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

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#### 8 Abstract

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Objective: Analyze through a systematic review of the effects of physical activity on 9 hemodialysis patients. Methods: The study followed the proposals of PRISMA (Preferred 10 Reporting Items in Systematic Reviews and Meta-Analyzes). The search for articles took 11 place on the digital platforms Medline, Pub Med, and Sports Discus, from February to 12 October 2019. Itwas found using word combinations specific to the research theme, and they 13 are aerobic exercise and renal insufficiency, aerobic exercise and dialysis treatment, strength 14 training and renal insufficiency, strength training, and renal insufficiency. Results: 43 articles 15 were identified. However, in the search criteria, 39 were excluded. No studies were excluded 16 by checking titles and abstracts. Finally, four of them were selected for a full reading. After 17 eligibility, all four were included for the final analysis. The PEDro scale identified a high 18 methodological quality of the selected studies. The studies showed significant improvements in 19 the neuromuscular, cardiovascular, cardiorespiratory, biochemical, and organic systems. In 20 addition to improvements in the evaluative aspects of quality of life. Methods: The study 21 followed the proposals of PRISMA (Preferred Reporting Items in Systematic Reviews and 22 Meta-Analyzes). The search for articles took place on the digital platforms Medline, Pub 23 Med, and Sports Discus, from February to October 2019. Itwas found using word 24 combinations specific to the research theme, and they are aerobic exercise and renal 25 insufficiency, aerobic exercise and dialysis treatment, strength training and renal insufficiency, 26 strength training, and renal insufficiency. Results: 43 articles were identified. However, in the 27 search criteria, 39 were excluded. No studies were excluded by checking titles and abstracts. 28 Finally, four of them were selected for a full reading. After eligibility, all four were included 29 for the final analysis. The PEDro scale identified a high methodological quality of the selected 30 studies. The studies showed significant improvements in the neuromuscular, cardiovascular, 31 cardiorespiratory, biochemical, and organic systems. In addition to improvements in the 32 evaluative aspects of quality of life. 33

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35 Index terms— physical activity; hemodialysis; chronic kidney disease.

#### <sup>36</sup> 1 Introduction

<sup>37</sup> hronic 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

#### 4 B) ELIGIBILITY CRITERIA AND STUDY SELECTION

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.

<sup>46</sup> These hormones regulate blood pressure, make red blood cells, and strengthen bones 5 . The repercussions of

47 CKD associated with hemodialysis treatment can lead to the loss of components of physical fitness that results

<sup>48</sup> in decreased functional capacity and mortality in this population **??**-7-8 . The CKD patient has several changes

49 in their bodies. Muscle loss is noted, characterized by musculoskeletal changes, which occur at an accelerated 50 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 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

 $\mathbf{63}$  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.

#### 80 2 II.

#### <sup>81</sup> 3 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.

# <sup>85</sup> 4 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.

97 Articles that presented intervention methods other than physical exercise were excluded; those who underwent 98 training with non-dialysis patients. And articles that applied physical activities and that found benefits for 99 patients with CKD on hemodialysis were included.

#### $_{100}$ 5 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. 101 The evaluation instrument for the selected studies was performed using the PEDro scale 15. The PEDro scale 102 is considered an appropriate tool in systematic reviews for qualitative analysis of quantitative studies. The 103 method consists of component classifications for the following categories: selection criteria, the equation between 104 groups, data collection methods, outcome factors. The components were classified into 0 (not identified) and 105 1 (identified). Studies with PEDro scores between 6 and 10 points, 4 and 5 points, and 0 and 3 points were 106 considered high, moderate, and low quality, respectively. All disagreements regarding the classification of PEDro 107 scores were resolved by a consensus discussion among the reviewers. 108

#### 109 6 III.

#### 110 7 Results

#### <sup>111</sup> 8 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 excluded. No 118 one was excluded by checking their titles and abstracts. Finally, four studies were selected for reading in full. 119 After eligibility, the four were included for the final analysis. The summary of articles, in table 1, was based on 120 a structured questionnaire that considered the following items: Authors, year of publication, sample (quantity, 121 sex, and age), training protocols, dependent variable, results. The average PEDro score for the studies included 122 in the review was  $6.25 \pm 0.5$  points, ranging from 3 to 6 points (Table 1). According to the established quality 123 criteria, the average quality of the studies included in this review is, therefore, high. Also, there was no high 124 degree of variation in quality between studies. All studies ??6-17-18-19 met the eligibility criteria. (Question 1 125 of the PEDro scale) and outcome measures. Likewise, all of them 16-17-18-19 performed a randomized crossover 126 design (question 2 of the PEDro scale). Only one study 16 concealed criteria (question 3 on the PEDro scale). 127 All studies ??6-17-18-19 showed similarity between groups (question 4 on the PEDro scale). None of the studies 128 presented blind methodological criteria (questions on the PEDro scale 5, 6, and 7). All studies ??6-17-18-19 129 showed results in more than 85% of the sample (question 8 on the PEDro scale), fulfilled criteria 9, related to 130 the intervention condition (question 9 on the PEDro scale), showed statistical comparisons between 131

#### <sup>132</sup> 9 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 ??6-17-19. 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 143 of lower limbs (squat and calf lengthening) and upper limbs (strengthening of claws), with 20 to 30 repetitions, 144 three times a week. Ikizler et al. 19 observed the effectiveness of aerobic training tied to a caloric restriction, 145 where the exercise was performed for 30 to 45 minutes, three times a week, and the caloric restriction was 146 designed to decrease calories in general. Watson et al. 17 One of the studies 18 took place at home, and 147 three studies took place in laboratories, requiring the use of cycle ergometers ??6-17-18. The selected studies 148 applied chronic interventions that were from 12 weeks 17 to 12 months 18. Regarding the responses resulting 149 from different physical training protocols, two findings observed an increase in muscle strength [17][18], three 150 151 studies verified aerobic capacity ??6-17-19, two studies obtained improvement in renal function [16][17][18], one 152 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 153 quality of life 16. Below are the results of the variables identified in the studies. 18 found significant results 154 between the exercise group (wrist:  $31.7 \pm 7.4$  in baseline to  $36.4 \pm 6.4$  kgf. Post-intervention; knee extensor: 155  $0.65 \pm 0.17$  in baseline for 0,  $70 \pm 0.17$  kgf. / Kg post-intervention) and the control group (wrist:  $35.5 \pm 8.8$  to 156  $36.5 \pm 9.2$  kgf. Post-intervention; knee extensor:  $0.66 \pm 0.15$  for  $0.62 \pm 0.13$  kgf / kg Watson et al.. 17 achieved 157

significant results both in the aerobic exercise group and in the resistance exercise group, however, the resistanceexercise group had a greater gain.

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## <sup>161</sup> 11 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).

# <sup>166</sup> 12 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 rate in the group that underwent intervention, from 37.0  $\pm$  10.9 to 35.1  $\pm$  11.4 ml/min / 1.73 m 2.

### 170 13 d) Oxidative stress and inflammatory response

171 Only the study by Ikizleret al. 19 recorded a change in these two components. Both oxidative stress and 172 inflammatory response decreased in the control group.

# <sup>173</sup> 14 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.

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 **??**6-17-18-19. 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 **??**6-18-19 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 IV.

- <sup>190</sup> 15 Results of Measures Taken
- 191 V.

# 192 16 Discussion

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 ??6-17-18-19 demonstrated positive neuromuscular, cardiovascular, cardiorespiratory, biochemical, systemic responses, and 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.

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.<sup>1</sup>

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Figure 1: Figure 1 :

#### $\mathbf{1}$

Studies	1	2	3	4	5	6	7	8	9	10	11	Tota
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

[Note: Legend: EGexercise 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; â??" -there was no significance concerning Baseline; ?the significant difference concerning baseline.]

Figure 2: Table 1 :

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[Note: a) Muscle strengthHirakiet al..]

Figure 3: Table 2 :

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#### 206 .2 Conflict of interest statement

- 207 The authors declare that there is no conflict of interest in the present study.
- $_{\rm 208}$  [Sesso] , R C Sesso .
- $_{\rm 209}$   $~[{\rm Sesso}~{\rm et~al.}]$  , R C Sesso , A A Lopes , Thomé , Fs , Lugon .
- 210 [Vi and Conclusion] , Vi , Conclusion .
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