after 8 weeks of intervention. The primary outcome was functional capacity using the 6-minute walk test (6MWT). Secondary outcomes were peripheral muscle strength, respiratory muscle strength, spirometric respiratory function, and laboratory data.

Laboratory tests

All subjects fasted overnight, predialysis and postdialysis urea results were collected from medical records to evaluate dialysis efficiency by calculating Kt/V (single pool). Additionally, plasma hemoglobin (g/dl), creatinine (mg/dl), phosphorus (mg/dl), potassium (mEq/L), and calcium (mg/dl) concentrations were evaluated. Blood samples were obtained 1 week before and after the end of the protocol at the hospital.

Evaluation of lower limb muscle strength

Lower limb muscle strength was measured using a portable hand-held dynamometer (MicroFet2, Hoggan Scientific, Salt Lake City, UT), with isometric maximal voluntary contraction of the quadriceps muscle. The measurement was performed with the patient sitting comfortably in an upright posture, with 90° knee flexion, hands on the respective lower limbs, hip stabilization with a seat belt device, and the evaluator positioned in front of the patient. The test began with the evaluator gradually applying force, with the dynamometer positioned distally on the dominant lower limb. The test was divided into three stages: the first moment with the patient initiating muscle contraction against the apparatus and the evaluator's hands, the second moment increasing strength in relation to the initial contraction, and during the third stage performing the maximum possible contraction, which is an isometric contraction, until reaching a range of motion of approximately 30° knee extension from the initial positioning. Five maximal contractions were performed with an interval of approximately 10 s between them, and the highest value of three reproducible maneuvers that did not differ by more than 5% from each other was used for analysis.[21]

Assessment of functional capacity

The 6MWT was used to assess functional capacity, following the guidelines of the American Thoracic Society (ATS).[22] Briefly, patients were monitored with a heart rate monitor, pulse oximeter, and the Borg scale. Blood pressure was measured at the beginning and end of the course. Prior to the test, patients were instructed to walk as fast as possible for 6 min without running, with the patient interrupting the test if he or she felt extremely tired or by the physical therapist when peripheral oxygen saturation was below 85%. The test was stopped for chest pain, intolerable dyspnea, leg cramps, staggering, diaphoresis, and pale appearance (as described in ATS guidelines).

Assessment of respiratory function

Spirometry was performed using the Micro Plus system (CareFusion, San Diego, CA). Participants completed at least three acceptable slow and forced expiratory maneuvers; at least two had to be reproducible, according to the criteria of the Brazilian Society of Pulmonology and Tisiology. The measured variables were forced vital capacity (FVC) in L, forced expiratory volume in 1 s (FEV1) in L, and FEV1/FVC ratio in percent.

Respiratory muscle strength was measured by maximal respiratory pressures (MIP and MEP) using the digital manovacuometer (MVD300 model; Globalmed, Porto Alegre, RS, Brazil), with pressure measurements from 0 to −300 cmH_2O for inspiratory pressure and from 0 to 300 cmH_2O for expiratory pressures. In both tests, three measurements were performed; the highest value was considered. The patient was placed in a sitting position, keeping his or her head and feet in a neutral position, following the guidelines for pulmonary function tests.[23]

Interventions

In the STG, passive stretching of the hamstrings, abductors and adductors of the hip and triceps sural muscles was performed. Three repetitions of 20 s stretching maintenance were performed for each muscle group, with a 30-s rest between repetitions.[24]

In the REG, each session lasted 30 min. Resistance exercises with shin pads were instituted for the lower limb muscle groups (quadriceps, adductors, abductors, and hip flexors), initially with a 50% strength workload, determined from isometric maximal voluntary contraction of the quadriceps muscle. In the test as described above, the load was maintained for five sessions. An additional 0.5 kg was added in the 6th, 12th, and 18th sessions. Three sets of 10 repetitions were established, with 2 min rest between sets.[25]

In both groups, treatment sessions were held three times a week for 8 weeks, totaling 24 sessions. All treatment sessions were performed individually during HD, always during the first 2 h in order to avoid efforts in the second half of the session, when dialysis-related complications such as cramps and blood pressure falls are more frequent.

Statistical analysis

Sample calculation processing was performed using Ene software, version 3.0 (Autonomous University of Barcelona, Spain), based on the clinical trial conducted by Orcy et al.[26] The primary variable was the functional capacity measured by the 6MWT. The sample size calculation was based on the detection of 68.50 m between groups, with a standard deviation of 113.60 m. Thus, the suggested sample size was at least 45 patients per group.

Histograms were created to test data normality, and all outcomes had normal distributions. The data were expressed as mean and standard deviation (SD). Adjusted between-group mean differences (MD) and 95% confidence intervals (CI) are also reported. We used linear mixed models by considering group, time, and group-by-time interaction terms. SPSS version 17.0 (Chicago, IL) was used for all analyses, with a 5% significance level established for comparisons. Intent-to-treat analysis was employed in the present study.

Cohen's d was used to determine the clinical effect size of the proposed physiotherapeutic interventions, with the interpretation based on the classification established by Cohen and Cohen[27]: 0.20, small effect; 0.50, moderate effect; ≥0.80, large effect.

RESULTS

Two hundred and sixty-one patients were initially recruited for the study. Of these, 154 were excluded for the following reasons: not agreed to participate (n = 121), severe heart disease (n = 25), and cognitive impairment (n = 8). Thus, 107 patients were included in the study. The patients were randomized as follows: 53 in the STG and 54 in the REG. Seven patients discontinued treatment in each group. In the REG, these were the reasons: death (n = 3), hospital transfer (n = 3), and waiver (n = 1). In the STG, the reasons were hospital transfer (n = 4) and waiver (n = 3). However, considering the intention-to-treat analysis, the same number of randomized patients were analyzed at the end of the study.

The personal and clinical variables of the patients before the intervention are described in Table 1. The expected, personal, and clinical parameters (age, hemodialysis duration, gender, hemodialysis shift [morning/afternoon], and CKD etiology) were similar ($p > 0.05$) in both groups at baseline.

The second column of Tables 2 and 3 shows the functional and pulmonary variables at baseline. Comparisons between groups revealed the following clinically relevant results in favor of REG: increase in lower limb muscle strength (MD = −1.99, 95% CI = −2.77 to −1.21; d = −0.53) and distance walked in the 6MWT (MD = −26.27, 95% CI = −45.40 to −7.14; d = −0.46).

With regard to the laboratory data, there was clinical difference only in the following outcomes: creatinine, with mean values after the intervention in the REG of 13.02 mg/dl (SD = 5.00) and in the STG of 10.04 mg/dl (SD = 3.87), MD = −1.52 (95% CI = −2.49 to −0.54), and d = −0.66; calcium, with mean values after the intervention in the REG of 9.76 mg/dl (SD = 1.04) and in the STG

TABLE 1 Clinical and personal characteristics of stretching (STG) and resistance exercise group (REG) before intervention

Variables	STG	REG	*p* value
Age (years)[a]	44.91 (8.77)	46.65 (9.46)	0.326
Hemodialysis time (years)[a]	3.70 (4.04)	4.22 (3.52)	0.475
Gender (male)[b]	26 (49.1%)	33 (61.1%)	0.210
Hemodialysis period[b]			
Morning	28 (52.8%)	29 (53.7%)	0.364
Vespertine	16 (30.2%)	11 (20.4%)	
Nocturnal	9 (17%)	14 (25.9%)	
CKD etiology[b]			
Hypertensive nephrosclerosis	24 (45.3%)	36 (66.7%)	0.172
Diabetic nephropathy	6 (11.3%)	4 (7.4%)	
Chronic glomerulonephritis	16 (30.2%)	10 (18.5%)	
Others	7 (13.2%)	4 (7.4%)	
Hemodialysis efficiency (Kt/V)[a]	1.60 (0.33)	1.49 (0.31)	0.316
Hemoglobin (g/dl)[a]	10.54 (1.45)	10.58 (1.54)	0.866
Urea (mg/dl)[a]	169.57 (43.85)	177.61 (47.26)	0.056
Creatinine (mg/dl)[a]	11.07 (4.51)	12.54 (4.16)	0.212
Phosphor (mg/dl)[a]	5.16 (1.63)	5.95 (2.09)	0.764
Potassium (mEq/L)[a]	5.57 (1.28)	5.95 (1.35)	0.902
Calcium (mg/dl)[a]	8.89 (1.04)	8.95 (0.95)	0.431

[a]Variables presented as mean (standard deviation).

[b]Variables presented in absolute number (percentage). No significant differences occurred ($p > 0.05$), nonpaired t test or Pearson's chi-square test.

TABLE 2 Comparison between groups of outcomes related to functional aspects

Outcomes	Preintervention[a]	Postintervention[a]	Group-by-time interaction	MD (CI 95%)	Cohen d (CI 95%)
Lower limbs strength (kgf)					
STG	14.98 (6.52)	15.97 (6.85)	F = 25.583, $p < 0.001$	−1.99 (−2.77, −1.21)[b]	−0.53 (−0.92, −0.15)[c]
REG	16.99 (7.05)	19.97 (7.67)			
6MWT (m)					
STG	360.94 (108.84)	412.45 (130.32)	F = 7.413, $p = 0.008$	−26.27 (−45.40, −7.14)[b]	−0.46 (−0.85, −0.08)[c]
REG	395.93 (128.73)	473.70 (132.24)			

Abbreviations: CI: confidence interval; MD: adjusted between-group mean difference; 6MWT: Six-minute walk test.

[a]Values presented as mean (standard deviation).

[b]Significant difference.

[c]Moderate clinical effect.

of 9.26 mg/dl (SD = 1.00), MD = −0.44 (95% CI = −0.78 to −0.10), and d = −0.50.

DISCUSSION

The results of this study indicate that 8 weeks of intradialytic resistance training provided clinical increases in functional capacity and lower limb muscle strength in patients on HD. Furthermore, this treatment promoted a clinical increase in creatinine and calcium plasma concentrations.

ESRD patients on HD have reduced functional capacity compared to healthy sedentary individuals. In turn, this reduction appears to be associated with a lower survival rate and affects the performance of their daily living

TABLE 3 Comparison between groups of outcomes related to pulmonary aspects

Outcomes	Preintervention[a]	Postintervention[a]	Group-by-time interaction	MD (CI 95%)	Cohen d (CI 95%)
MIP (cmH_2O)					
STG	67.77 (24.38)	70.58 (24.41)	F = 1.443, $p = 0.232$	−2.32 (−6.14, 1.51)	−0.06 (−0.44, 0.32)
REG	66.93 (22.17)	72.06 (21.64)			
MEP (cmH_2O)					
STG	72.58 (28.66)	80.13 (31.69)	F = 1.195, $p = 0.277$	−4.25 (−11.95, 3.46)	−0.04 (−0.42, 0.34)
REG	69.46 (18.92)	81.26 (25.88)			
FVC (L)					
STG	1.58 (0.47)	1.52 (0.51)	F = 4.587, $p = 0.035$	−0.15 (−0.28, −0.01)[b]	−0.33 (−0.71, 0.05)
REG	1.61 (0.51)	1.70 (0.58)			
FEV_1 (L)					
STG	1.56 (0.47)	1.51 (0.51)	F = 5.280, $p = 0.024$	−0.15 (−0.28, −0.02)[b]	−0.31 (−0.69, 0.07)
REG	1.59 (0.50)	1.68 (0.57)			
FEV_1/FEV (%)					
STG	98.94 (2.58)	100.00 (0.01)	F = 2.070, $p = 0.153$	0.58 (−0.21, 1.38)	0.00 (−0.38, 0.38)
REG	98.31 (4.09)	100.00 (0.10)			

Abbreviations: CI: confidence interval; FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; MIP: maximal inspiratory pressure; MD: adjusted between-group mean difference; MEP: maximal expiratory pressure.

[a]Values presented as mean (standard deviation).

[b]Significant difference.

activities.[28] In the present study, 8 weeks of resistance training promoted an observable clinical effect, data that indicate a potential application in nephrology centers. Several factors appear to be associated with reduced functional capacity in patients maintained on HD, including anemia, uremic myopathy, cardiovascular abnormalities, and comorbidities such as diabetes mellitus.[29] In this sense, a previous study reported the survival of ESRD patients on HD increased by approximately 5% per 100 m covered in the 6MWT.[26] Additionally, walking distance was an independent predictor of survival for this population. The results of increased functional capacity in the resistance exercise protocol of the present study corroborate other studies that used other aerobic and resistance exercise protocols.[30,31]

Therapeutic strategies aimed at increasing the functional capacity of this population have been tested as part of the treatment of CKD patients. From this perspective, intradialytic strength training positively impacts against reduced functional capacity of ESRD patients on HD.[32]

Peripheral muscle strength may influence functional capacity that is assessed by the 6MWT. The present study demonstrated an increase in lower limb muscle strength in ESRD patients maintained on HD following an intradialytic resistance training protocol. Resistance training is known to improve the quality of life,[33] perhaps due to the increase of lower limb muscle strength, which enables greater independence of the individual.

CKD patients have skeletal muscle dysfunction that culminates in decreased muscle strength and aerobic capacity that significantly reduces the exercise tolerance.[34] Furthermore, reduced skeletal muscle strength may be a potent predictor of mortality among ESRD patients.[35] In this sense, due to the adaptations inherent to this type of intervention, resistance training is the main strategy to combat the reduction of muscle strength in this population. Moreover, both in this study and in previous studies,[24,25,36] resistance training was demonstrated and suggested to be a safe and satisfactory nonpharmacological intervention in this population to increase muscle strength.

The strength improvement observed in HD patients who received 18 weeks of strength training was related to the neuromuscular adaptations resulting from the type of training.[36] Additionally, acute strength training can promote an anabolic environment, thereby increasing lean body mass, improving muscle strength, and attenuating the muscle catabolism process in HD patients.[37] Strength training has also been indicated to maintain/increase strength and skeletal muscle mass in ESRD patients on HD and should therefore be routinely included in the treatment of this population.[38]

Muscle impairment in CKD patients results in a series of changes that affect the peripheral and respiratory muscles. The pathophysiological basis of these changes includes muscle atrophy of type I and type II fibers, and impairment in oxygen uptake, transport, and consumption, among others.[37]

Unlike previous findings, there were no significant differences in respiratory muscle strength assessed by MIP and MEP. A possible explanation for this finding is that the utilized training protocol not capable of producing sufficient stress to the inspiratory and expiratory muscles to the point of promoting structural and functional adaptations related to muscle strength that generated clinically important improvements. This deficiency may have been due to the short treatment period (8 weeks). However, these conditions apparently prevented patients undergoing the intradialytic resistance training program from presenting improvements related to spirometric lung volumes.

In turn, serum calcium and creatinine concentrations showed moderate clinical increases in ESRD patients after participating in the intradialytic resistance training program, data that confirm findings previously observed in the literature.[24,30] Improvements related to exercise-induced dialysis efficiency provide better welfare and higher quality of life for this population, due to the reduction of complications inherent to the hemodialysis process.[38]

This study had some limitations. It was conducted at a single hemodialysis center, a design that makes it difficult to generalize our findings to other dialysis populations. Another limitation was the nonapplication of a nutritional status questionnaire, and the initial nutritional status of each patient was not known.

CONCLUSION

Resistance exercises applied for 8 weeks and performed during the intradialytic phase was an effective therapeutic strategy for CKD patients when compared to a control group submitted to stretching, mainly because it increased functional capacity and lower limb muscle strength.

CONFLICT OF INTEREST

None

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REFERENCES

1. Quaggin SE. Kindling the kidney. N Engl J Med. 2016;374:281–3.
2. Work Group, International Society of Nephrology. Chapter 1: definition and classification of CKD. Kidney Int Suppl. 2018;3: 19–6264.
3. Groopman EE, Marasa M, Cameron-Christie S, Petrovski S, Aggarwal VS, Milo-Rasouly H, et al. Diagnostic utility of exome sequencing for kidney disease. N Engl J Med. 2019;380: 142–51.
4. Ku E, Mitsnefes MM. Cardiovascular disease in young adults with incident ESRD. Nat Rev Nephrol. 2019;15:390–1.
5. Modi ZJ, Lu Y, Ji N, Kapke A, Selewski DT, Dietrich X, et al. Risk of cardiovascular disease and mortality in young adults with end-stage renal disease. JAMA Cardiol. 2019;4:353–62.
6. Morton RL, Tong A, Howard K, Snelling P, Webster AC. The views of patients and carers in treatment decision making for chronic kidney disease: Systematic review and thematic synthesis of qualitative studies. BMJ. 2010;340:c112.
7. Morishita S, Tsubaki A, Shirai N. Physical function was related to mortality in patients with chronic kidney disease and dialysis. Hemodial Int. 2017;21:483–9.
8. Phillips JK, Boyd R, Krockenberger MB, Burgio G. Progression of anemia and its relationship with renal function, blood pressure, and erythropoietin in rats with chronic kidney disease. Vet Clin Pathol. 2015;44:342–54.
9. Go AS, Hsu C, Yang J, Tan TC, Zheng S, Ordonez JD, et al. Acute kidney injury and risk of heart failure and atherosclerotic events. Clin J Am Soc Nephrol. 2018;13:833–41. CJN.12591117.
10. Phan O, Burnier M, Wuerzner G. Hypertension in chronic kidney disease – Role of arterial calcification and impact on treatment. Eur Cardiol Rev. 2014;9:115–9.
11. Oka T, Hamano T, Sakaguchi Y, Yamaguchi S, Kubota K, Senda M, et al. Proteinuria-associated renal magnesium wasting leads to hypomagnesemia: a common electrolyte abnormality in chronic kidney disease. Nephrol Dial Transplant. 2018;34:1154–62.
12. Bello AK, Alrukhaimi M, Ashuntantang GE, Basnet S, Rotter RC, Douthat WG, et al. Complications of chronic kidney disease: current state, knowledge gaps, and strategy for action. Kidney Int Suppl. 2017;7:122–9.
13. Fassbinder TRC, Winkelmann ER, Schneider J, Wendland J, Oliveira OB. Functional capacity and quality of life in patients with chronic kidney disease in pre-dialytic treatment and on hemodialysis - a cross sectional study. J Bras Nefrol. 2015;37:47–54.
14. Fiaccadori E, Sabatino A, Schito F, Angella F, Malagoli M, Tucci M, et al. Barriers to physical activity in chronic hemodialysis patients: a single-center pilot study in an Italian dialysis facility. Kidney Blood Press Res. 2014;39:169–75.
15. Masajtis-Zagajewska A, Muras K, Nowicki M. Effects of a structured physical activity program on habitual physical activity and body composition in patients with chronic kidney disease and in kidney transplant recipients. Exp Clin Transplant. 2018; 24:569–75.
16. Guio BM, Gomes CP, da Costa FB, Oliveira A d S d, Duarte MT, Leite Júnior M, et al. Benefcial effects of intradialytic cardiopulmonary rehabilitation. J Bras Nefrol. 2017;39:275–82.
17. Cheema BS, Chan D, Fahey P, Atlantis E. Effect of progressive resistance training on measures of skeletal muscle hypertrophy, muscular strength and health-related quality of life in

patients with chronic kidney disease: a systematic review and meta-analysis. Sport Med. 2014;44(8):1125–38.
18. Watson EL, Gould DW, Wilkinson TJ, Xenophontos S, Clarke AL, Vogt BP, et al. Twelve-week combined resistance and aerobic training confers greater benefits than aerobic training alone in nondialysis CKD. Am J Physiol Physiol. 2018;314:F1188–96.
19. Parsons TL, Toffelmire EB, King-Van Vlack CE. Exercise training during hemodialysis improves dialysis efficacy and physical performance. Arch Phys Med Rehabil. 2006;87: 680–7.
20. Siddiqui M, Darain H, Sah S. Effect of progressive resistive exercise training in improving mobility and functional ability of middle adulthood patients with chronic kidney disease. Saudi J Kidney Dis Transplant. 2015;26:912.
21. Coronell C, Orozco-Levi M, Méndez R, Ramírez-Sarmiento A, Gáldiz JB, Gea J. Relevance of assessing quadriceps endurance in patients with COPD. Eur Respir J. 2004; 24:129–36.
22. ATS. Committee on proficiency standards for clinical pulmonary function laboratories. ATS statement. Am J Respir Crit Care Med. 2002;166:111–7.
23. Souza RB. Pressões respiratórias estáticas máximas. J Pneumol. 2002;28:S155–65.
24. Ribeiro R, Coutinho GL, Iuras A, Barbosa AM, Souza JAC d, Diniz DP, et al. Effect of resistance exercise intradialytic in renal patients chronic in hemodialysis. J Bras Nefrol. 2013; 35:13–9.
25. Chen JLT, Godfrey S, Ng TT, Moorthi R, Liangos O, Ruthazer R, et al. Effect of intra-dialytic, low-intensity strength training on functional capacity in adult haemodialysis patients: a randomized pilot trial. Nephrol Dial Transplant. 2010;25:1936–43.
26. Orcy RB, Dias PS, Seus TL, Barcellos FC, Bohlke M. Combined resistance and aerobic exercise is better than resistance training alone to improve functional performance of haemodialysis patients - results of a randomized controlled trial. Physiother Res Int. 2012;17:235–43.
27. Cohen J. Chapter 4 – Differences between correlation coefficients. Statistical power analysis for the behavioral sciences. Cambridge: Academic Press; 2013:109–43.
28. Painter P. Physical functioning in end-stage renal disease patients: update 2005. Hemodial Int. 2005;9:218–35.
29. Garcia RSA, Lucinda LMF, Ramos FA, Bueno GDS, GMR d O, Bonisson LS, et al. Factors associated with functional capacity in hemodialysis patients. Artif Organs. 2017;41: 1121–6.
30. Sheng K, Zhang P, Chen L, Cheng J, Wu C, Chen J. Intradialytic exercise in hemodialysis patients: a systematic review and meta-analysis. Am J Nephrol. 2014;40:478–90.
31. Pellizzaro CO, Thomé FS, Veronese FV. Effect of peripheral and respiratory muscle training on the functional capacity of hemodialysis patients. Ren Fail. 2013;35:189–97.
32. Kouidi EJ, Grekas DM, Deligiannis AP. Effects of exercise training on noninvasive cardiac measures in patients undergoing long-term hemodialysis: a randomized controlled trial. Am J Kidney Dis. 2009;54:511–21.
33. Bennett PN, Fraser S, Barnard R, Haines T, Ockerby C, Street M, et al. Effects of an intradialytic resistance training programme on physical function: a prospective stepped-wedge randomized controlled trial. Nephrol Dial Transplant. 2016;31:1302–9.
34. Johansen KL. Physical functioning and exercise capacity in patients on dialysis. Adv Ren Replace Ther. 1999;6:141–8.
35. Isoyama N, Qureshi AR, Avesani CM, Lindholm B, Barany P, Heimburger O, et al. Comparative associations of muscle mass and muscle strength with mortality in dialysis patients. Clin J Am Soc Nephrol. 2014;9:1720–8.
36. Kirkman DL, Mullins P, Junglee NA, Kumwenda M, Jibani MM, Macdonald JH. Anabolic exercise in haemodialysis patients: A randomised controlled pilot study. J Cachexia Sarcopenia Muscle. 2014;5:199–207.
37. McIntyre CW, Selby NM, Sigrist M, Pearce LE, Mercer TH, Naish PF. Patients receiving maintenance dialysis have more severe functionally significant skeletal muscle wasting than patients with dialysis-independent chronic kidney disease. Nephrol Dial Transplant. 2006;21:2210–6.
38. Wu Y, He Q, Yin X, He Q, Cao S, Ying G. Effect of individualized exercise during maintenance haemodialysis on exercise capacity and health-related quality of life in patients with uraemia. J Int Med Res. 2014;42:718–27.

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