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*Published in:*  
Disability and Rehabilitation

*DOI:*  
[10.1080/09638288.2020.1766581](https://doi.org/10.1080/09638288.2020.1766581)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2022

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Zelko, A., Rosenberger, J., Skoumalova, I., Kolarcik, P., Madarasova Geckova, A., van Dijk, J. P., & Reijneveld, S. A. (2022). The effects of an intradialytic resistance training on lower extremity muscle functions. *Disability and Rehabilitation*, 44(2), 275-281. <https://doi.org/10.1080/09638288.2020.1766581>

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To cite this article: Aurel Zelko, Jaroslav Rosenberger, Ivana Skoumalova, Peter Kolarcik, Andrea Madarasova Geckova, Jitse P. van Dijk & Sijmen A. Reijneveld (2020): The effects of an intradialytic resistance training on lower extremity muscle functions, *Disability and Rehabilitation*, DOI: [10.1080/09638288.2020.1766581](https://doi.org/10.1080/09638288.2020.1766581)

To link to this article: <https://doi.org/10.1080/09638288.2020.1766581>



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Published online: 24 May 2020.



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## The effects of an intradialytic resistance training on lower extremity muscle functions

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### ABSTRACT

**Purpose:** The loss of muscle functions is a significant health issue among dialysis patients. Poor muscle strength negatively affects a patient's mobility, independence and quality of life. The aim of the study was to assess the effects of an intradialytic resistance training (IRT) on lower extremity muscle functions among dialysed patients.

**Materials and methods:** Ninety patients were allocated into an experimental group ( $n=57$ ) or control group (CNG) ( $n=33$ ) according to the location of the dialysis service center. Fifty-eight patients completed the study follow-up. The intervention regarded 12-week IRT, while the controls remained physically inactive during hemodialysis. In both groups of patients, we assessed lower extremity muscle functions by a diagnostics of maximal isometric force generated during hip flexion (HF), hip extension (HE), and knee extension (KE) contractions at baseline, after the 12-weeks intervention and after a further 12-weeks follow up.

**Results:** We found that improvements in HE between baseline and post-intervention were significantly larger for the experimental than the CNG (difference 32.0, 95% CI = 12.3–51.8,  $p=0.002$ ). For the other primary outcomes, we found no differences between the groups, and neither for the two other indices of muscle strength (HF and KE). At 12-weeks follow-up, we found no statistically significant differences between the two groups.

**Conclusions:** Our findings indicate that exercise during dialysis not just suppresses adverse effects in muscle strength and functioning, but effectively and safely increases lower extremities muscle function in a relatively short time.

### ARTICLE HISTORY

Received 9 January 2020  
Revised 4 May 2020  
Accepted 5 May 2020

### KEYWORDS

Intradialytic exercise;  
resistance training; muscle  
functions; hemodialysis;  
patients

### ► IMPLICATIONS FOR REHABILITATION



- Regular, progressive, resistance training realized during dialysis is well tolerated and safe for exercise interventions in hemodialysis patients.
- A 12-weeks intradialytic resistance training is effective in the prevention and clinical management of muscle function loss among hemodialysis patients.
- The range of improvements in muscle functions, demonstrated by the assessment of maximal isometric force, varied severely during different lower extremity movements of hemodialysis patients.

## Introduction

Hemodialysed patients (HDPs) frequently suffer from muscle weakness [1], frailty [2], and falls [3,4]. This continuous loss of muscle mass and functions across life-time spent on dialysis therapy causes frequent health problems in HDP. In chronic kidney disease, these health risks factors are primarily caused by deregulated proteolytic synthesis and degradation balance [5,6], mitochondrial dysfunctions [7], and impaired satellite cells functions [8]. Moreover, hemodialysis therapy alone is an activator of several mechanisms of cellular protein catabolism [9]. The permanent

decline in muscle functions of HDP is associated with a decrease of functional independence [10], mobility, quality of life [4] and is associated with increased mortality and morbidity risks [11].

To counteract muscle weakness in HDP, various approaches have been proposed to apply traditional exercise interventions in the clinical settings of dialysis centers. Evidence on exercise effects mostly regards changes in aerobic capacity and physical functioning during endurance training. Evidence is scarce on the effects of exercise interventions on muscle strength and functions. The inconsistency in conclusions of previous studies is due to differences in disease severity of the patients included in these

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studies and due to differences in the organization (intra-/inter-dialytic) and modality of the exercise interventions offered (endurance-, strength-, or combined training) [12,13].

In HDP, resistance training prevents deterioration of muscle mass and function and is accepted as an instrument for maintaining of favorable functional efficiency [14,15]. The importance of muscle functions for patients undergoing maintenance dialysis is emphasized by the evidence that muscle strength and functions are independent predictors of mortality [16,17] and hospitalization [18,19] among HDP. Due to these functional and prognostic relevancies, we decided to assess the effects of resistance training for patients during dialysis.

The methodology and the organization of strength training programs determine the range and rate of the resulting morphological and neurological adaptations. In a supine position, which is typically maintained during intradialytic exercise because of the dialysis, the activation of lower extremity muscle groups is different from that in a seated or standing position [20,21]. Most studies among HDP reported the change in muscle strength by assessments of maximal isometric force during knee extension (KE), preferably in the seated position [22–26]. Only Johansen et al. [27] realized and reported the additional testing of the maximal isometric strength during hip flexion (HF) and hip abduction (HA). No other studies are available that report the effects of intradialytic resistance training (IRT) on lower extremity muscle strength by assessing the maximal strength during various muscle movements. However, isolated functional assessments probably have limited explanatory value, especially among chronically diseased patients [28,29]. Therefore, the aim of our study was to evaluate the effects of IRT on three different indicators of lower extremity muscle functions.

## Methods

### Study design

We conducted a quasi-experimental, two-group, pre-post comparative study with 12 weeks follow-up at three dialysis centers (Fresenius Medical Care Dialysis Services in Kosice, Logman East in Kosice and Fresenius Medical Care Dialysis Services in Banska Bystrica). The study design and protocol were reviewed and approved by the Ethics Committee of the Pavol Jozef Safarik University in Kosice (approval no. 14N/2017); the protocol was registered at ClinicalTrials.gov (ID: NCT03511924). All methods, assessments and data acquisitions were conducted according to relevant ethics guidelines and regulations, based on the Helsinki Declaration (Helsinki Declaration of 1975, as revised in 2013) and followed the official protocol of study [30].

**Table 1.** Inclusion and exclusion criteria used to assess the eligibility of patients.

Inclusion criteria
– Over 30 years of age
– Diagnosed with CKD-5
– Treated by dialysis therapy at least for last three months
Exclusion criteria
– Lower extremity amputation
– Severe dementia or retardation
– Acute intercurrent disease
– Probability of one year mortality higher than 25% according to the Charlson comorbidity index [31]

### Participants

Inclusion criteria regarded age older than 30 years and being in hemodialysis therapy for at least three months prior to the start of the study. From three dialysis centers, all 198 dialysis patients were screened and selected according to the inclusion and exclusion criteria (Table 1) through their nephrologists, yielding 126 eligible patients (63.6% eligible patients). These received oral and written information about the possibility to participate in the study, leading to 90 patients signing a written informed consent (71.4% response rate) prior to the study.

### Patient allocation

Patients attended dialysis therapy in both sites in Kosice were allocated into the experimental group (EXG,  $n=57$ ), while patients from the Banska Bystrica dialysis center were allocated into the control group (CNG,  $n=33$ ). After the allocation procedure, the investigatory team members and participating patients were informed about the group assignment structure.

### Intervention

*Experimental condition.* Patients allocated to the EXG participated in a 12-week IRT which they performed under the supervision of training assistants, three times per week. IRT sessions were 40 min length, composed of 3-min warming-up, 30-min of conditioning, and 7-min of cooling-down and stretching. To perform effective exercises on supine position during dialysis, we used external pressure generated by elastic bands and over-balls (TheraBand®, Akron, OH). These external loading resources were fixed on a construction of the dialysis bed, and during exercises patients pulled or pushed against them. The program included three exercises ((A) unilateral push and pull of over-ball against a leg board, (B) bilateral knee squeeze of over ball, and (C) unilateral straight leg raise against the band pressure).

The progress of the IRT program was individual and depended on a patient's physical capabilities of the patient. During the first two weeks of the IRT program, patients performed an initial program, which consisted of three sets of three different exercises (12 up to 15 repetitions of each exercise) of lower extremity muscles. Once a patient was capable to safely complete a session of the planned initial program as planned, then the number of repetitions in the next session increased with three repetitions for each exercise. If a patient reached the maximal number (18) of repetitions per exercise during a session, then for the next session the number of sets was increased with one set. When the patient was able to perform five sets with 18 repetitions for each exercise, then we made the IRT harder by applying a stiffer elastic band or an over-ball with higher hardness. Vice versa, if a patient failed to complete the entire training session, or had obvious difficulties, the IRT was facilitated by lowering number in all above steps sequentially. This methodology of training progressivity enabled us to maintain the patient's safety during IRT and ensured the subjective intensity of training to be between "moderate" and "hard". To control the patient's training progress during IRT, we registered the number of repetitions and series for each of exercise independently on the patient's training log-book.

*Control condition.* Patients allocated to the CNG group received their standard nephrology care. Through the 12-weeks control period, all CNG patients maintained their standard treatment regimen and maintained their customary dietary and physical activity patterns. The CNG patients were informed about the clinical benefits and effects of regular physical activity in dialysed patients and

during the control period they were receiving increased attention from the research team members.

### Measures

The *primary outcome* of the study was the change of maximal isometric force generated during the contractions of lower extremity muscles involved in hip and knee joint movements. We chose the primary outcome in this study based on those used in previous studies that were most sensitive to strength training during dialysis and based on feasibility in a multicenter design of our study. A detailed description of outcomes assessments is described in the protocol article [30]. Maximal isometric forces generated during three lower extremity movements (KE, HF, and hip extension (HE)) were assessed by a hand-held dynamometer (Universal digital force gauge HF 500, SAUTER GmbH, Balingen, Germany). All tests were administered by one member of the investigatory team (AZ), which was not blinded to the intervention. The assessments of maximal isometric contraction force using hand-held dynamometers had excellent inter-rater reliability and accuracy [29]. The standard errors of measurements were 5.34–7.29 for HE, 6.39–6.71 for HF, and 8.76–9.30 for KE contraction. The accuracy of the device used for assessment was verified with standard weights and the margin of error was below 5%. During the assessments, patients were in a supine position with arms safely and comfortably placed on the bed. The measurements of the KE of the dominant leg were done at a knee angle of 90° from full extension. The hand-held, portable dynamometer was placed on the patient's ankle and was stabilized during the performance of the physical examination. During the assessments of HF and HE of the lower limb the patient held the dominant leg in a straightened position, while the dynamometer was placed proximally to the ankle, on the anterior surface of the lower leg for the HF force assessments and on the posterior surface of the lower leg for the HE force assessments. The patients were instructed to perform a maximal isometric contraction and hold it for 5 s. The tests were repeated within 30-s rest intervals, and the higher measured values of two consecutive tests were used for the analysis. The administrator was not blinded to the allocation of patients. The changes of maximal isometric forces were calculated as post-intervention measure minus baseline measure (measure unit: Newton, N). To avoid an experimental error in data processing and analysis, we included a patient's age and baseline measures of muscle strength as statistical covariates.

*Background variables* regarded a patient's clinical data were extracted from the latest electronic medical record of patient completed before the start of the intervention. Extracted data contained (A) patient's age and gender, (B) body composition parameters (body weight and body height), and (C) nephrological clinical data containing the Charlson comorbidity index [31], dialysis adequacy ( $Kt/V$ ), over-hydration, and concentrations of C-reactive protein, parathyroid hormone, hemoglobin, albumin, ferritin, phosphates, calcium, potassium, and sodium. The body mass index was calculated as body weight in kilograms divided by the square of the body height in meters (BMI,  $\text{kg}/\text{m}^2$ ).

The primary outcome measures were collected in both groups before and after the 12-week intervention period and also at the 12-week follow up. The background variables were collected only before the start of the intervention.

### Power analysis

We estimated that 27 patients per group would be required to have 80% power to detect an effect size of 0.60 in change of maximal forces measured during isometric contraction of lower extremities muscles between EXG and CNG (two-tailed,  $\alpha$  level of 0.05). We therefore planned to enroll at least 78 patients (i.e.,  $2 \times 39$ ), anticipating a 70% retention during this study. This approach was based on the results from previously published articles, which reported changes in maximal lower extremity muscle strength on similar groups of dialysed patients who underwent IRT [22,24,32].

### Statistical analysis

First, we assessed background variables and compared them between two study groups by  $\chi^2$  tests for categorical (binary) variables and Student's *t*-test for continuous variables for possible differences.

Second, we assessed the effects of the intervention by comparing the changes of the primary outcome measures between baseline and post intervention for EXG versus CNG. We estimated the between-group differences in change by analysis of covariance, with patients' group allocation as the fixed factor, the change scores of primary outcome indices as the dependent value and age plus baseline values of primary outcome indices as covariates [33]. We performed this on an intention-to-treat basis, i.e., including all patients who completed the baseline assessments of the primary outcomes. We repeated all analyses on the basis of complete-case-analyses, i.e., including only patients with complete baseline, and post-intervention assessments. Applied statistical tests were all two-tailed and the level of significance was set at an  $\alpha$  level of 0.05. Data analyses were carried out using the statistical software package IBM SPSS 22.0 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Version 22.0, IBM Corp., Armonk, NY).

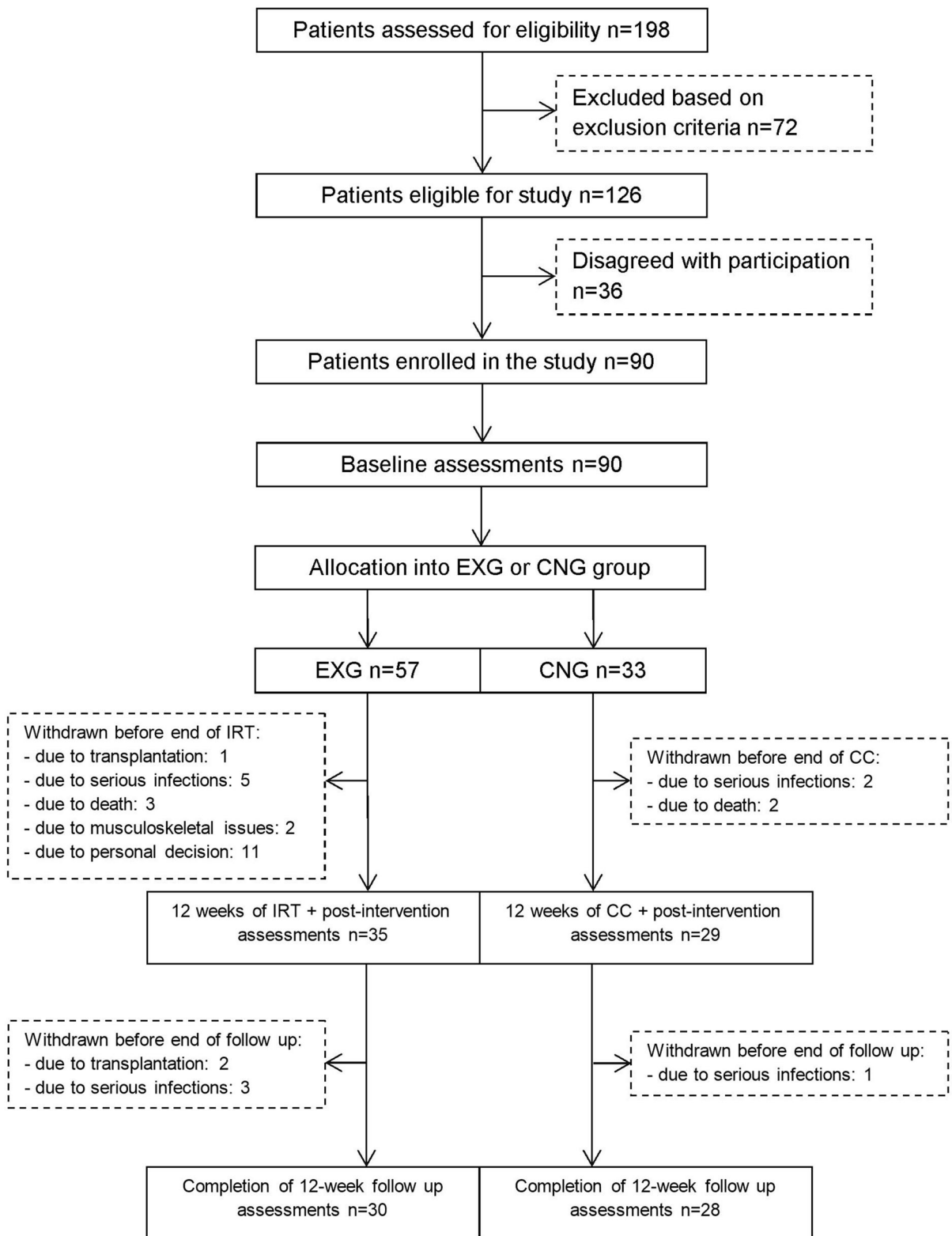
## Results

### Patient flow

From an initial study sample of 90 patients, 64 completed the 12-week intervention and 58 completed the 12-week follow up period. Drop-out rates in our study were similar in both groups, and reflected patient characteristics at baseline. Drop-outs were due to mortality, transplantation, serious infections, personal decision, and musculoskeletal issues. No adverse effects occurred during training intervention or muscle strength assessments. Musculoskeletal complications leading to discontinuation of patients were not related to the training intervention; they however were mainly due to interdialytic activities and accidents. In patients that completed the exercise intervention, the compliance was adequate with an average rate of 83%. The detailed patients flow summary (Figure 1) containing numbers of patients completed the intervention and follow up is presented in the CONSORT diagram [34].

### Comparison of groups at baseline

The mean age of patients enrolled in the study ( $n = 90$ ) was 62.6 (standard deviation: 12.8). Among the enrolled patients, 61% was male and the BMI was 26.1 (5.5)  $\text{kg}/\text{m}^2$ . The mean duration of dialysis therapy was 49.1 (45.9) months. Baseline patients' characteristics and their differences between EXG and CNG are



(EXG = Experimental group; CNG = Control group; IRT = Intradialytic resistance training; CC = Control condition).

**Figure 1.** CONSORT flowchart of patients summarizing their eligibility assessment, enrolment, and allocation to the experimental and control groups of the study, and drop-out of patients at the two further measurements. EXG: experimental group; CNG: control group; IRT: intradialytic resistance training; CC: control condition.

**Table 2.** Baseline patients' characteristics and their differences between EXG and CNG group.

Variable	EXG (n = 30)	CNG (n = 27)	p Value
Age	61.7 (11.5)	67.1 (9.5)	0.056
Gender (male/female)	19/11	15/13	0.451
Body mass index (kg/m <sup>2</sup> )	27.3 (5.8)	24.3 (4.5)	0.035 <sup>a</sup>
Duration of dialysis therapy	46.4 (51.2)	49.5 (51.7)	0.717
Dialysis adequacy (Kt/V)	1.5 (0.2)	2.0 (0.3)	0.001 <sup>b</sup>
Over-hydration index (%)	11.6 (6.0)	11.9 (6.8)	0.861
C-reactive protein (mg/l)	12.4 (10.3)	8.3 (10.4)	0.170
iPTH (pg/ml)	396.6 (378.8)	388.6 (443.3)	0.941
Hemoglobin (g/l)	114.4 (14.2)	113.1 (12.7)	0.732
Albumin (g/l)	39.4 (2.7)	37.07(4.3)	0.016 <sup>a</sup>
Ferritin (ng/ml)	642.7 (595.6)	844.5 (298.3)	0.107
Phosphates (mmol/l)	1.7 (0.4)	1.5 (0.5)	0.122
Calcium (mmol/l)	2.2 (0.2)	2.4 (0.1)	0.001 <sup>b</sup>
Potassium (mEq/l)	5.2 (0.7)	5.2 (0.7)	0.694
Sodium (mEq/l)	138.1 (3.3)	138.6 (2.5)	0.569
Hip flexion (N)	112.7 (47.1)	97.5 (28.4)	0.144
Hip extension (N)	168.3 (69.0)	141.6 (45.2)	0.090
Knee extension (N)	155.2 (48.4)	132.9 (48.6)	0.085

iPTH: intact parathyroid hormone; EXG: experimental group; CNG: control group. Data are presented as mean  $\pm$  standard deviation, *p* Values determined by the unpaired Student's *t*-test.

<sup>a</sup>Differences between groups significant at  $p < 0.05$ .

<sup>b</sup>Differences between groups significant at  $p < 0.01$ .

**Table 3.** Comparison of differences in changes of primary outcomes and 95% confidence intervals (CI) from baseline to first post-measurement between the two groups.

Group	Hip extension (N)	Hip flexion (N)	Knee extension (N)
EXG	+12.4 (38.7)	+14.9 (32.0)	+0.6 (47.9)
CNG	-14.1 (34.0)	+3.1 (25.9)	-0.3 (38.7)
Mean difference	32.0 (9.9) <sup>a</sup>	14.2 (7.6)	4.3 (10.7)
95% CI	12.3–51.8	-1.0 to 29.5	-17.0 to 25.6

EXG: experimental group; CNG: control group.

Data are presented as mean change  $\pm$  standard deviation. Change in primary outcome indices calculated as post intervention values minus baseline values. *p* Values determined by ANOCA. *p* Value calculated for intention-to-treat analysis ( $n = 90$ , EXG = 57, CNG = 33).

<sup>a</sup>Difference between groups significant at  $p < 0.01$ .

summarized in Table 2. At baseline, we found significant differences between the groups in body mass index, dialysis adequacy, and concentrations of albumin and calcium. We analyzed data on primary outcomes with adjustment for body mass index, dialysis adequacy, and concentrations of albumin and calcium and found that these factors did not affect our findings.

#### Comparison of differences in changes of primary outcomes from baseline to first post-measurement between groups

We found that the change of HE was significantly greater in the EXG compared to the CNG (difference 32.0, 95% CI = 12.3–51.8,  $p = 0.002$ ). Two other indices of muscle strength, HF and KE did not show significant differences in change between the EXG group and CNG group (Table 3).

#### Comparison of differences in changes of primary outcomes from baseline to second post-measurement between groups

We compared the changes in the primary outcome indices after follow up between the groups and we found no significant difference in change between EXG and CNG in any of three followed muscle strength parameters (Table 4).

**Table 4.** Comparison of differences in changes of primary outcomes and 95% confidence intervals (CI) from baseline to second post-measurement between the two groups.

Group	Hip extension (N)	Hip flexion (N)	Knee extension (N)
EXG	+1.4 (51.6)	+2.1 (33.6)	-5.0 (39.9)
CNG	-14.2 (32.8)	-2.8 (26.5)	-12.2 (39.3)
Mean difference	21.4 (11.2)	6.3 (7.0)	8.4 (10.1)
95% CI	-1.1 to 43.9	-1.0 to 29.5	-11.8 to 28.5

EXG: experimental group; CNG: control group.

Data are presented as mean change  $\pm$  standard deviation. Change in primary outcome indices calculated as post follow up values minus baseline values. *p* Values determined by ANOCA. *p* Value calculated for intention-to-treat analysis ( $n = 90$ , EXG = 57, CNG = 33).

#### Complete case analysis of differences between groups

HE increased with statistical significance after the intervention (difference 30.9, 95% CI = 11.9–49.9,  $p = 0.002$ ) and also after follow-up period (difference 23.3, 95% CI = 0.9–45.7,  $p = 0.042$ ) in the EXG compared to the CNG. No significant differences were found during between-group analysis of changes in HF and KE during the intervention, or the follow up period.

#### Discussion

Physical activity plays an important role in the prevention of muscle loss in end-stage renal disease. The main goal of this quasi-experimental study was to evaluate the effects of IRT on the lower extremities' muscle strength of hemodialysis patients. We found beneficial effects of IRT on muscle function, i.e., a significant increase of the maximal isometric force produced during HE (+10.2%) in EXG which significantly differed from the change observed in CNG (-11.2%). During the follow-up, we found this effect not to continue in the intention-to treat-analysis, but to continue in the complete case analysis.

We found an effect of IRT on HE, which can only be compared to the findings of Johansen et al. [27] on the change of maximal strength of the hip joint muscles during IRT. In that study, IRT improved patients' HA strength and HF strength much more (+81.2% and +80.3%, respectively). These differences in Johansen's study are higher probably because the authors assessed the HA and HF strength by three repetitions maximum tests, because these tests assessed different hip joint movements, and maybe also because patients were at average younger than in our study. Our findings demonstrate how important strength training is for maintaining favorable muscle functions in HDP, and confirm the importance of IRT in these patients as first shown by Johansen et al. [27].

Importantly, we found that the IRT leads to functional improvements only for maximal HE contraction force, but not for KE (EXG: +6.1%; CNG: -1.4%) and HF (EXG: +18.4%; CNG: +5.5%). Most evidence on the beneficial effects of IRT regards improvements in maximal KE strength ranging from +15.6% up to +60.3% [22–25]. We could not confirm the improvement in maximal isometric force during KE contraction as found by Kirkman et al. [24], even though the baseline values of our sample were very similar. The lack of improvement for KE is partially due to the type and characteristics of the training intervention as offered. Only one of the three exercises applied during IRT enables patients to fully activate knee extensors. A second contributing factor may be our modified method of assessment of KE contraction force. The assessment was realized in the supine position of the patient, whereas the standard position for assessment of KE force is the sitting position of the patient. These two factors must be considered during the evaluation of evidence regarded

the change of maximal isometric force during knee extensors contraction. Therefore, multiple muscle function tests should be applied for more accurate and valid assessments of muscle functions, to come to more final conclusions regarding the effects of IRT on these muscles.

We found that the intradialytic training improved HE right after the intervention but this effect decreased at follow-up, confirming the beneficial effects of exercise on patient's muscle functions. This finding shows that generally, exercise should be continued to maintain the improved functioning. Dialysis patients are at high risk of falls, movement disabilities and immobilization. These health risks are closely related to loss of muscle functions that occurred after the initiation of hemodialysis therapy and worsen during the life-time spend on dialysis. The improvements in patient's muscle strength detected in our study are an important demonstration of how intradialytic exercise intervention acted against health-related risks among HDPs. To improve the effectiveness of interventions and reach the full potential of patient's adaptability, it is necessary to create personalized activity prescriptions for every patient. Significant improvements in patient's physical functioning are achievable also by application of endurance training, combined training [35], or training interventions including electrical muscle stimulation [36,37].

Our study has some important strengths. We used a quasi-experimental design that was realized in a clinical setting of dialysis service units. All interventions and instruments used during the research were applied during regular dialysis therapy and all methods were adapted to maximize patient's safety while keeping reasonable validity and reliability. The gold standard for assessment of lower extremity muscle contraction characteristics is computer-controlled isokinetic dynamometry. Due to patient safety and protection of patient's vascular access, we used hand-held dynamometry during dialysis to assess muscle functions. This has shown acceptable validity and reliability for lower extremity strength assessments [29]. Contrary to other studies, we applied three different muscle strength tests, leading to more accurate and validate data about the change of muscle functions during the experiment.

Our study also has some limitations. First, the allocation of patients was realized based on the dialysis center location, leading to baseline differences in body mass index, dialysis adequacy, albumin and calcium level between EXG and CNG which could confound our findings. However, we controlled this imbalance in baseline variables by assessing differences in muscle function changes between groups by analysis of co-variance statistical model with adjustments for baseline values of body mass index, dialysis adequacy, albumin and calcium level. This showed that our findings were not influenced by these factors. Small changes in findings after adjustment show that the potential bias due to the use of geographical location was probably small. Second, we had no concealment of group allocation during the study, which may have biased outcome measurements. The absence of blinding is typical for "exercise" intervention studies and cannot be avoided completely during the application of intradialytic training intervention.

A 12-week IRT is effective in the prevention and clinical management of muscle function loss among hemodialysis patients. Besides the suppression of adverse effects in muscle functioning, our results suggested that exercise during dialysis effectively and safely increases lower extremities muscle function in a relatively short time. To incorporate the regular physical activity into the clinical care of dialysis patients remains an important challenge. We believe that the digital health instruments and technologies

could be an efficient and long-term suitable solution for this purpose. For future research, we are strongly recommending to include various types of diagnostic tools for the assessments of muscle functions among HDP.

## Acknowledgements

We appreciate the co-operation of the representatives and staff of dialysis centers involved in the implementation of this study. Special acknowledgements go to Peter Mizla MD and Peter Javorsky MD for organizational support during study planning and implementation.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## Funding

This work was supported by the Slovak Research and Development Agency under the Contract No. APVV-16-0490 and was supported by the Internal Research Grant System of the Pavol Jozef Safarik University under the Contract No. VVGS-2019-1069.

## Data availability

The data that support the findings of this study are available from the corresponding author, AMG, upon reasonable request.

## References

- [1] Tangvoraphonkchai K, Hung R, Sadeghi-Alavijeh O, et al. Differences in prevalence of muscle weakness (sarcopenia) in haemodialysis patients determined by hand grip strength due to variation in guideline definitions of sarcopenia. *Nutr Clin Pract*. 2018;33(2):255–260.
- [2] Young HML, Eborall HC, Conroy S, et al. Living with frailty and falls: a qualitative study exploring the experiences of patients with end-stage renal disease receiving haemodialysis. *Physiotherapy*. 2019;105(Suppl. 1):e28–e29.
- [3] Kono K, Nishida Y, Yabe H, et al. Sarcopenia as a risk factor for falls in patients undergoing maintenance hemodialysis: a cohort study. *Physiotherapy*. 2015;101(Suppl. 1):e782–e783.
- [4] Wang AY, Sherrington C, Toyama T, et al. Muscle strength, mobility, quality of life and falls in patients on maintenance haemodialysis: a prospective study. *Nephrology (Carlton)*. 2017;22(3):220–227.
- [5] Adey D, Kumar R, McCarthy JT, et al. Reduced synthesis of muscle proteins in chronic renal failure. *Am J Physiol Endocrinol Metab*. 2000;278(2):E219–E225.
- [6] Du J, Hu Z, Mitch WE. Molecular mechanisms activating muscle protein degradation in chronic kidney disease and other catabolic conditions. *Eur J Clin Invest*. 2005;35(3):157–163.
- [7] Su Z, Klein JD, Du J, et al. Chronic kidney disease induces autophagy leading to dysfunction of mitochondria in skeletal muscle. *Am J Physiol Renal Physiol*. 2017;312(6):F1128–F1140.



- [8] O'Sullivan TF, Smith AC, Watson EL. Satellite cell function, intramuscular inflammation and exercise in chronic kidney disease. *Clin Kidney J.* 2018;11(6):810–821.
- [9] Ikizler TA, Pupim LB, Brouillette JR, et al. Hemodialysis stimulates muscle and whole body protein loss and alters substrate oxidation. *Am J Physiol Endocrinol Metab.* 2002;282(1):E107–E116.
- [10] Oller GASAdO, Ribeiro RdCHM, Travagim DSA, et al. Functional independence in patients with chronic kidney disease being treated with haemodialysis. *Rev Lat Am Enfermagem.* 2012;20(6):1033–1040.
- [11] Torino C, Manfredini F, Bolognani D, et al. Physical performance and clinical outcomes in dialysis patients: a secondary analysis of the EXCITE trial. *Kidney Blood Press Res.* 2014;39(2–3):205–211.
- [12] Clarkson MJ, Bennett PN, Fraser SF, et al. Exercise interventions for improving objective physical function in patients with end-stage kidney disease on dialysis: a systematic review and meta-analysis. *Am J Physiol Renal Physiol.* 2019;316(5):F856–F872.
- [13] Johansen KL. Resistance exercise in the hemodialysis population – who should do the heavy lifting? *Am J Nephrol.* 2016;44(1):29–31.
- [14] Rhee CM, Kalantar-Zadeh K. Resistance exercise: an effective strategy to reverse muscle wasting in hemodialysis patients? *J Cachexia Sarcopenia Muscle.* 2014;5(3):177–180.
- [15] McLeod JC, Stokes T, Phillips SM. Resistance exercise training as a primary countermeasure to age-related chronic disease. *Front Physiol.* 2019;10:645.
- [16] Kittiskulnam P, Chertow GM, Carrero JJ, et al. Sarcopenia and its individual criteria are associated, in part, with mortality among patients on hemodialysis. *Kidney Int.* 2017;92(1):238–247.
- [17] Matsuzawa R, Matsunaga A, Wang G, et al. Relationship between lower extremity muscle strength and all-cause mortality in Japanese patients undergoing dialysis. *Phys Ther.* 2014;94(7):947–956.
- [18] Musso CG, Jauregui JR, Macías Núñez JF. Frailty phenotype and chronic kidney disease: a review of the literature. *Int Urol Nephrol.* 2015;47(11):1801–1807.
- [19] Kutner NG, Zhang R, Huang Y, et al. Gait speed and mortality, hospitalization, and functional status change among hemodialysis patients: a US Renal Data System Special Study. *Am J Kidney Dis.* 2015;66(2):297–304.
- [20] Worrell TW, Perrin DH, Denegar CR. The influence of hip position on quadriceps and hamstring peak torque and reciprocal muscle group ratio values. *J Orthop Sports Phys Ther.* 1989;11(3):104–107.
- [21] Rochette L, Hunter SK, Place N, et al. Activation varies among the knee extensor muscles during a submaximal fatiguing contraction in the seated and supine postures. *J Appl Physiol (Physiol).* 2003;95(4):1515–1522.
- [22] Cheema B, Abas H, Smith B, et al. Progressive exercise for anabolism in kidney disease (PEAK): a randomized, controlled trial of resistance training during hemodialysis. *J Am Soc Nephrol.* 2007;18(5):1594–1601.
- [23] Chen JL, Godfrey S, Ng TT, 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(6):1936–1943.
- [24] Kirkman DL, Mullins P, Junglee NA, et al. Anabolic exercise in haemodialysis patients: a randomised controlled pilot study. *J Cachexia Sarcopenia Muscle.* 2014;5(3):199–207.
- [25] Hellberg M, Höglund P, Svensson P, et al. Randomized controlled trial of exercise in CKD—the RENEXC Study. *Kidney Int Rep.* 2019;4(7):963–976.
- [26] Martins do Valle F, Valle Pinheiro B, Almeida Barros AA, et al. Effects on intradialytic resistance training on physical activity in daily life, muscle strength, physical capacity and quality of life in hemodialysis patients: a randomized clinical trial. *Disabil Rehabil.* 2019;29:1–7.
- [27] Johansen KL, Painter PL, Sakkas GK, et al. Effects of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: a randomized, controlled trial. *J Am Soc Nephrol.* 2006;17(8):2307–2314.
- [28] Cuk I, Prebeg G, Sreckovic S, et al. Generalization of muscle strength capacities as assessed from different variables, tests, and muscle groups. *J Strength Cond Res.* 2017;31(2):305–312.
- [29] Mentiplay BF, Perraton LG, Bower KJ, et al. Assessment of lower limb muscle strength and power using hand-held and fixed dynamometry: a reliability and validity study. *PLoS One.* 2015;10(10):e0140822.
- [30] Zelko A, Skoumalova I, Kolarcik P, et al. The effects of intradialytic resistance training on muscle strength, psychological well-being, clinical outcomes and circulatory micro-ribonucleic acid profiles in haemodialysis patients: protocol for a quasi-experimental study. *Medicine (Baltimore).* 2019;98(19):e15570.
- [31] Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373–383.
- [32] Molsted S, Harrison AP, Eidemak I, et al. The effects of high-load strength training with protein- or nonprotein-containing nutritional supplementation in patients undergoing dialysis. *J Ren Nutr.* 2013;23(2):132–140.
- [33] Saeed S, Moodie EEM, Strumpf EC, et al. Evaluating the impact of health policies: using a difference-in-differences approach. *Int J Public Health.* 2019;64(4):637–642.
- [34] Schulz KF, Altman DG, Moher D, CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *PLoS Med.* 2010;7(3):e1000251.
- [35] Wilund KR, Viana JL, Perez LM. A critical review of exercise training in hemodialysis patients: personalized activity prescriptions are needed. *Exerc Sport Sci Rev.* 2020;48(1):28–39.
- [36] Suzuki Y, Kamiya K, Tanaka S, et al. Effects of electrical muscle stimulation in frail elderly patients during haemodialysis (DIAL): rationale and protocol for a crossover randomised controlled trial. *BMJ Open.* 2019;9(5):e025389.
- [37] Taylor MJ, Schils S, Ruys AJ. Home FES: an exploratory review. *Eur J Transl Myol.* 2019;29(4):8285.