Global Journal of Medical Research: F
Diseases
Volume 20 Issue 7 Version 1.0 Year 2020
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Effects of Physical Activity on Patients with Chronic Kidney Disease on Hemodialysis: A Systematic Review

By Denis Vianna Guerra Peixe, Leandro de Oliveira Sant'Ana, Janine Meirelles dos Santos Ramos & Fabiana Rodrigues Scartoni

Catholic University of Petrópolis

Abstract- Objective: Analyze through a systematic review of the effects of physical activity on hemodialysis patients.

Methods: The study followed the proposals of PRISMA (Preferred Reporting Items in Systematic Reviews and Meta-Analyzes). The search for articles took place on the digital platforms Medline, Pub Med, and Sports Discus, from February to October 2019. Itwas found using word combinations specific to the research theme, and they are aerobic exercise and renal insufficiency, aerobic exercise and dialysis treatment, strength training and renal insufficiency, strength training, and renal insufficiency.

Results: 43 articles were identified. However, in the search criteria, 39 were excluded. No studies were excluded by checking titles and abstracts. Finally, four of them were selected for a full reading. After eligibility, all four were included for the final analysis. The PEDro scale identified a high methodological quality of the selected studies. The studies showed significant improvements in the neuromuscular, cardiovascular, cardiorespiratory, biochemical, and organic systems. In addition to improvements in the evaluative aspects of quality of life.

Keywords: *physical activity; hemodialysis; chronic kidney disease.*

GJMR-F Classification: *NLMC Code: WJ 378*

EFFECTSOFPHYSICALACTIVITYONPATIENTSWITHCHRONICKIDNEYDISEASEONHEMODIALYSISASYSTEMATICREVIEWS

Effects of Physical Activity on Patients with Chronic Kidney Disease on Hemodialysis: A Systematic Review

Denis Vianna Guerra Peixe [α], Leandro de Oliveira Sant'Ana [σ], Janine Meirelles dos Santos Ramos [ρ] & Fabiana Rodrigues Scartoni [ω]

Abstract- Objective: Analyze through a systematic review of the effects of physical activity on hemodialysis patients.

Methods: The study followed the proposals of PRISMA (Preferred Reporting Items in Systematic Reviews and Meta-Analyzes). The search for articles took place on the digital platforms Medline, Pub Med, and Sports Discus, from February to October 2019. Itwas found using word combinations specific to the research theme, and they are aerobic exercise and renal insufficiency, aerobic exercise and dialysis treatment, strength training and renal insufficiency, strength training, and renal insufficiency.

Results: 43 articles were identified. However, in the search criteria, 39 were excluded. No studies were excluded by checking titles and abstracts. Finally, four of them were selected for a full reading. After eligibility, all four were included for the final analysis. The PEDro scale identified a high methodological quality of the selected studies. The studies showed significant improvements in the neuromuscular, cardiovascular, cardiorespiratory, biochemical, and organic systems. In addition to improvements in the evaluative aspects of quality of life.

Conclusion: We can say that the use of a physical activity to help patients with chronic kidney disease on hemodialysis, guarantees benefits in functional capacity, whether using aerobic training or combined training.

Keywords: *physical activity; hemodialysis; chronic kidney disease.*

I. Introduction

Chronic kidney disease (CKD) occurs when there is kidney damage resulting in slow, gradual, and irreversible loss of kidney functions. The CKD can also be called chronic renal failure[1]. In Brazil, the number of patients with his type of pathology who underwent treatment increased from 122 thousand in 2016 in a survey carried out by the Brazilian Chronic Dialysis Survey [2]. The number of people who managed to have a kidney transplant reached 5.7 thousand, a number that has been growing 10% every year[3].

The kidneys are the organs that filter all nutrients and other substances processed in the body. What is beneficial for the body is used and offered for organic demands, and what is harmful is eliminated in the urine. These organs are of great importance, as they are the ones that make the metabolic and hydro electrolytic balance of the organism 1-4. The kidneys also play another role: the release of some hormones into the blood. These hormones regulate blood pressure, make red blood cells, and strengthen bones [5]. The repercussions of CKD associated with hemodialysis treatment can lead to the loss of components of physical fitness that results in decreased functional capacity and mortality in this population[6-7-8]. The CKD patient has several changes in their bodies. Muscle loss is noted, characterized by musculoskeletal changes, which occur at an accelerated rate. This loss occurs due to a sedentary lifestyle, obesity, nutritional imbalance that occurs in conjunction with the reduction of protein synthesis and insulin resistance, two metabolic changes[9].

Another change noticed is the constant fatigue, where the patient has tiredness and lack of energy to perform the most common activities of daily life. This fatigue can be linked to psychological changes, such as depression, because the patient is away from social life, due to the severity of the treatment, abnormal levels of urea and hemoglobin, due to improper kidney function, nutritional deficits, caused by poor food intake[9].

Bearing in mind that the number of people who develop CKD and that this number has been progressively increasing [10], studies are needed that show the effectiveness of structured exercise programs that benefit this audience.

As a form of prevention, patients should be encouraged to practice physical exercises to mitigate the changes caused by CKD. According to the American College of Sports Medicine[11], individuals affected by chronic kidney disease should perform

Author α ρ ω: Department of Physical Education, Catholic University of Petrópolis, RJ, Brazil.
Author σ: Post Graduate Program in Physical Education, Federal University of Juiz de Fora, Brazil.
Author σ: Strength Training Studies and Research Laboratory, Federal University of Juiz de Fora, Brazil.
Author σ ρ ω : Laboratory of Sport and Exercise Sciences, Catholic University of Petrópolis, Brazil.
Corresponding Author ω: PhD., Endereço: Barão do Amazonas Street, 124 – Center, Petrópolis - RJ, 25685-100. Catholic University of Petrópolis. e-mail: fabiana.scartoni@ucp.br

aerobic exercises for 3 to 5 days a week, lasting 20 to 60 minutes continuously. If the amount is not supported, sessions of 3 to 5 minutes should be performed intermittently, to accumulate 20 to 60 minutes per day. Resistance exercises should also be performed two to three times a week, with at least one set. This series should contain 8 to 10 movements, covering the main muscle groups. The number of repetitions can vary from 10 to 15.

Knowing the importance of the practice of physical activity in the prevention of diseases, patients affected by some kidney injury should be encouraged to physical activity, which is a possibility to mitigate the changes caused by the disease and by the treatment of hemodialysis or peritoneal dialysis itself, slowing the progression of the disease[12].

A study carried out with patients undergoing hemodialysis performed aerobic training and found benefits such as a decrease in resting heart rate (HR), systolic and diastolic blood pressure (BP) at rest, reduced body fat, and triglycerides increased cardiovascular resistance and reduced platelet aggregation. The study also showed benefits with resistance muscle training such as increased strength, power, and muscular endurance, in addition to providing an improvement in the performance of daily activities such as getting up from a chair and climbing a ladder[13].

However, studies related to physical activity with individuals with CKD are scarce, which consequently generates a relevant limitation regarding a subject that has a demand for more information and consistent directions. Therefore, the objective of this study is to conduct a systematic review of the effects of physical activity on patients on hemodialysis.

II. Methods

a) Search strategy

The structure in this study followed the proposals of PRISMA (Preferred Reporting Items in Systematic Reviews and Meta-Analyzes)[14]. Studies that analyzed the effects of physical activity in chronic renal patients undergoing hemodialysis will be considered for this review as well as both sexes in adulthood.

b) Eligibility criteria and study selection

To compose our study, the search for articles took place on the digital platforms MedLine, Pub Med, and Sports Discus, between February to October 2019. Also, the following criteria were considered: studies with interventions performed on humans, available and free of charge, classified as clinical trials. The articles were found by words combinations to the specific research topic, and they are: "aerobic exercise" and "renal insufficiency", "aerobic exercise" and "dialysis treatment", "strength training" and "renal insufficiency", "strength training" and "renal insufficiency". Also, the references of all selected articles were analyzed.

The selection of studies was carried out by two independent people who, in case of disagreement, sought a consensus. The evaluation consisted of a selection of studies using the analysis of the title, followed by the analysis of the abstract and the analysis of the full text. With the disagreement between the two evaluators, a third party will be asked to complete the process. The relevant articles were obtained and evaluated by the inclusion and exclusion criteria described below.

Articles that presented intervention methods other than physical exercise were excluded; those who underwent training with non-dialysis patients. And articles that applied physical activities and that found benefits for patients with CKD on hemodialysis were included.

c) Risk of bias in individual studies

To assess the risk of bias, the researchers carried out an analysis of the methodological quality of the studies. The evaluation instrument for the selected studies was performed using the PEDro scale[15]. The PEDro scale is considered an appropriate tool in systematic reviews for qualitative analysis of quantitative studies. The method consists of component classifications for the following categories: selection criteria, the equation between groups, data collection methods, outcome factors. The components were classified into 0 (not identified) and 1 (identified). Studies with PEDro scores between 6 and 10 points, 4 and 5 points, and 0 and 3 points were considered high, moderate, and low quality, respectively. All disagreements regarding the classification of PEDro scores were resolved by a consensus discussion among the reviewers.

III. Results

a) The selection process of articles related to research

As a way of elucidating the research, a process was carried out to identify all possible studies, which could contribute to it. After searching the scientific databases (Pub Med., MedLine and Sports Discus), screening was carried out by checking the title and the summary of the studies found. Those who did not fit the survey were excluded. The studies went through an eligibility process, where all of them were read in full. Because of this, some studies were excluded, taking into account their methodological quality, according to the standards of standardization of the PRISMA scale (Preferred Reporting Items in Systematic Reviews and Meta-Analyses).

After using the keywords, 43 articles were identified. However, in the search criteria, 39 were

Global Journal of Medical Research (F) Volume XX Issue VII Version I Year 2020

excluded. No one was excluded by checking their titles and abstracts. Finally, four studies were selected for reading in full. After eligibility, the four were included for the final analysis. The summary of articles, in table 1, was based on a structured questionnaire that considered the following items: Authors, year of publication, sample (quantity, sex, and age), training protocols, dependent variable, results.

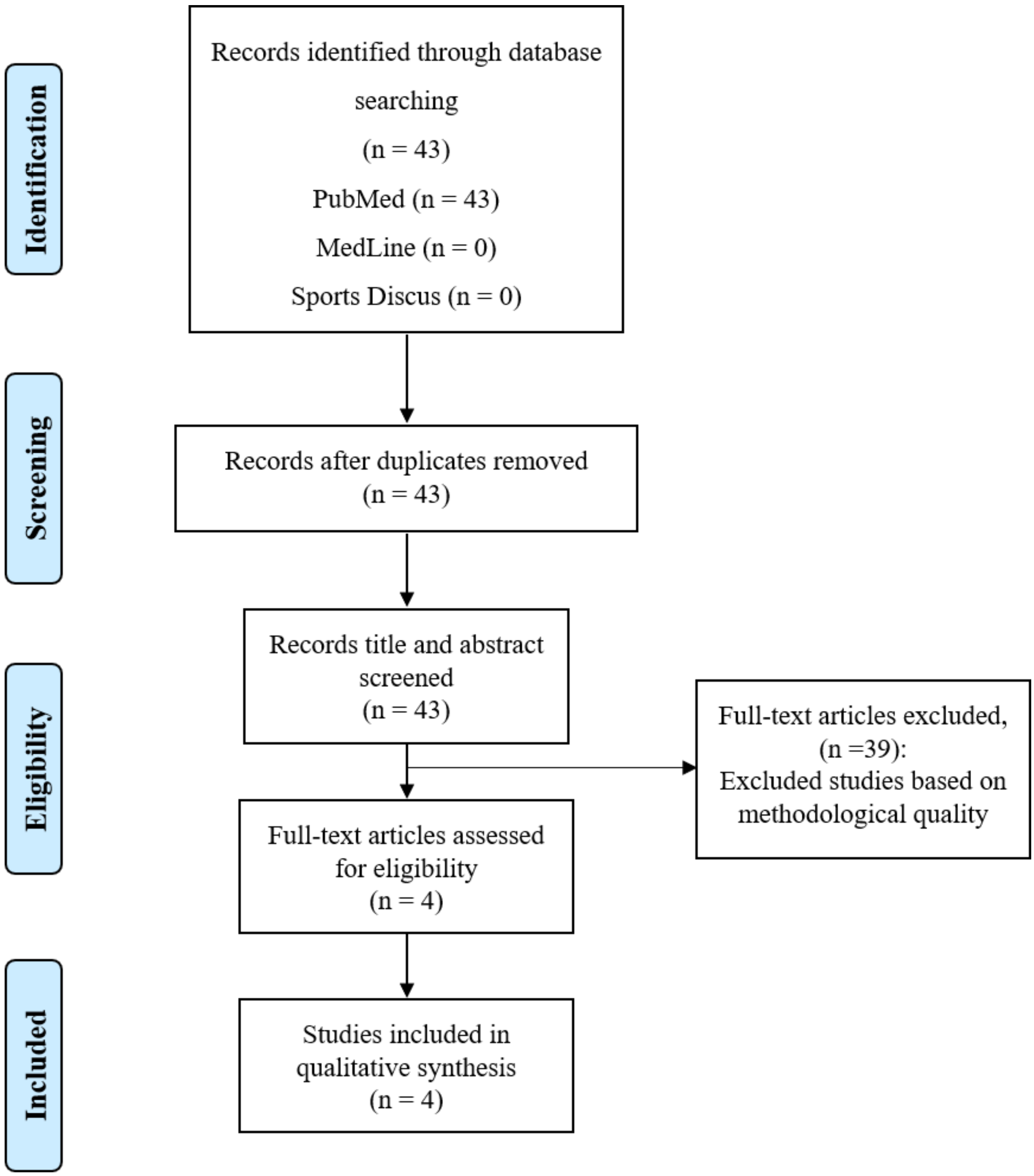

Figure 1: Flowchart of the selection process for articles related to research

b) The methodological quality of selected studies

The average PEDro score for the studies included in the review was 6.25 ± 0.5 points, ranging from 3 to 6 points (Table 1). According to the established quality criteria, the average quality of the studies included in this review is, therefore, high. Also, there was no high degree of variation in quality between studies. All studies [16-17-18-19] met the eligibility criteria. (Question 1 of the PEDro scale) and outcome measures. Likewise, all of them [16-17-18-19] performed a randomized crossover design (question 2 of the PEDro scale). Only one study 16 concealed criteria (question 3 on the PEDro scale). All studies[16-17-18-19] showed similarity between groups (question 4 on the PEDro scale). None of the studies presented blind methodological criteria (questions on the PEDro scale 5, 6, and 7). All studies[16-17-18-19] showed results in more than 85% of the sample (question 8 on the PEDro scale), fulfilled criteria 9, related to the intervention condition (question 9 on the PEDro scale), showed statistical comparisons between groups (question 10 on the PEDro scale) and provided specific measures and measures of variability (question 11 on the PEDro scale).

Table 1: PEDro score of methodological quality for included studies

Studies	1	2	3	4	5	6	7	8	9	10	11	Totality
Headleyet al.. (2014)	1	0	1	1	0	0	0	1	1	1	1	6
Hirakiet al.. (2017)	1	0	0	1	0	0	0	1	1	1	1	5
Emma et al.. (2018)	1	0	0	1	0	0	0	1	1	1	1	5
Ikilzeret al.. (2018)	1	0	0	1	0	0	0	1	1	1	1	5

Legend: EG - exercise group; *CG* - control group; *W* - women; *M* - men; *AT* - aerobic training; *CAPWV-* Central aortic pulse wave velocity; *HRQL* - health-related quality of life; *ET-1* - endothelin; *RT* - resistance training; *SM* - superior members; *LL* - lower limbs; *GFR* - glomerular filtration rate; *AEG* - aerobic exercise group; *CEG* - combined exercise group; *DG* - diet group; *BP* - blood pressure; *TPR* total peripheral resistance-; *TPRI* - total peripheral resistanceindex; *MAP* - mean arterial pressure; *SV* - stroke volume; *SVI* - stroke volume index; *CO* - cardiac output; *CI* - cardiac index; ↔ - there was no significance concerning Baseline; ↑ - the significant difference concerning baseline.

c) Characteristics of selected studies

In the selected articles (Table 2), the publications were from 2014[16] to 2018[17]. The sample of these studies totaled 234 individuals, where 148 were men, and 86 were women one of the selected articles used only men in its sample[18]. Three studies used men and women in their sample[16-17-19]. None of the findings used only women in their interventions. The sample sizes in the studies found ranged from 36[18] to 111 individuals[19].

The findings found in the present study, identified different protocols for the intervention, being the aerobic training [16], aerobic training combined with resistance training[17-18], and aerobic training together with caloric restriction[19]. These protocols were used to observe positive changes in the variables of body composition, muscle strength, aerobic capacity, and markers of renal function. Headley *et al.*.[16] performed an aerobic training, three times a week, starting with 15 to 30 minutes, reaching up to 55 minutes (5 minutes of warm-up, 45 minutes of activity and 5 minutes of relaxation), where the patients remained between 50 to 60% of the VO_{2peak}.

Hiraki *et al.*.[18] applied aerobic and resistance training, consisting of 30 minutes of walking plus strengthening of lower limbs (squat and calf lengthening) and upper limbs (strengthening of claws), with 20 to 30 repetitions, three times a week. Ikizler *et al.* [19] observed the effectiveness of aerobic training tied to a caloric restriction, where the exercise was performed for 30 to 45 minutes, three times a week, and the caloric restriction was designed to decrease calories in general. Watson *et al.* [17] performed a combined training of aerobic and resistance exercise, being 20 minutes of aerobic (thus guaranteeing the duration of the session) and 3 sets of leg press and knee extension, with the load set at 70% of 1 RM, with 12 to 15 repetitions.

One of the studies[18] took place at home, and three studies took place in laboratories, requiring the use of cycle ergometers[16-17-18]. The selected studies applied chronic interventions that were from 12 weeks[17] to 12 months 18. Regarding the responses resulting from different physical training protocols, two findings observed an increase in muscle strength[17-18], three studies verified aerobic capacity[16-17-19], two studies obtained improvement in renal function[16-18], one study investigated the oxidative stress and inflammatory response [19], one study looked at power[17], one study investigated the pulse wave velocity of the central aorta and the improvement of some aspects of health-related quality of life [16]. Below are the results of the variables identified in the studies.

Table 2: Selected studies that used physical exercise in patients with CKD.

Authors	Year	Sampling	Training protocols	DependentVariables	Results
Headleyet *al.*,	2014	N= 30 women /16 men 35 a 70 years GE: M: 9 / H: 16 GC:W: 7 / H: 14	16 weeks/ 3x w./ cycle ergometer AT 5' warm 45' stimulus Intensity: 50-60% $VO_{2\ peak}$ 5' coll down	CAPWV Vascular Function QRVS	↔ CAPWV ↑ET-1 no EG (20,6%) ↑ aerobiccapacity aeróbica (8,3% no EG) ↑QRVS (physical functioning, vitality, and bodily pain)
Hirakiet *al.*,	2017	N= 36 men 68,7 ± 6,8 years	12 months AT 30' de day walking RT Strengthening of claws (MMSS), squat and calf enlargement (lower limbs) - 1 series, from 20 to 30 repetitions per exercise, at least 3 times a week	Muscle strength (wrist and knee extensor muscle) Alterationof renal function	↑Muscle strength ↑TGF in both groups
Ikizleret *al.*,	2018	N= 47 women /64 man 60 ± 11 years	4 months AEG 30'- 45'/ 3x without / treadmill, elliptical cross-training, Nu-Step cross-training and inclined exercise bike / 60 - 80% $VO_{2\ max}$	Oxidative stress and inflammation Body composition Cardiorespiratory Fitness ($VO_{2\ peak}$)	↑ oxidative stress and the inflammatory response ↔ AEG body weight ↑ body weight DG ↔ $VO_{2\ peak}$
Watson *et al.*,	2018	N= 54 AEG= 27	12 weeks / 3x sem. AEG 30' treadmill, cycling or	Muscle strength Quadriceps muscle volume	↑ Muscular strength (895 + - 408 to 1510 + - 658 kg) ↑Relative VO2 (AEG: +

	CEG= 27	rowing 70-80% of HR_{max} CEG Leg press and knee extension 3 sets 12-15 repetitions / 70% of 1RM 20 'of treadmill, cycling or rowing	Femoral rectum Cardiorespiratory fitness CardiacBioreactivity	1.1ml. Kg-1. Min-1, 5.1%, P = 0.4; GEC: + 0.6ml. Kg-1. Me-1, 2.1%, P = 0.4) ↑ Capacity↔ ↑ TPR e TPRI ↔ MAP; ↔ SV; ↔ SVI; ↔ CO e ↔ CI

Legend: EG - exercise group; *CG* - control group; *W* - women; *M* - men; *AT* – aerobic training; *CAPWV* - Central aortic pulse wave velocity; *HRQL* - health-related quality of life; *ET-1* - endothelin; *RT* - resistance training; *SM* - superior members; *LL* – lower limbs; *GFR* - glomerular filtration rate; *AEG* - aerobic exercise group; *CEG* - combined exercise group; *DG* - diet group; *BP* - blood pressure; *TPR* total peripheral resistance -; *TPRI* - total peripheral resistance index; *MAP* - mean arterial pressure; *SV* - stroke volume; *SVI* - stroke volume index; *CO* - cardiac output; *CI* - cardiac index; ↔- there was no significance concerning baseline; ↑ - the significant difference concerning baseline.

IV. Results of Measures Taken

a) *Muscle strength*

Hirakiet al..[18] found significant results between the exercise group (wrist: 31.7 ± 7.4 in baseline to 36.4 ± 6.4 kgf. Post-intervention; knee extensor: 0.65 ± 0.17 in baseline for 0, 70 ± 0.17 kgf. / Kg post-intervention) and the control group (wrist: 35.5 ± 8.8 to 36.5 ± 9.2 kgf. Post-intervention; knee extensor: 0.66 ± 0.15 for 0.62 ± 0.13 kgf / kg Watson et al.. 17 achieved significant results both in the aerobic exercise group and in the resistance exercise group, however, the resistance exercise group had a greater gain.

b) *Aerobic capacity*

The study by Headley et al..[16] observed a significant improvement in this capacity, obtaining an increase of 8.3% in the EG. Watson et al. [17] found in their study, a significant improvement in the group of combined exercises (an increase of +0.6 ml · kg-1 · min -1 2.1 %%, p = 0.04) for the group of aerobic exercises. (an increase of + 1.1 ml · kg -1 · min -1, 2.1 %%, p = 0.04).

c) *Renal function*

The exercise group in the study by Headley et al..[16] showed a 20.6% reduction in the ET - 1 rate. In the study by Hirakiet al.[18], renal function decreased in the GFR ratein the group that underwent intervention, from 37.0 ± 10.9 to 35.1 ± 11.4 ml/min / 1.73 m^2.

d) *Oxidative stress and inflammatory response*

Only the study by Ikizleret al.[19] recorded a change in these two components. Both oxidative stress and inflammatory response decreased in the control group.

e) *Central aortic pulse wave velocity*

Only one study by Headley et al.[16] verified this variable. There was no significant difference in both the EG and the CG, thus showing that the exercise was not effective.

V. Discussion

With the increasing incidence of CKD, with this research, we seek to verify whether the use of physical activity causes benefits in CKD patients undergoing hemodialysis treatment and what should be the best intervention method to be prescribed for this audience. A total of 43 articles were found, and of these, only 4 met our criteria [16-17-18-19]. Because of this, it is worth mentioning the presence of very few studies that investigate the effectiveness of the physical activity in patients who are in these conditions. The articles used to integrate this research obtained results in the variables offered by aerobic training [16-18-19] and resistance training associated with aerobic [17].

Regarding the study by Watson et al..[17] that verified the intervention of aerobic training with resistance training, the results obtained had great significance in muscle strength, quadriceps volume, and rectus femoris. There were also small gains in the relative VO_{2peak} and an improvement in the distance covered. Total peripheral resistance and its index increased only in the resistance training group, and blood pressure did not change. The studies by Headley et al.[16], Hirakiet al.[18] and Ikizleret al.[19], which verified only the intervention of aerobic training, had an increase in aerobic capacity, improved vasoactive balance and some aspects of health-related quality of life, increased renal function, decreased body composition (body weight, BMI, waist-hip and the percentage of body fat), oxidative stress and inflammatory response.

The PEDro scale demonstrated that the selected studies were rated at a high level for methodological quality [15]. However, studies related to our purpose are still scarce. It is known how important physical activity is in the treatment of any organic abnormalities. Selected studies [16-17-18-19] demonstrated positive neuromuscular, cardiovascular, cardio-respiratory, biochemical, systemic responses, and quality of life aspects. However, given these results and the need for more information on the subject, more studies should be carried out to promote the reduction of knowledge gaps that still exist.

VI. Conclusion

After analyzing the studies that were used to integrate this research, we can say that the use of physical activity as a way to assist patients with CKD on hemodialysis, guarantees benefits in functional capacity, whether using aerobic training or combined training. It is worth emphasizing the need for further studies to verify which other variables may change with the use of physical activity.

Conflict of interest statement

The authors declare that there is no conflict of interest in the present study.

Acknowledgment

Catholic University of Petrópolis (UCP)
Juiz de Fora of Federal University (UFJF)

References Références Referencias

1. Cavalcanti, C. Physical activity level in depressive symptoms in patient underground hemodialysis: A cross-section studies. Fisioter.Pesqui. 2014; 21 (2): 161-6. doi: 10.1590/1809-2950/49921022014.
2. Sesso RC; Lopes AA, Thomé FS, Lugon JR, Martins CT. Brazilian Chronic Dialysis Census 2014. J Bras Nefrol. 2016; 38h54min- 61. doi: org/10.5935/0101-2800.20160009.
3. Sesso RC, Lopes AA, Thomé, FS, Lugon, JR; Watanabe, Y; Santos DR. J BrasNefrol. 2014; 36(1): 48-53. doi: 10.5935/0101-2800.20140009.
4. Dantas FFO, Figueirôa NMC. Evaluation of the effects of intradialytic aerobic training in chronic renal patients. Rev Health Care 2014; 12 (42): 22-8.doi: 10.13037/rbcs. vol12n42.2471
5. Brazil. Ministry of Health. Brazilian Society of Nephrology. Ministry of Health 2015. Available from: https://bvsms.saude.gov.br/dicas-em-saude/2083-insuficiencia-renal-cronica.
6. Anand S. Association of self-reported physical activity with laboratory markers of nutrition and inflammation: The Comprehensive Dialysis Study. Journal of Renal Nutrition. 2011; 21(6), 429-437.
7. Johansen KL. Association of body size with health status in patients beginning dialysis. The American Journal of Clinical Nutrition. 2006; 83(3), 543-549
8. Nascimento MM. Malnutrition and inflammation are associated with impaired pulmonary function in patients with chronic kidney disease. Nephrology, Dialysis, and Transplantation. 2004; 19(7), 1823-1828.
9. Cheema B, Abas H, Smith B, O'Sullivan AJ, Chan M, Patwardhan A,et al. Investigation of skeletal muscle quantity and quality in end-stage renal disease. Nephrology (Carlton). 2010; 15(4):454-63.
10. Salgado Filho N, Brito D. Chronic kidney disease: the great epidemic of this millennium. J Bras Nefrol. 2006; 28 (2), p. 1–5.
11. American College of Sports Medicine (ACSM).2014. Disponível em: www.acsm.org.
12. Painter P. Exercise: a guide for the people on dialysis. Madison: Medical Education Institute. 2000.
13. Segura - Orti E, Johansen KL. Exercise in end-stage renal disease. Semin Dial. 2010; 23(4):422-30.
14. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and Elaboration. PLoS medicine. 2009; 6(7), e1000100.
15. Shiwa SR, Costa LOP, Moser ADL, Aguiar IC, de Oliveira LVF. PEDro: The physiotherapy evidence database. Fisioter Mov. 201; 24(3):523-33.
16. Headley S, Germain M, Wood R, Joubert J, Milch C, Evans E, et al.Short-term aerobic exercise and vascular function in stage 3 CKD: a randomized controlled study. Am J Kidney Dis. Elsevier Inc. 2014; 64: 222-229.
17. Watson EL, Gould DW, Wilkinson TJ, Xenophontos S, Clarke AL, Vogt BP, Viana JL, Smith AC. Twelve-week combined resistance and aerobic training confer greater benefits than aerobic training alone in nondialysis CKD. Am J Physiol Renal Physiol. 2018; 314: 1188-1196. doi:10.1152/ adrenal.00012.2018.
18. Hiraki K, Shibagaki Y, Izawa KP, Hotta C, Wakamiya A, Sakurada T, et al. Effects of home exercise on patients with pre-dialysis chronic kidney disease: a pilot randomized study and feasibility. BMC Nephrol. 2017; 18 (1): 198-204. doi: 10.1186 / s12882-017-0613-7.
19. Ikizler TA, Robinson-Cohen C,Ellis C, Headley SAE, Tutlle K, Wood RJ, et al. Metabolic effects of diet and exercise in patients with moderate to severe CKD: A randomized clinical trial. J AmSocNephrol. 2017; ASN. 2017010020. 10.1681 / ASN.2017010020.