Magna Scientia UCEVA (2022) 2:1, 60-68
ISSN: 2805-6884 e-ISSN: 2805-6701
https://doi.org/10.54502/msuceva.v2n1a6

Systematic Review | Medicine

Effects of physical exercise on functional capacity in hemodialysis patients. A systematic review

Efectos del ejercicio físico sobre la capacidad funcional en pacientes con hemodiálisis. Una revisión sistemática

Maria Augusta Ruy-Barbosa Emily Pereira dos Santos Gabriel Pereira Sofía Tomaselli Arioni Thabata Caroline de Oliveira Santos and Rafael Luiz Pereira*

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Correspondence: gutabarbosa92@gmail.com
Department of Physiology. Federal University of Paraná, Curitiba, Brazil.
Physical Performance Studies Center. Federal University of Paraná, Curitiba, Brazil.

First draft submitted: 16-12-2021
Accepted for publication: 29-04-2022
Published on line: 01-07-2022

Key words:

Chronic kidney disease;
Functional Capacity;
Hemodialysis;
Intradialytic training protocols
Physical exercise.

Palabras clave:

Capacidad funcional;
Ejercicio físico;
Enfermedad crónica de riñón;
Hemodiálisis;
Protocolos de entrenamiento intradiálisis

Citation:

Ruy Barbosa MA, Santos EP, Pereira G, Arioni ST, Santos TCO, Pereira RL. Effects of physical exercise on functional capacity in hemodialysis patients. A systematic review. *Magna Scientia UCEVA* 2022; 2:1 60-68. *https://doi.org/10.54502/msuceva.v2n1a6*

Abstract

The aim of this study was to conduct a systematic review in order to evaluate the main effects of intradialytic physical exercise on different parameters of functional capacity in dialytic patients. The clinical question that guided the objective of this study was developed using the PICO method (Population, Intervention, Comparation and Outcome)." Where *i*) population: patients on hemodialysis; *ii*) intervention: physical exercise; *iii*) comparison: active vs sedentary patients; and *iv*) outcome: functional capacity. The combinations of the following keywords were used: CKD, physical exercise, exercise, physical training and hemodialysis. The selection of studies was performed using the PubMed database and only studies dating from 2011 to 2021 were selected. The search results led to 53 studies. The following steps were carefully analyzed, such as the title, abstract and the full paper description to evaluate whether they met the following inclusion criteria: *i)* target audience of the studies should be patients on hemodialysis; *ii*) outcomes that analyze different parameters of functional capacity; iii) Intervention using physical exercise; and *iii)* intradialytic exercise. The final results indicate that intradialytic physical exercise can cause significant changes in the evaluated outcomes of functional capacity, such as increased strength, improvement of cardiorespiratory function, and improvement of locomotor activity. It was concluded that intradialytic training protocols should be encouraged in clinical practices because they are responsible for causing beneficial changes in the functional capacity of hemodialytic patients.

Resumen

El objetivo de este estudio fue realizar una revisión sistemática para evaluar los principales efectos del ejercicio físico intradiálisis sobre diferentes parámetros de capacidad funcional en pacientes dializados. La pregunta clínica que orientó el objetivo de este estudio fue desarrollada mediante el método PICO (Population, Intervention, Comparation and Outcome). Donde: *i*) población: pacientes en hemodiálisis; *ii*) intervención: ejercicio físico; *iii*) comparación: pacientes activos vs sedentarios; y *iv*) resultado: capacidad funcional. Se utilizaron las combinaciones de las siguientes palabras clave: ERC, ejercicio físico, ejercicio, entrenamiento físico y hemodiálisis. La selección de estudios se realizó utilizando la base de datos PubMed y solo se seleccionaron estudios que datan de 2011 a 2021. Los resultados de la búsqueda encontraron 53 estudios. Se analizaron cuidadosamente los siguientes pasos, como el título, el resumen y el artículo completo, para evaluar si cumplían con los siguientes criterios de inclusión: *i*) el público objetivo de los estudios debe ser pacientes en hemodiálisis; *ii*) resultados que analizan diferentes parámetros de la capacidad funcional; *iii*) intervención mediante ejercicio físico; y *iii*) ejercicio intradiálisis. Los resultados finales indican que el ejercicio físico intradiálisis puede provocar cambios significativos en los resultados de la capacidad funcional, como aumento de la fuerza, mejora de la función cardiorrespiratoria, y mejora de la actividad locomotora. Se concluyó que los protocolos de entrenamiento intradiálisis deben ser incentivados en la práctica clínica porque son los responsables de provocar cambios beneficiosos en la capacidad funcional de los pacientes en hemodiálisis.

Introduction

Chronic kidney disease (CKD), is defined as an abnormality in the structure or function of the kidneys with implications for individual's health, which will vary according to the cause, severity and rate of progression of the disease [1]. In more severe cases, patients have renal failure, which requires renal replacement therapies such as hemodialysis or kidney transplantation. Therefore, early diagnosis is very important, since dialysis treatment unfortunately affects the patient's life expectancy, besides being very expensive, representing an expressive expenditure for public health care especially in developing countries [1]. In addition, CKD represents a risk factor in the development of cardiovascular diseases, affecting also functional and cognitive functions that are associated with increased morbidity and mortality. Some studies have shown a 60% increasing in the risk of mortality among people with CKD with low daily levels of physical activity when compared to those with normal levels [2–4], suggesting that the regular practice of physical exercise can be an important modulator of several risk factors for the worsening of the disease which also includes functional capacity. Patients on hemodialysis have a lower functional capacity, that is aggravated by sedentary lifestyle and muscle degradation caused by the disease [5], leading to a loss of autonomy, with a subsequent decrease in life quality, that is associated with higher mortality levels.

Intradialytic physical exercise has been used as an important tool in the promotion of physical activity in patients with CKD on hemodialysis. Some studies have demonstrated physical and functional improvements [6,7], and also in addition, intradialytic physical exercise may be related to the potentiation of the beneficial effects of dialysis [8]. These combined factors demonstrate the importance of physical exercise, and more specifically, intradialytic exercise, for patients in advanced stages of CKD. Nevertheless, physical exercise is still seen with enough caveats in clinical practice. It is speculated that factors associated with the disease itself such as anemia, fatigue, intolerance to physical exertion, in addition to the fear of clinical complications, lack of prepared professionals, lack of knowledge about the benefits of physical activity and low motivation of patients, are barriers to the implementation of these practices in treatment centers [9]. Despite concern about the possible complications that physical exercise can cause to be valid, a meta-analysis [10], demonstrated that the risks for adverse events are very low. Thus, the aim of this study was to analyze through a systematic review the effects of intradialytic physical exercise on functional capacity in hemodialysis patients.

Methods

Study type

This study is characterized as a systematic review according to the procedures described in the literature, following the recommendations of Sampaio (2007) [11]. It was performed in peer-reviewed journals indexed in the PubMed database.

Descriptors for the selection of studies

The clinical question that guided the aim of this study, was developed using the PICO method (Population, Intervention, Comparation and Outcome). Where: *i*) population: patients on hemodialysis; *ii*) intervention: physical exercise; *iii*) comparison: active vs sedentary patients; and *iv*) outcome: functional capacity. For this, the question that directed this systematic review was *"Are there effects of intradialytic physical exercise on functional capacity in hemodialysis patients?"*. In order to answer this question, the combinations of the following descriptors were used: CKD; physical exercise; exercise; physical training and hemodialysis. The selection of descriptors was based on the descriptors in Health Sciences (DeCs) and the Medical Subject Headings (MeSH). The searches were carried out using the Boolean operator and thus the combination applied to the searches were: (CKD and physical exercise) and (exercise) and (physical training) and (hemodialysis).

Inclusion and exclusion criteria

The inclusion criteria used for the study were as follows: *i*) target audience of the studies should be patients on hemodialysis; *ii*) outcomes that analyze different parameters of functional capacity; *iii*) intervention using physical exercise; and *iv*) intradialytic physical exercise. Exclusion criteria were: *i*) articles prior to 2011; *ii*) articles that were not original; *iii*) articles that were not published in english or portuguese languages; *iv*) animal studies; *v*) books, book chapters, monographs, dissertations, theses, review articles, case studies, abstracts, letter to the editor, editorial and consensus.

Data base and search strategy

The search was conducted in May 2021 in peer-reviewed journals and indexed in PubMed electronic databases. The time interval comprised the period from January 2011 to May 2021. The search in database and the selection of titles, abstracts and articles, were carried out by two researchers independently, according to the pre-established inclusion and exclusion criteria. In cases of disagreement among the researchers, a third researcher was consulted at the consensus meeting.

Methodological quality score

The studies selected in this systematic review, were analyzed for their methodological quality using the criteria proposed by Downs and Black (1998) [12]. A checklist of 27 questions, evaluating the domains of communication, external validity, internal validity (bias), confounding variables/selection bias and statistical power. The answers are scored with score 1 (when the criterion that characterizes quality is present) and 0 (when the criterion that characterizes quality is absent), except in question (5) in which three answers are allowed (score from 0 to 2) and in question (27) in which, five answers are allowed (score from 0 to 5). Thus, the maximum score that a study can obtain, is 31. The studies of better methodological quality, have achieved higher scores.

Overall data description and study design

Initially, 53 articles were found in PubMed database. The first stage comprised the reading of all the titles of the selected articles and 5 articles (9.43%), were excluded. The articles excluded were systematic reviews. Thus, 48 studies were analyzed by reading the abstracts, from which, 28 were excluded, where: 39 (28%) did not meet the inclusion criteria 1 (n=11); 32 (14%) did not meet the inclusion criteria 2 (n=9); 7 (14%) did not meet the inclusion criteria 3 (n=2); e 32 (14%) were review articles (n=9). In the next step, the 20 selected articles were read fully two times, the pre-established criteria for inclusion and exclusion, were followed. A total of 13 articles were excluded after full checking, from which, 15% did not meet the inclusion criteria 2 (n=3); 10% did not meet inclusion criteria 3 (n=2); 30% did not meet inclusion criteria 4 (n=6); 10% were reviews (n=2); and 5% did not present the results (n=1). Thus, a total of 7 (seven) articles were assigned for this review, the steps performed for studies selection are illustrated in figure 1.

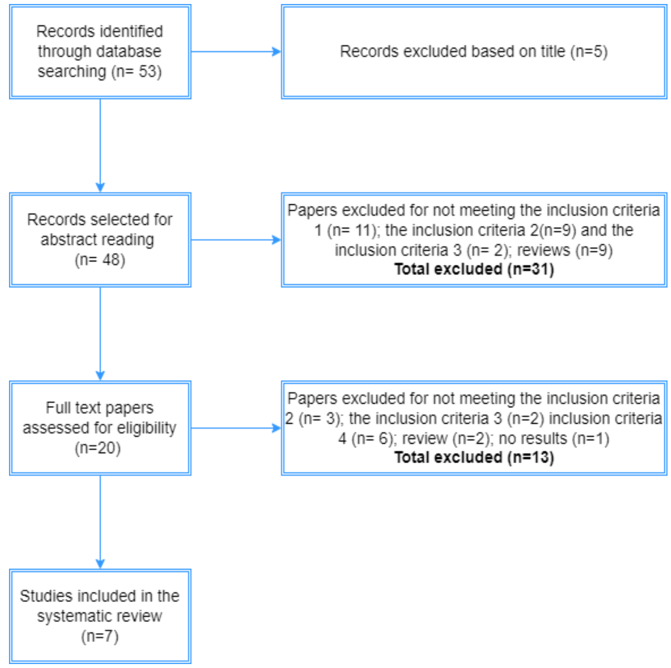


Figure 1 Flowchart with the selection steps of the articles

For the evaluation of methodological quality score of the eligible articles for this systematic review, the criteria proposed by Downs and Black (1998) were used, with a maximum score of 31. Thus, the highest score was 30 for one article [6]. Two articles achieved a score of 26 [13,14], an article reached 24 points [7], an article reached 23 points [15], an article reached 22 [16] and an article reached 20 points, the lowest score [17]; data is shown in table 1. Thus, the mean score of analyzed article was 24.42.

The years of articles publication varied between 2013 [14] and 2020 [6,13]. Only three articles had differences between control and training group [6,13,15]. One article conducted the research with patients in the final stage of renal disease [15]. All studies included men and women. Regarding the analysis of functional capacity, all studies evaluated cardiorespiratory capacity through the 6-minute walk test, except for the studies carried out by Sovatzidis et al. [13] and Castro et al. [17], who used the NSRI walking test and Gait speed in 4m, respectively. Only one article used only one functional capacity parameter [15], while all others evaluated more than one parameter.

Regarding the type of exercise proposed, two studies used aerobic training [13,15], two studies used concurrent training, with aerobic training and resistance training [7,14] and three studies used resistance training [6,16,17].

Table 1 Methodological quality of the analyzed studies

Questions-reporting/external validity/internal validity/power																											
Author	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total
Torres et al [16]	1	1	1	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	0	1	1	1	0	0	0	0	5	22
Sovatzidis et al [13]	1	1	1	1	2	1	1	1	1	1	0	0	1	0	0	1	1	1	1	1	1	1	1	0	0	1	5	26
Castro et al [17]	1	1	1	1	0	0	0	0	1	1	0	0	1	0	0	1	1	1	1	1	1	1	0	0	0	1	5	20
Anding et al [7]	1	1	1	1	1	1	1	1	1	1	0	0	1	0	0	1	1	1	1	1	1	1	0	0	0	1	5	24
Silva et al [14]	1	1	1	1	2	1	1	1	1	1	1	1	1	0	0	1	1	1	0	1	1	1	0	0	0	1	5	26
Groussard et al [15]	1	1	1	1	1	1	1	0	1	1	0	0	1	0	0	1	1	1	0	1	1	1	1	0	0	1	4	23
Exel et al [6]	1	1	1	1	2	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	5	30

In only one study, there was an attempt to blind the participants and researchers in relation to the type of intervention proposed, where the control group performed stretching exercises [6]. Only one study reported an adverse effect during training, where an arm hematoma in which, it was located a fistula in one of the patients; however, according to the authors, this event was not directly related to training [17]. All this information has been synthesized and described in table 2.

Results

This study aimed to analyze, through a systematic review, the effects of intradialytic physical exercise on the functional capacity of hemodialysis patients with CKD. After analyzing the results, it was observed that all the selected studies indicated that an intradialytic physical exercise protocol could increase the functional capacity of patients with CKD, aerobic or resisted, independently. This test is intended to analyze cardiorespiratory capacity. It is an easy test to perform and requires little equipment, besides being widely validated by the literature. The test consists of traveling as far as possible in six minutes and should be performed in a flat environment according to American Thoracic Society standards. All studies that used the 6MWT protocol, observed a positive change, with an increasing in the distance covered after the exercise.

These characteristics directly reflect oxygen consumption (VO2), which is low in CKD patients due to various conditions including anemia, electrolyte imbalance, hyperparathyroidism, and respiratory problems. Several studies have shown an increasing in VO2max during endurance, which reinforces the hypothesis that the improvement in walking tests, may be related to this factor. Another aspect that may have influenced the test results is muscle strength and function. Muscle strength is related to the ability to walk, go up and down stairs, get on and off buses and various other activities of daily living. The improvement of muscle strength can mean that CKD patients improve autonomy, independence, and provide greater social interaction. This explains the fact that, even in the protocols that used only resistance training, there was an increasing in distance and improvement in walking tests. Thus, the improvement of muscle strength and function, represents an important gain in functional capacity.

The mechanisms by which strength and muscle mass gain are explained by the effects of resistance exercise, which has as characteristic of a metabolism increasing and protein synthesis, leading to an increasing in the muscle cross-section area. In addition, exercise can raise levels of growth factors such as IGF-1, already observed in hemodialysis patients. In general, studies have shown that intradialytic physical exercise can be an important strategy against sedentary lifestyle that is already reinforced among patients undergoing hemodialysis, bringing several benefits such as increased strength and physical fitness, which directly affect the functional capacity, autonomy, and quality of life of these patients. In addition, it has been demonstrated that both aerobic and resistance exercise can be used thinking in improving these capabilities, and that these training models do not require sophisticated equipment besides not offering risk to their practitioners.

Table 2 Synthesis of the analyzed articles in the systematic review

Authors	Experimental design	Exercise protocol	Evaluated functional capacity parameters	Main findings
Torres et al [16]	36 patients underwent intradialytic resistance training three times per week during three months. Comparisons were made between baseline values and the obtained values at the end of the training protocol	Exercise protocol consisted of the leg flexion and extension; arms and hip abduction. The exercises were performed with body weight or extra weights according to individual physical capacity	Cardiorespiratory capacity (6MWT); lower limbs strength (sit and stand test in 30 seconds); handgrip strength (dynamometer)	A mean increasing of 28.66 in a covered distance of 6MVT test (p<0.001); a mean increasing of 1.9 replicates in the sit and stand test (p<0.003); average increasing of 5kg in handgrip strength (p<0.001).
Sovatzidis et al [13	20 patients were divided into two groups. Training group (GT) (n=10) and control group (CON) (n=10). TG patients underwent intradialytic aerobic training, 3 times per week during sixth months.	Aerobic training consisted of pedaling in an ergometer cycle. The initial five minutes consisted of warm -up, in the remaining time, both, duration and exercise load, were self-selected. The final five minutes, were back to resting. Exercise intensity was measured using the Borg scale (6-20)	Cardiorespiratory capacity (NSRI walking test); lower limbs strength (sit and stand test in 60 seconds); handgrip strength (dynamometer)	In TG, there was an increasing of 8% in the walking test (p<0.001); 11% in the sit and d stand test (p<0.001) and 1% in handgrip strength (p<0.002), when compared to baseline values. Differences were statistically significant when compared to control group (CG)
Castro et al [17]	43 patients underwent intradialytic resistance training three times per week during 39 months. Comparisons were made between the baseline and the obtained values at the end of training protocol	The exercise protocol was directed by the main muscle groups of the lower and posterior limbs. The load adjustment was performed using Borg scale (6-20). All exercises consisted of 3-4 sets per 5 replicates and one last training session lasted on average, 50 minutes	Self- selected gait speed test (4m); lower limbs strength (sit and stand test in 30 seconds); handgrip strength (dynamometer)	An increasing in gait speed test ranged from 0.99 ± 0.29m.s^{-1} to 1.26 ± 0.22m.s^{-1} (p<0.003)
Anding et al [7]	46 patients underwent intradialytic resistance training twice a week during 12 months. Comparisons were made between the baseline values (6-12 months after training)	Aerobic training consisted of pedaling in an ergometer cycle for 30 minutes, then patients performed a resistance training with the aim of recruiting 8 different muscle groups. The exercise was performed in 2 sets of 1 resting minute. A load progression was performed through evaluation of the maximum replicate test, which was periodically performed	Cardiorespiratory capacity (6MWT); locomotor activity (time up and go); lower limbs strength (sit and stand test in 60 seconds)	An average increasing of 43 m in a covered distance of 6MWT when compared to baseline values and after 12 weeks of training (p<0.002); an increasing in lower limbs strength after six months with a mean increasing of 3.8 replicates in the sit and stand test (p<0.053) and 12 months with a mean increasing of 7.5 replicates (p<0.0001); a decreasing in tug test execution time, which represents an increasing in gait speed test after 6 and 12 months of training (p<0.002, p<0.0001), respectively.
Silva et al [14]	56 patients underwent intradialytic concurrent (aerobic and resistance) three times per week during 16 months. Analysis were carried out between the baseline state and at the end of the experiment	Aerobic training consisted of pedaling in an ergometer cycle for 10 minutes, with intensity adjustment based on heart rate, followed by ten minutes of strength training for the lower and upper limbs with the aid of additional weights, such as medicine balls and TheraBand, as well as isometric exercises.	Cardiorespiratory capacity (6MWT); lower limbs strength/knee extension (dynamometer)	An average increasing of 54.37m in a covered distance of 6MWT (p<0.001); while the perception of exertion was evaluated using the Borg scale (CR-10), during the decreasing test (p<0.001) and an increasing in knee extension strength (p<0.001).

6MWT= 6 minutes walk test; rpm = rotations per minute.

Table 2 Continued

Authors	Experimental design	Exercise protocol	Evaluated functional capacity parameters	Main findings
Groussard et al [15]	18 patients were divided into two groups. Training group (GT) (n=8) and control group (CON) (n=10). TG patients underwent intradialytic aerobic training, 3 times per week during three months. Comparisons were made between control and training groups.	Aerobic training consisted of pedaling in an ergometer cycle. The intensity maintained was ranged from 55-65% of the peak power; previously analyzed before the beginning of the protocol exercise. The time in exercise increased progressively upon the second week, from this, participants should pedal for 30 minutes at 50 rpm. The exercise intensity was adjusted according to heart rate.	Cardiorespiratory capacity (6MWT)	A significant increasing of 23.4% in a covered distance of 6MVT test only in the treatment group after 3 months (p<0.001); there were not significant differences in the control group.
Exel et al [6]	93 patients were divided into two groups. stretching group (n=46) and resistance training group (n=47). The training sessions were held 3 times per week during 8 months. Comparisons were made among two groups at the end of the training.	Stretching training was performed in the thigh posterior muscles, hip aduation and abduction and sural triceps. Passive stretching was performed in 3 sets of 20 seconds each with 30 interval seconds. Stretch training lasted 30 minutes and performed only on lower limbs using the shin shin. The load underwent progressive adjustments throughout the sessions; participants performed 3 sets of 10 replicates with 2 interval minutes.	Cardiorespiratory capacity (6MWT); lower limbs strength/knee extension (dynamometer)	An increasing of 1.98 kgf in the strength of lower limbs, was evidenced in the resistance training group (p<0.001); no significant changes in the strength of the stretching group, was observed. An average increasing of 77.77m in the covered distance (6MWT), was observed in the resistance training group. The covered distance was higher among the resistance training group when compared to stretching group at the end of the eight weeks, demonstrating an interaction between type of training and time (F= 7.413; p<0.008).

6MWT= 6 minutes walk test; rpm = rotations per minute.

Discussion

Despite the analysis variation in relation to the parameters of physical capacity, most tests were proposing to analyze similar outcomes. Among them, we highlight the 6-minute walking test, used in 5 of the 7 articles analyzed here [6,7,14–16].

Only one study [13], used the NSRI walking test protocol, which consists of walking 50m, climbing 22 steps, going down 22 steps and walking over 50m. The aim of this test is to perform all the steps in the shortest possible time, which was observed after the proposed aerobic exercise protocol. Another study evaluated gait through the 4m gait speed test, a protocol consisted of walking 4m in the shortest possible time. This test does not assess cardiorespiratory capacity but rather the dynamic balance and self-selected speed [17]. In this study, the resistance exercise protocol was also responsible for increasing gait speed.

These changes which was observed in walking tests, may be related with two distinct factors, improvement in oxygen consumption and muscle function. Muscle damage in CKD, results from a series of changes that affect both peripheral and respiratory muscles. The pathophysiology of these changes, includes atrophy of type I and type II muscle fibers, in addition to deficiencies in capture, oxygen utilization and transport [18].

It is known that patients with CKD, suffer of a marked loss of strength and muscle mass. The results found in this systematic review, indicate that intradialytic physical exercise, whether aerobic or resisted, may provide significant gains in CKD stenght in patients. Exel et al. [6], associated these gains with neural adaptations that occur after strength training. Meanwhile, in a research carried out by Torres et al. [16], a strength increasing was accompanied by a muscle hypertrophy increasing, which was evaluated by muscle biopsy. In fact, strength training, can promote an anabolic environment, favoring a increase in lean mass, a muscle strength increasing and catabolism process attenuating in patients with CKD [6]. Strength training has also been indicated in strength maintenance and acquisition in patients in disease final stages and should be encouraged as a form of treatment in this population [20].

Only one study did not focus on muscle strength evaluation [15]. Two studies evaluated muscle strength through the maximum knee extension strength, measured with a dynamometer [6,14]; two studies evaluated strength through muscle endurance in the sit-stand up test in 60 seconds [7,13] and two studies through the sit and stand up test in 30 seconds [15,17].

Another aspect that may explain the gains in functional capacity are the anti-inflammatory effects provided by physical exercise. The state of chronic inflammation, present in patients with CKD, is one of the causes that lead to a decreased functional capacity, since systemic inflammation can induce proteolysis, leading to muscular atrophy [5,21]. Intradialytic physical exercise has been shown to increase levels of IL-10, an anti-inflammatory cytokine [22], the same effect was observed in pre-dialysis patients, where 30 minutes of aerobic exercise was responsible for increasing IL-6 and IL-10 levels. These results reinforce the idea of an important immune system and physical exercise interactions [23].

Conclusion

Based on the results exposed here in this systematic review, we conclude that intradialytic physical exercise is capable of improving efficiently functional capacity through a cardiorespiratory capacity increasing, dynamic balance, locomotor activity and lower and upper limbs strength in patients with CKD and, should be encouraged in clinical practice in order to provide a less sedentary lifestyle, improvement in functional capacity, autonomy and life quality of hemodialysis patients.

Consent for publication

The authors read and approved the final manuscript.

Competing interest

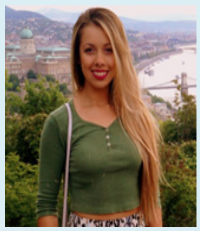
The authors declare no conflict of interest. This document only reflects their point of views and not that of the institution to which they belong.

Acknowledgments

We would like to thank Dr. Danilo Candido de Almeida (Nephrology Division, School of Medicine, Federal University of São Paulo, São Paulo, Brazil), Dr. Juan Sebastian Henao Agudelo (Unidad Central del Valle del Cauca, Colombia) and Dr. Ricardo Fernandez (Department of Physiology. Federal University of Paraná, Curitiba, Brazil) for the helpful comments and critical reading of the manuscript.

Author details

Maria Augusta Ruy-Barbosa



Master of Science in exercise physiology and health from Federal University of Paraná - UFPR. Graduated in physical education (2018) and sports physiology (2022). Currently, she is currently attached to the following institutions: Department of Physiology. Federal University of Paraná, Curitiba, Brazil and Physical Performance Studies Center. Federal University of Paraná, Curitiba, Brazil.

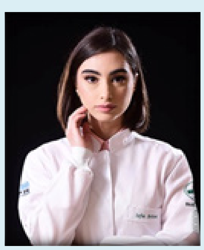
Emily Pereira dos Santos

Is pursuing her bachelor's degree in Pharmacy in the Federal University of Paraná, Brazil. Is currently in her third year as part of the science initiation program at the Kidney Physiology Laboratory. Has experience with clinical evaluation and biocompatibility evaluation of medical devices under European regulations. Is an intern at the Health's Secretary of Curitiba, working with sanitary requirements and regulations for healthcare establishments, and medical devices, cosmetics, drugs and food industries.

Gabriel Pereira

Doctoral student in the Department of Medicine, Discipline of Nephrology, Federal University of São Paulo – UNIFESP. Graduated in Biomedicine and completed a Master's degree in Physiology at the Federal University of Paraná – UFPR, investigating the effects of physical exercise in experimental model of glomerular lesion. Currently aim is to elucidate the effects of redox modulation in the context of glomerular lesion, with focus on the thioredoxin antioxidant system.

Sofia Tomaselli Arioni



Master student in the Department of Physiology at the Federal University of Parana–UFPR, Brazil, currently investigating the impact of fish oil supplementation in the improvement of the kidney function of neonatally overfed rats. Is graduated in Biomedicine at UFPR and during three years took part of the University's Scientific Initiation Program, researching the impact fish oil supplementation over the kidney function of Walker tumor bearing rats.

Thabata Caroline de Oliveira Santos

Doctoral student in the Department of Physiology, Federal University of Paraná. Graduated in Biology and completed a Master's degree in Physiology at UFPR, investigating the role of STAT3 signaling pathway in experimental model of glomerular lesion. Currently aim is to elucidate the modulatory effect of physical exercise on the STAT3 signaling pathway.

Rafael Luiz Pereira

Is Doctor in Sciences (Medicine-Nephrology) from the Federal University of São Paulo – UNIFESP (Brazil) with collaborative period in Istituto di Ricerche Farmacologiche Mario Negri (Italy) with a Post-doctorate in Immunology at University of São Paulo - USP (Brazil).
He is currently Associate Professor in the Department of Physiology, at the Federal University of Parana – UFPR (Brazil). Dr Pereira has experience in Experimental models of renal disease, renal inflammation and chronic kidney diseases.

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