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Literature review

Effects of exercise on individuals with chronic kidney disease: an evidence gap map

Efeitos do exercício em indivíduos com doenças renais crônicas: um mapa de evidências

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ABSTRACT

Introduction: Despite compromised exercise capacity and quality of life, patients with chronic kidney disease (CKD) are extremely inactive. Thus, exercise plays an essential role in disease management and has been strongly recommended, regardless of disease severity. Mapping the main evidence about this topic allows an evidence-based practice. **Objective:** To summarize the effects of exercise-based interventions prescribed for patients with CKD by producing an evidence gap map. **Methods:** After a comprehensive search in electronic databases, the eligible studies were analyzed by two reviewers. The data was extracted and plotted into a matrix linking interventions and outcomes. The narrative synthesis included only the findings of the studies published in the last five years. The confidence level was assessed as recommended. **Results:** In total, 75 reviews published between 2005 and 2022 were included in the map, but only 50 were described in the narrative synthesis. We found 179 associations, especially positive, based on the analysis of plotting 20 interventions categorized into seven groups and 27 outcomes categorized into 13 groups. Negative, potentially negative, and adverse effects were not reported, which indicates that exercise is safe for patients with CKD. **Conclusion:** The mapped evidence were mainly high confidence level, corroborating the role of prescribing exercise for patients with CKD as a safe and positively effective intervention for multiple outcomes with highlights for physical fitness, clinical outcomes, quality of life and wellbeing.

Keywords: kidney diseases; exercise; evidence-based practice; systematic review.

RESUMO

Introdução: A despeito do comprometimento da capacidade funcional e redução de qualidade de vida, pacientes com doença renal crônica (DRC) são extremamente inativos. Sendo assim, o exercício apresenta papel essencial no manejo da doença e tem sido fortemente recomendado, independentemente da severidade da doença. Mapear as principais evidências sobre a temática oportuniza a prática baseada em evidências. **Objetivo:** Sumarizar os efeitos de intervenções baseadas em exercícios físicos em pacientes com DRC a partir da elaboração de um mapa de evidências. **Métodos:** Após busca abrangente nas bases de dados, os estudos elegíveis foram analisados por duas revisoras. Os dados foram extraídos e plotados em uma matriz associando intervenções e desfechos. A síntese narrativa incluiu somente os achados relativos aos estudos de revisão publicados nos últimos cinco anos. O nível de confiança foi avaliado conforme recomendado. **Resultados:** Ao todo, 75 estudos de revisão publicados entre 2005 e 2022 foram incluídos no mapa, porém apenas 50 foram descritos na síntese narrativa. Encontramos 179 associações, principalmente positivas, a partir da análise da plotagem de 20 intervenções categorizadas em sete grupos e 27 desfechos em 13 grupos. Não foram reportados efeitos negativos, potencialmente negativos ou adversos, sugerindo que a prática de exercício é segura para pacientes com DRC. **Conclusão:** As evidências mapeadas apresentam, em sua maioria, alto nível de confiança, corroborando o papel da prescrição do exercício para pacientes com DRC como intervenção segura e com efeitos majoritariamente positivos para múltiplos desfechos, com destaque para aptidão física, desfechos clínicos, e qualidade de vida e bem-estar.

Palavras-chave: nefropatias; exercício físico; prática clínica baseada em evidências; revisão sistemática.

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Introduction

Chronic kidney disease (CKD) is a clinical syndrome with slow and progressive evolution resulting from irreversible morphofunctional alteration of the kidney for more than three months [1]. It can be classified into five stages according to the glomerular filtration rate (G1-G5), three according to albuminuria (A1-A3), and three groups (i.e., pre-dialysis, dialysis, and transplantation) [1,2]. Treatment and control of risk factors for their development (i.e., diabetes, hypertension, obesity, cardiovascular disease, and smoking) are the main ways to prevent disease [3].

Worldwide, more than 850 million people have CKD, which is responsible for 2.4 million deaths annually [4]. CKD is part of noncommunicable chronic diseases with a silent development, increased prevalence, high mortality, and high costs for health systems worldwide [3]. Its prevalence in the Brazilian population is still uncertain, but it is estimated that 3 to 6 million Brazilians have CKD [5]. This population has a mortality rate of 15 to 30 times higher than healthy individuals due to the impairment of 60-65% of the functional capacity with a consequent lower quality of life [6]. Commonly, there is the presence of multiple symptoms (i.e., restless leg syndrome, sleep disorder, depression, anxiety, muscle cramps, fatigue) that may be associated with metastatic cancer [7].

One of the most frequent complaints of patients is the reduction of functional exercise capacity manifested by decreasing exercise tolerance and reducing performance in daily life activities [8]. Both the hemodialysis procedure (HD) and uremic myopathy are associated with the breaking of muscle proteins that affects peripheral and proximal muscles and, consequently, physical capacity [8].

Recently, exercise has been considered a first-rate treatment for various chronic diseases, including psychiatric, neurological, metabolic, cardiovascular, pulmonary disease, and musculoskeletal disorders, and cancer [9]. Given this scenario, exercise has been successfully used as an adjuvant treatment in improving CKD and reducing its progression [10]. Among the benefits of exercise programs for patients with CKD and transplanted, the improvement of functional exercise capacity and quality of life stand out, regardless of the type of exercise, intensity, or duration of intervention [11]. Since CKD patients are extremely inactive, exercise promotes positive cardiovascular effects, as well as improves the efficacy of dialysis [12]. Thus, patients with CKD should be encouraged to exercise and increase their physical activity levels [10]. However, there may be differences in results according to the stage of the disease and dialysis or transplantation, which suggests the need for study designs based on the prescription of a wide variety of exercises and the importance of evidence-based practice [13].

Given the diversity of exercise, physical activity, and body practices, as well as prescription strategies, sector or service, and supervision/guidance, the evidence gap map allows mapping the effects of physical exercise in patients with CKD considering different contexts [14]. The map provides friendly access to existing knowledge,

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contributing to professional updates/training and favoring evidence-based practice [14]. In addition to pointing out the role of physiotherapy professionals in hemodialysis and nephrology services, this professional can contribute as a member of the team in healthcare setting and, hence, reduce healthcare costs of this service according to their skills, especially the prescription of exercises [15].

Therefore, this evidence gap map aimed to summarize the effects of exercise-based interventions prescribed for patients with CKD.

Methods

This evidence gap map is based on the methodology developed by the International Initiative for Impact Evaluation (3IE) and adapted by the Latin American and Caribbean Center on Health Sciences Information in the Pan American Health Organization and the World Health Organization (Bireme/PAHO/WHO) [16]. Accordingly, it is a method of evidence synthesis based on the review of specific area/thematic literature reviews, followed by the development of an evidence matrix from the plot of interventions and outcomes [14]. Although previously written according to the recommendations, the protocol was not registered elsewhere. However, consultation with the protocol can be performed upon request to the authors responsible for the study. The scope of the study was defined through the acronym PCC, as described below:

Population or problem: Patients with CKD, regardless of sex, race-ethnicity, age, socioeconomic status, education, and presence of associated comorbidities;

Concept: Multiple and/or nonspecific outcomes in health;

Context: Interventions based on physical exercises, regardless of the modality, frequency, duration of the session and/or the intervention, intensity, public or private sector, and level of health care.

Information sources

Potentially eligible citations were identified and recovered from the searches conducted in the electronic databases Cochrane Library, Physiotherapy Evidence Database, PubMed, and Virtual Health Library on April 26, 2022.

Search strategy

The search strategy was elaborated by one of the reviewers (TLVDPO) to provide a comprehensive and understanding search of the literature. The descriptors and alternative terms were defined and selected in English and Portuguese after consulting the health descriptors (DECS/Mesh): population or problem (kidney failure, kidney failure, chronic renal insufficiency, chronic renal failure, and their respective terms Alternatives) and context (exercise, exercise therapy, breathing exercise, exercise, and movement techniques, muscle stretching exercises, high-intensity interval training, and their respective alternative terms). Having seen the interest in mapping multiple outcomes, no terms regarding outcomes were included. Although there are no restrictions on the date of publication, we use filters (i.e., type of study and language) when available in order to identify review studies of interest.

Eligibility criteria

We considered eligible: (1) Systematic review studies (systematic reviews with or without meta-analysis, and overview systematic review) available in full text (2), which (3) evaluated the effects of exercise-based interventions for (4) patients with CKD, regardless of age, sex, race-ethnicity, socioeconomic status, education and presence of associated comorbidities. Primary studies, letters to the editor, opinion articles, comments, publications from annals of congresses, and ongoing review protocols were excluded.

There was no restriction on the date of publication, but only systematic review studies published in English, Portuguese, and Spanish were included. The option for language restriction was a choice of reviewers to minimize possible evidence interpretation errors due to language barriers.

Evidence selection

The analysis and selection of the studies occurred through the Rayyan application for bibliographic management. Two independent reviewers (TLVDPO, LGdSdM) screened titles and abstracts. After the resolution of disagreements by consensus and verification of eligibility from consultation with the full text, ineligible studies were excluded. Citations of studies considered potentially relevant by at least one reviewer were analyzed through the full text.

Extraction and analysis of data

Data extraction and analysis were performed by two reviewers (TLVDPO, LGdSdM) in a standardized excel spreadsheet and according to the protocol previously elaborated at the beginning of the review. The characterization data of the review studies (i.e., study title, year and country of publication, type, and design of the review) and main interventions, outcomes, and effects (i.e., no effect, not reported, potentially negative, negative, inconclusive, potentially positive, positive) were extracted from the reading of the full text.

After completing data extraction, the categories and subcategories of interventions and outcomes were defined based on the literature on the subject. The results were analyzed and reported in an evidence matrix based on plotting interventions and outcomes. The concentration and quality of the evidence were presented according to different colors and graphic elements. Finally, the interactive version of the evidence map was built using the Tableau ® tool.

Evidence quality assessment

The methodological quality assessment of the included review studies was performed by two reviewers (TLVDPO, LGdSdM) using the instrument A MeaSurement Tool to Assess Systematic Reviews (AMSTAR 2) [17]. Studies that did not meet the requirements of this instrument were not included in this map to avoid reporting evidence without assessing the confidence level.

Results

A total of 495 potentially eligible citations were identified, but only 75 studies were included in the map after screening and verification of eligibility (Figure 1). The map in its interactive version is available in the evidence map.

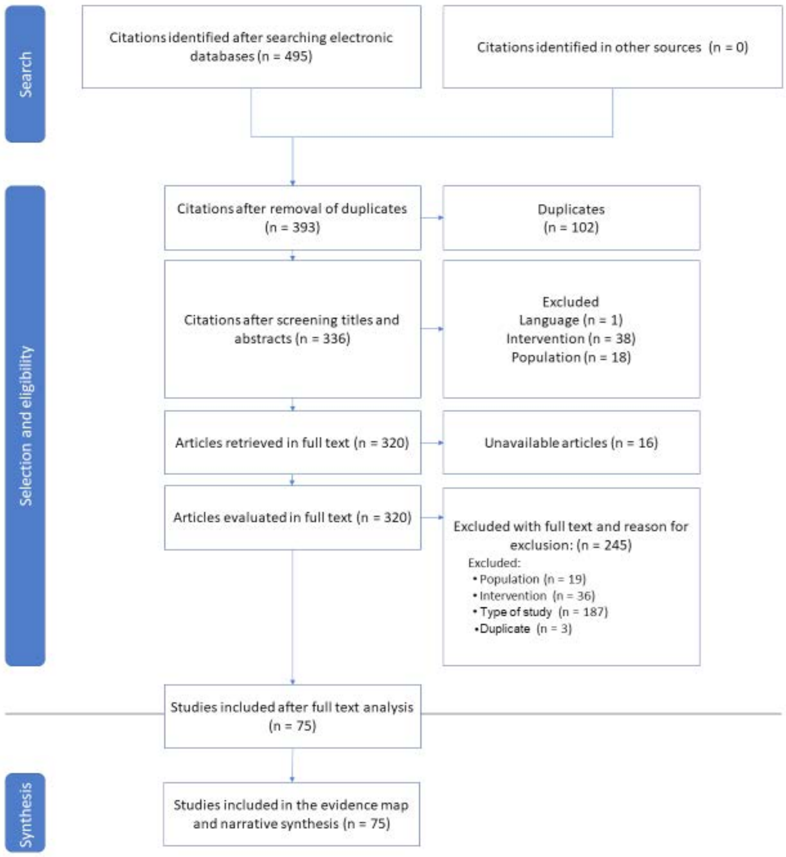

Figure 1 - Map evidence flowchart
Source: adaptation of the Reporting standards for Systematic Evidence Syntheses recommendation [18]

We analyzed publications between 2005 and 2022 with a predominance of systematic review and meta-analysis studies (n = 37), which mostly evaluated effectiveness (n = 65). Additionally, we included six meta-analysis studies, 27 systematic review studies, and four Cochrane-type systematic reviews. The narrative synthesis privileged the publications of the last five years (n = 50).

Focus countries indicate where the primary studies included in the reviews were conducted. Among them, we observed 45 countries in 23 studies, with emphasis on Brazil (n = 10), China (n = 14), Australia (n = 6), Canada (n = 3), United States of America (n = 3), Japan (n = 2), and Taiwan (n = 2). We emphasize that we did not analyze the primary studies included in the systematic reviews. Therefore, data from the same primary study may have been systematized in more than one review. Thus, the analysis of the amount and concentration of evidence must be done with caution.

Target population

The study sample consisted mainly of adults (n = 40), with only three studies with patients of all ages and seven that did not inform age or age group. As for sex, only one study focused on male participants, while 19 studies included patients of both sexes (n = 19), and another 30 did not report whether included only males or females or both of them.

Patients with CKD covered all stages of classification, hemodialysis, and kidney transplants. Additionally, patients with restless legs syndrome (n = 3), overweight or obesity (n = 1), diseases related to oxidative stress (n = 1), and hypertension (n = 1) were evaluated. Unfortunately, there were no considerations related to race-ethnicity, socioeconomic status, or other health inequities.

Interventions and outcomes

The 50 studies included in the narrative synthesis evaluated the effect of 20 types of interventions divided into seven groups: Stretching, Physical Activity, Physical Activity and Exercise, Exercise, Combined and/or Multimodal Intervention, Integrative and Complementary Practices, and Others. These interventions were associated with 27 health outcomes distributed into 13 groups: Physical Fitness, Muscular Fitness, Anthropometric and Body Composition Outcomes, Clinical Outcomes, Epidemiological Outcomes, Renal Outcomes, Fatigue, Level of Physical Activity, Quality of Life and Well-being, Mental Health, Optimization of Dialysis, Adverse Effects, and Others.

Overall, there were 179 associations between interventions and outcomes. It is important to highlight that the same intervention can be applied to more than one outcome and vice versa. The Physical Exercise intervention group was the most associated (127 associations), followed by the Combined and/or Multimodal Intervention group (31 associations). Among the outcomes, the Physical Fitness group received 39 associations, while Clinical outcomes had 26 associations, and Quality of Life and Well-being received 25 associations.

Effects of interventions on outcomes

The effects of the interventions were mainly positive (88 associations) and potentially positive (38 associations). However, we found inconclusive effects (35 associations), as well as interventions without effect (16 associations). No study reported a negative or potentially negative effect for the analyzed interventions. The main associations found were highlighted in Table I.

We observed a positive effect mainly for physical fitness (32 associations), quality of life (10 associations), cardiovascular outcomes (8 associations), muscular fitness (7 associations), restless legs syndrome (6 associations), and depression (5 associations). For potentially positive effects, the most frequent outcomes were quality of life (9 associations) and muscle fitness (5 associations). There were more inconclusive effects for physical fitness and quality of life and well-being (4 associations), cardiovascular outcomes (3 associations), and musculoskeletal outcomes (4 associations).

Exercise-based interventions had no negative effects, but we observed 35 associations with inconclusive effects. Additionally, no exercise-related adverse effects have been reported for patients with CKD.

Table I - Main associations between interventions and outcomes based on the evidence map analysis

Interventions	Effect, n	Outcomes
Stretching	Positive, 2	Restless legs syndrome
	No effect, 1	Adverse effects
Physical activity	Positive, 2	Prognosis
Physical activity and/or unspecified exercise	Inconclusive, 5	Physical fitness, depression, adverse effects, fatigue, quality of life
Neuromuscular electrical stimulation	No effect, 2	adverse effects, restless legs syndrome
	Positive, 2	physical fitness, muscle fitness
	Inconclusive, 4	cardiovascular outcomes, musculoskeletal outcomes, muscle mass, multiple or nonspecific
Exercise + Health education	Positive, 1	Physical fitness
Exercise + Neuromuscular electrical stimulation	Potentially Positive, 3	Physical fitness, Muscle fitness
Exercise + Behavior change techniques	Potentially Positive, 3	Physical fitness, Multiple or nonspecific, Quality of life
Exercise + Integrative and Complementary Practices + Sports	Positive, 1	Depression
	Potentially Positive, 5	Anxiety, depression, fatigue, level of physical activity, quality of life
Aerobic exercise	Potentially Positive, 5	Musculoskeletal outcomes, Depression, Optimization of dialysis, Quality of life
	Positive, 26	Physical fitness, muscular fitness, cardiovascular outcomes, musculoskeletal outcomes, depression, glomerular filtration, body mass index, quality of life, restless legs syndrome, time duration of exercise
	No effect, 7	Cardiovascular outcomes, musculoskeletal outcomes, body mass index, optimization of dialysis, quality of life, cardiovascular risk
	Inconclusive, 10	Anxiety, physical fitness, cardiovascular outcomes, musculoskeletal outcomes, glomerular filtration, inflammatory markers, quality of sleep, quality of life
Aerobic exercise + stretching	No effect, 1	Sleep quality

Table I - Continuation

Interventions	Effect, n	Outcomes
Aerobic exercise + resistance	Potentially Positive, 10	Anxiety, muscle fitness, musculoskeletal outcomes, depression, glomerular filtration, inflammatory markers, multiple or nonspecific, quality of life
	Positive, 30	Physical fitness, muscular fitness, cramp, cardiovascular outcomes, fatigue, body mass index, inflammatory markers, quality of sleep, quality of life, optimization of dialysis
	Inconclusive, 13	Muscle fitness, musculoskeletal outcomes, adverse effects, glomerular filtration, body fat, body mass index, inflammatory markers, proteinuria, quality of life, multiple or nonspecific
	No effect, 1	Optimization of dialysis
Aerobic exercise + resistance + stretching	Potentially Positive, 1	Anxiety
	Positive, 3	Physical fitness
Aerobic exercise + resistance + respiratory muscle training + neuromuscular electrical stimulation	Positive, 6	Physical fitness, muscular fitness, musculoskeletal outcomes, optimization of dialysis, quality of life
	No effect, 1	Adverse effects
Aerobic Exercise + Telehealth	Inconclusive, 1	Cardiovascular outcomes
	Potentially Positive, 1	Quality of life
	Positive, 8	Physical fitness, muscular fitness, depression, cardiovascular outcomes, body fat, quality of life
Home-based exercise	Potentially Positive, 1	Muscle fitness
Multiple or non-specific exercise	Inconclusive, 2	optimization of dialysis, proteinuria
	Potentially Positive, 2	cardiovascular outcomes
	Positive, 4	physical fitness, depression, optimization of dialysis, quality of life
	No effect, 2	adverse effects, quality of life
Resistance exercise	Potentially Positive, 5	Physical fitness, muscle fitness, muscle mass, quality of life
Upper Limb Musculature Training	Positive, 2	Maturation of arteriovenous fistula
Respiratory Muscle Training	Potentially Positive, 1	Quality of life
	Positive, 1	Muscle fitness
Yoga	Potentially Positive, 1	Musculoskeletal outcomes

Source: own elaboration

Confidence level

Regarding the critical appraisal analysis, studies were classified as high (n = 34; 68%), moderate (n = 9; 18%), low (n = 5; 10%), or critically low confidence level. (n = 2; 4%).

Lastly, the associations between interventions and outcomes can be observed according to the effect found and the level of confidence obtained through the application of AMSTAR 2 (Table II).

Table II - Associations between interventions and outcomes according to effect and confidence level

Confidence level	Effect	Intervention category	Outcome category
High	Positive	Stretching	Other (restless legs syndrome)
		Physical activity	Epidemiological outcomes (prognosis)
		Exercise	Physical and muscular fitness Anthropometric and body composition outcomes (body mass index) Clinical outcomes (cardiovascular, musculoskeletal and metabolites) Renal outcomes (glomerular filtration) Fatigue Optimization of dialysis Others (cramping, restless legs syndrome, sleep quality, inflammatory markers, maturation of arteriovenous fistulas and exercise duration time) Quality of life and well-being Mental health (depression)
		Combined and/or multimodal intervention	Physical and muscular fitness Anthropometric and body composition outcomes (body fat) Clinical outcomes (cardiovascular and musculoskeletal) Optimization of dialysis Quality of life and well-being Mental health (depression)
		Others	Physical and muscular fitness
		Integrative and complementary practices	Others (inflammatory markers)
	Potentially positive	Exercise	Physical and muscular fitness Anthropometric and body composition outcomes (Muscle mass) Clinical outcomes (cardiovascular and musculoskeletal) Renal outcomes (Multiple or nonspecific) Others (inflammatory markers) Quality of life and well-being Mental health (anxiety, depression)
		Combined and/or multimodal intervention	Physical and muscular fitness Anthropometric and body composition outcomes (multiple or nonspecific) Clinical (cardiovascular) outcomes Fatigue Level of physical activity Quality of life and well-being Mental health (anxiety, depression)
		Integrative and complementary practices	Clinical outcomes (musculoskeletal)

Table II - Continuation

Confidence level	Effect	Intervention category	Outcome category
Moderate	Positive	Exercise	Physical and muscular fitness Anthropometric and body composition outcomes (body mass index) Quality of life and well-being
		Combined and/ or multimodal intervention	Physical fitness
	Potentially positive	Exercise	Muscle fitness Clinical outcomes (cardiovascular and musculoskeletal) Renal outcomes (glomerular filtration) Optimization of dialysis
		Combined and/ or multimodal intervention	Physical fitness Renal outcomes (multiple or nonspecific) Quality of life and well-being
Low	Positive	Exercise	Physical and muscular fitness Anthropometric and body composition outcomes (body mass index) Clinical (cardiovascular) outcomes Other (restless legs syndrome)
		Combined and/ or multimodal intervention	Stretching Other interventions (neuromuscular electrical stimulation)
	Inconclusive	Exercise	Renal outcomes (glomerular filtration) Optimization of dialysis
	No effect	Stretching	Adverse effects
		Exercise	Other outcomes (sleep quality)
		Other interventions	Other outcomes (restless legs syndrome)
Critically low	Positive	Exercise	Muscle Fitness Clinical (cardiovascular) outcomes

Source: own elaboration

Discussion

The present study developed an interactive evidence gap map on the effects of exercise-based interventions prescribed for patients with CKD. Overall, 50 review studies were included in the narrative synthesis of this evidence gap map and reported a variety of exercise modalities prescribed for patients with CKD.

Exercise-based interventions were mostly effective and can be considered safe, while no significant negative and/or adverse effects were reported. Therefore, the evidence map contributes to understanding the role of these interventions in the healthcare of patients with CKD, favoring the translation of knowledge and the identification of important gaps to be investigated.

The general characterization showed a higher proportion of systematic reviews and meta-analyses (56%) [19-46], whose sample consisted of adults. The restricted approach of participants from a wide age group and/or children is compatible with the greater concentration of epidemiological data in adults [47] between 20-65 years [5]. This situation limits the recognition and even the management of CKD in earlier stages, which tends to result in case studies with renal impairment at an advanced stage [47,48]. It should be added that studies on CKD are carried out mainly after the start of dialysis treatment or transplantation, despite CKD being associated with risk factors, which include health inequalities among them [49]. Additionally, this population has a high mortality, i.e., approximately 50% of the elderly survive about five years after starting dialysis [50]. These points may contribute to explaining the profile of patients analyzed in the studies.

All CKD classification stages were analyzed, dependent or not on dialysis and kidney transplant recipients. A previous study pointed out that the studies are mainly focused on patients with end-stage CKD who undergo regular dialysis [48], and preferably the exercise protocols occurred within the first two hours after the start of dialysis to avoid cardiovascular instability [35]. This point may justify our findings as only ten included studies were performed with patients without dialysis or kidney transplantation [23,27,28,30,31,37,40,48,51,52] and three did not make it clear whether the studied population was or not dependent on renal replacement therapy [29,44,53]. In patients without dialysis treatment (pre-dialysis) or transplanted, combined aerobic and exercises have a potential effect in delaying the deterioration of renal function [30].

Literature was prominently published in China [19,36,41,48,54] and Brazil [33, 34,38,43,46,55,56]. Brazil is a prominent country on the global stage since presents one of the largest populations on chronic outpatient dialysis and one of the highest rates of annual kidney transplants. Thus, CKD is a relevant public health problem with increasing prevalence worldwide, but it is getting worse in countries like China and Brazil due to the rapid demographic transition associated with the persistence of economic, health, and social inequalities [5,57]. Still, CKD may be associated with risk factors, such as sociodemographic conditions, lifestyle, and chronic diseases [49], which may also justify the greater literature in these regions.

Multiple interventions were found, and hence, different outcomes. These findings may be associated with a high burden of symptoms observed in these patients [7]. According to a previous systematic review, about thirty symptoms are prevalent in patients with CKD, which may vary according to the stage of the disease [7]. It is also important to consider the methodology adopted, which favors the analysis of comprehensive evidence, especially in comparison with the specificity of systematic reviews, for example.

Among the interventions, the modality of aerobic exercises combined with resistance exercises presented the most evidence [8,23,24,27,28,35,36,43,46,48, 56,58]. This exercise modality has been strongly recommended for promoting positive effects on functional exercise capacity, muscle function, body composition, restless legs syndrome, sleep quality, fatigue, quality of life, inflammatory markers, depressive symptoms, and blood pressure [8,23,24,27,28,35,36,46,48,56,58,59]. As expected, multicomponent exercise tends to have a wide range of physiological and psychosocial effects, given that it combines different exercise modalities. It should be added that these findings are consistent with the recent literature, especially focused on exercises prescription for middle-aged and elderly individuals, intending to offer more comprehensive and potentially effective interventions.

In our study, we found 25 associations related to clinical outcomes, which include cardiovascular and musculoskeletal outcomes, especially when aerobic exercise was prescribed. Exercises have been strongly suggested for patients with CKD, mainly due to the positive antihypertensive effects even in shorter interventions (i.e., less than six months in duration), which can lead to a reduction of 5.61 mmHg in systolic pressure and 2.87 mmHg in stages 2-5 of non-dialysis patients [48]. In patients with CKD stages 3-4, in contrast, there is an effect of aerobic exercise on the estimated glomerular filtration rate and exercise tolerance, although limited, but not on blood pressure [44]. However, the findings must be analyzed with caution due to the confidence level being considered low to moderate. Despite this, the findings reiterate previous recommendations available in the KDIGO Clinical Practice Guideline (2021) on Blood Pressure Management in CKD, which suggest that patients with elevated BP and CKD be advised to perform moderate-intensity physical activity for at least 150 minutes a week [60].

Another aspect worth mentioning concerns the association between CKD and obesity. In this study, we found 39 associations between exercise and physical fitness, 11 associations with anthropometric and body composition outcomes, 14 cardiovascular outcomes, and four related to inflammatory markers, among others. These associations are closely related to obesity in patients with CKD, with a greater number of positive associations related to aerobic exercise and the combination of aerobic and resistance exercise [8,23,25,27,28,33-37,39-41,43,44,46,48,51,52,54-56,58,61-64].

We found 88 associations with positive effects after exercises performed during hemodialysis or on days without dialysis [8,21-24,27-29,32,34-37,39,41,43, 44,46,48,51,53–56,58,59,61-66]. Heiwe and Jacobson [13] emphasize that exercise should be one of the care components for adults receiving dialysis, especially for cardiovascular risk factors management. Additionally, it should be mentioned that aerobic capacity is improved by regular exercise training programs, regardless of the type of exercise, intensity, or duration of intervention [13]. Any training modality performed for 2 to 12 months can significantly improve depression and functional exercise capacity, contributing to a better prognosis and survival of adults undergoing dialysis [50].

Three studies evaluated the association between exercise and telehealth with positive effects for outcomes such as physical fitness [64]. Stevenson et al. [67] reported that the use of a physical activity monitoring application (step count) does not promote statistically significant effects for increasing the level of physical activity but favors the management of dietary sodium intake and fluid management. It is important to highlight that this evidence is of low quality, with inconclusive effects due to methodological limitations, as well as the heterogeneity of modalities and types of interventions [67]. Conversely, the combination of aerobic exercise and virtual reality, results in positive and potentially positive effects on quality of life [64], regardless of the exercise modality [64]. Telehealth has been widely investigated and considered a potential strategy to reduce costs, expand access to health care, provide opportunities for chronic conditions management, and promote a more active and healthier lifestyle. Although it was not the focus of the mapping proposed in this study, determining its applicability to patients with CKD is an important perspective to be analyzed in the future, both in primary and secondary studies.

Respiratory muscle training was evaluated in 4 studies, and it showed positive effects on respiratory muscle function, psychosocial outcomes, biochemical markers, functional exercise capacity, adequacy of dialysis, and aerobic capacity [34,62,65], in addition to potentially promoting effects positive concerning the quality of life [22] in the absence of adverse events [62].

Regarding physical activity, a systematic review and meta-analysis study demonstrated that increased physical activity levels were associated with reduced mortality in patients with end-stage CKD treated with hemodialysis [20]. However, the authors point out that the scarcity of well-designed, controlled, and randomized clinical trials with a sufficient number of participants compromises the generalizability of the findings [20]. It is relevant to mention that the definition of the search strategy, although comprehensive, may have privileged the identification of interventions that emphasized the prescription of exercises to the detriment of the promotion of the physical activity. Similarly, the search strategy may have limited the publications related to body practices. Although this has been minimized by the adoption of highly inclusive eligibility criteria, it would be interesting to improve and deepen the search for evidence related to these types of interventions.

Five studies reported that exercise performed in exercise centers and/or at home had positive effects on quality of life [59,66]. Concerning anxiety and depression, these interventions lead to potentially positive effects [24]. A recent study conducted in the United States observed positive effects of home-based exercise on frailty in patients with end-stage CKD, including improvement in muscle strength, walking speed, level of physical activity, depression, and weight loss [68]. It is necessary to consider that 35% of patients with CKD are frail, being eligible for kidney transplantation [68]. However, the long wait for the transplant leads to ineligibility as these individuals become more fragile [68]. Some patients report a fear of exercising during dialysis, but the literature is still limited about home-based exercises for this population [50]. In this sense, Sheng et al. [69] suggest greater viability of intradialytic exercise, minimizing the occurrence of complications and reducing the dropout rate as it does not require extra time for training.

We found 14 associations between exercise and cardiovascular outcomes [36,40,41,43–45,48,56, 61, 63, 64]. A recent meta-analysis reported that 463 million adults are currently living with diabetes worldwide, i.e., 1 in 11 adults aged 20 to 79 years have diabetes [53]. Among these subjects, 35% may develop end-stage CKD after five years, and 18% will die from diabetic nephropathy within 20 years [53]. Given this scenario, physical activity has a protective effect and may delay the progression of diabetic nephropathy [53]. Similarly, a systematic review reinforced the importance of exercise for this population, especially for reducing mortality related to cardiovascular events [61]. Additionally, a meta-analysis showed that exercise is a potential strategy in the prevention and treatment of numerous health conditions, including CKD [19].

Restless legs syndrome (i.e., a movement disorder characterized by a strong urge to move the limbs, especially the legs, which may present with dysesthesias, exacerbated at night or during periods of inactivity) is common in patients with end-stage CKD, significantly affecting sleep quality and, hence, increasing the risk of developing depression and anxiety [24]. Among the included studies, three studies evaluated the effects of exercise in relieving symptoms of restless legs syndrome and found positive effects from interventions of intradialytic stretching and regular aerobic exercises [21,32]. Likewise, the combination of aerobic and resistance exercise also had positive effects on this outcome [24].

Three studies reported an inconclusive effect [20,28,64], and four did not observe significant effects [21,41,62,63]. In contrast, no studies reported adverse events (i.e., any injury or disease exacerbation attributed to the exercise regimen), which could include headaches, hypotension, angina, or even fistula-related problems. This evidence reinforces the role of exercise in the care of patients with CKD, as it is a widely effective and safe intervention.

A previous review study described how challenging it is for dialysis center staff to promote regular exercise practice, as only 25% of patients can exercise without any difficulty [70]. In addition, the health services routine makes counseling by the team incipient and irregular, which perpetuates the lack of knowledge of the benefits and types of exercise that can be performed by patients [70]. Another important point to be analyzed is that, despite the positive and relevant results, few hemodialysis services have physiotherapists in their CKD care team. Thus, the evidence described warns against underestimating the contribution of this professional in hemodialysis clinics and nephrology services [71]. This scenario may also be associated with the high annual expenses for hemodialysis and peritoneal dialysis in Brazil, with 75% of the population depending exclusively on the SUS [72].

Given current trends of the increasing prevalence of CKD, it is imperative to carry out economic evaluation studies in this area to provide a greater understanding of the cost-effectiveness of interventions and encourage the adoption of preventive actions, early diagnosis, and treatment of CKD [73]. Lastly, more studies are needed that include a wide age range and race-ethnicity, sex, health condition, social capital, and education, among other health inequalities, thus providing opportunities for the elaboration and implementation of a health agenda that meets the real demands of countries with marked social inequality, such as Brazil.

Limitations and strengths

This evidence gap map is mostly clinical due to the scope of the study and methodological choices. However, it may be a limitation of the current literature that tends to emphasize and reproduce the biomedical model to the detriment of the biopsychosocial model. Given this scenario, the findings are restricted, which may compromise the applicability of the map concerning health management.

This study does not describe the duration of interventions, intensity, frequency, volume, and progression of exercises. This information can be found in the full text of the primary studies included in the analyzed review studies. The evidence map does not assess the risk of bias. However, this limitation was minimized through the use of AMSTAR 2 for critical appraisal evaluation. Despite the expressive number of studies with a high level of confidence, possibly related to the choice of population and the number of Cochrane-type review studies included, the use of AMSTAR 2 evidences the need to improve the development of protocols for literature reviews, as well as their conduction and description of the main findings, regardless of the performance of meta-analysis.

This study has several strengths that deserve to be highlighted. Among them is the ability to access evidence on exercise-based interventions for patients with CKD and their main clinical outcomes in a user-friendly graphical presentation. Although it does not have statistical analysis, access to studies is provided through hyperlinks. Additionally, the findings were accompanied by the confidence level, contributing to the critical analysis of the evidence and, hence, clinical decision-making. Finally, it is worth considering that the map favors the identification of knowledge gaps, which may be the subject of future studies.

Recommendations

Given the current scenario, the regular practice of exercises has been strongly recommended due to its physiological and psychosocial benefits, mainly for chronic disease treatments such as CKD, regardless of severity. Therefore, the evidence reiterates the role of exercise in the care of these patients and highlights the need to encourage the implementation of exercise programs for this population and encourage increase levels of physical activity. Additionally, the regulation of the participation of the physiotherapy professional as a member of the multidisciplinary team in nephrology centers is imperative and may have a substantial impact on health expenses, reduction of the accelerated progression of the disease, and, consequently, the reduction of morbidity and mortality in this population.

Conclusion

Evidence supports the recommendation of exercise prescriptions for patients with CKD. In general, we observed mostly positive and potentially positive associations between different types of regular intradialytic, interdialytic, and home exercise for clinically relevant outcomes, such as physical fitness, cardiovascular outcomes, mental health, and quality of life, regardless of CKD severity. Finally, we found no negative effects or adverse events reported for this population.

Potential conflict of interest
No conflicts of interest potentially relevant to this article were reported.

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Authors' contribution
Conception and design of the research: Ostolin TLVDP, Moura LGS; **Data collection:** Ostolin TLVDP, Moura LGS; **Data analysis and interpretation:** Ostolin TLVDP, Moura LGS; **Manuscript writing:** Moura LGS; **Critical review of the manuscript for important intellectual content:** Ostolin TLVDP.

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