



A systematic review of trials investigating the efficacy of exercise training for functional capacity and quality of life in chronic kidney disease patients

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Received: 31 October 2020 / Accepted: 6 June 2021 / Published online: 19 June 2021
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Abstract

Objective To investigate the efficacy of exercise training on functional capacity and quality of life in chronic kidney disease.

Data sources SCOPUS, CINAHL, Science Direct, Web of Science, MEDLINE, ProQuest, Physiotherapy Evidence Database (PEDRO), and Google Scholar databases were searched between 2010 and December 2020.

Methods Randomized controlled trials were included if they involved any types of exercise training (aerobic, resisted and respiratory ex.) conducted with chronic kidney disease patients. Three authors independently screened articles, extracted data, and assessed the methodological quality using PEDro scale, and two authors released any confliction. Modified Sackett Scale was used to determine the level of evidence for each outcome.

Results Out of 130 papers screened, 13 studies with 619 participants met the inclusion criteria. The frequency of the treatment ranged from three to four sessions per week for a period ranging from 8 to 24 weeks. According to the Pedro scale, the quality of studies ranged from good (three studies) to fair (ten studies). All included studies showed positive effects on the measured outcomes (functional capacity and quality of life in chronic kidney disease).

Conclusion Exercise programs for chronic kidney disease patients provide beneficial clinical outcomes and optimize functional capacity and quality of life in those patients. Future studies still need to focus on high-quality evidence and studies evaluating the adverse effects of exercise.

Keywords Chronic kidney disease · Exercise training · Quality of life · Functional capacity

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Introduction

Studies of chronic kidney disease (CKD) in several countries have reported that about 12% of the population presents CKD. This rate increases with increasing age [1]. Persons diagnosed with CKD present high morbidity and mortality due to cardiovascular diseases (CVD), low quality of life (QOL), limitation of functional capacity, and metabolic, musculoskeletal disorders [2].

The mortality rate of CKD patients on dialysis is higher than that for individuals in the age-matched population. In Saudi Arabia, the rate of CKD increased in the last three decades due to the rapid changes in lifestyle and high population growth. By the end of 2014, a total of 15,782 dialysis patients were receiving treatment in 187 dialysis centers in the Kingdom of Saudi Arabia, 14,366 of them treated by hemodialysis (HD) and the remaining 1416 by peritoneal

dialysis (PD) [3]. The correlation between physical inactivity and poor physical and social outcomes is well established for patients presenting with CKD [4]. Compared with other populations, these patients exhibit reduced physical activity in association with metabolic acidosis, inflammation, and malnutrition, which in turn can induce reduced neuromuscular functioning, reduced exercise tolerance, and reduced cardiorespiratory fitness [5, 6]. Also, we should consider behavioral and pathophysiological factors, such as muscle mass or anemia, and logistical factors, such as time spent on dialysis and traveling to the clinic, as all these factors may contribute to the worsening of physical activity [7].

It is well known that exercise therapy programs lead to an improvement in the functional capacity and life quality of CKD patients due to a positive effect on skeletal and cardiac muscles as well as improved vascular health. Therefore, regular physical activity is strongly recommended for CKD patients [8, 9].

Patients presenting with CKD and their relatives experience different kinds of stress during the duration of their illness and treatment because of the chronicity of the disease and its long-term treatment. Patients report discomfort and disruption in life as they spend hours in dialysis treatments. CKD also stresses the relatives because the treatment is lifetime and because of the financial costs of the treatment [10].

Methods

SCOPUS, CINAHL, Science Direct, Web of Science, MEDLINE, ProQuest, Physiotherapy Evidence Database (PEDRO), and Google Scholar were searched without restrictions regarding language or the year of publication. The keywords “exercise training,” “quality of life,” “functional capacity,” and “CKD patient” were used to search from 2010 until December 2020. The screening for eligibility was conducted using the Rayyan QCRI software for systematic reviews [11].

Three independent reviewers (AAI, OWA, and MRA) assessed titles and abstracts of the trials identified by the search against the eligibility criteria (Table 1). All the articles considered potentially eligible were obtained in full text, and additional manual screening of reference lists of the eligible studies was performed. The exclusion criteria for this

study included studies based on animal data, studies including subjects who were healthy in experimental settings, and study designs other than RCT such as quasi-experimental, systematic review, case studies, and reports.

The quality of the included studies was assessed using the PEDro scale [12]. Three authors (AAI, OWA, MRA) rated the included studies using the PEDro scale, with any conflict being resolved by two authors (HMH and WKA). The following classification was used for rating the methodological quality: a PEDro score of < 4 indicated poor quality, a score of 4–5 indicated fair quality, a score of 6–8 indicated good quality, and a score of 9–10 indicated excellent quality [13]. The methodological quality of the studies was assessed according to the criteria of the PEDro scale 10, which scores 11 items, namely: (1) eligibility criteria, (2) random allocation, (3) hidden allocation, (4) baseline comparability, (5) blind subjects, (6) blind therapists, (7) blind assessors, (8) proper follow-up, (9) intent to treat analysis, (10) group comparisons, and (11) point estimates and variability. Items are scored as present 1 or absent 0, generating a maximum sum of 10 points, and the first item is not counted. For the interpretation of results, we used the Modified Sackett Scale to determine the level of evidence for each outcome [14].

Results

The initial search of all engines resulted in a total of 130 studies: Scopus “27”, Science direct “25”, PEDro “10”, Medline “23”, CINAHL “10”, Web of Science “10”, Google Scholar “5”, and ProQuest “20”. After filtering the articles against the eligibility criteria, 13 trials were included in the review [15–27]. The selection process of the studies is completely described in the flowchart of Fig. 1. The final included trial had a total of 619 patients presenting with CKD, both sexes included, aged ≤ 80 years old. The characterization of the sample, exercise programs, and the main outcomes are illustrated in Table 2. The studies were arranged in descending order according to the scores in the PEDro score. The quality of the selected studies according to the PEDro scale was fair and good: three studies were of good quality [18, 19, 24] with the level of evidence 1b (Moderate) based on the Modified Sackett Scale, and the other ten studies were fair [15–17, 20–23,

Table 1 The inclusion criteria of the study

Design	Randomized controlled trials (RCTs). Published from 2010 until December 2020 in English language
Participants	Applied on single or both genders of age ≤ 80
Intervention	Any exercises training (aerobic, resisted ex and respiratory ex)
Out come measures	quality of life using scales of Quality of LifeQOL 36 or 1.3 functional capacity through the 6-min walk test or shuttle walk test
Comparison	Exercises training (aerobic, resisted ex and respiratory ex) versus control

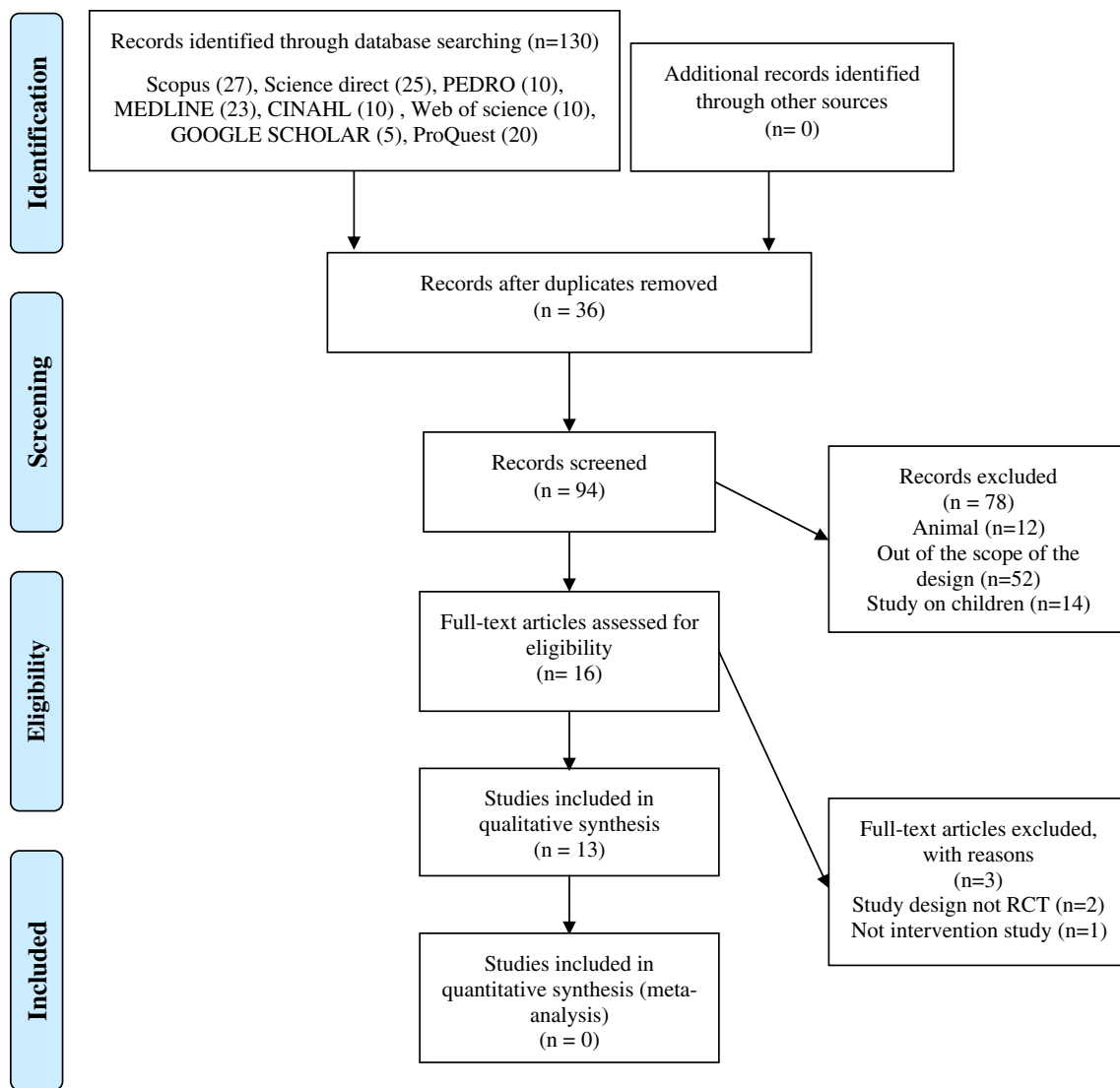


Fig. 1 PRISMA flow diagram of studies through the review [7]

25–27] with a level of evidence 2b (Limited). Regarding the intervention in the selected studies (aerobic, resisted, and respiratory exercises) [15–27], the frequency ranged from 3 to 4 sessions per week for the period ranging from 8 to 24 weeks. The exercise protocol was carried out for HD patients during dialysis in eleven studies [17–27] and for non-dialysis day in one study [15]. Further, in one study, exercise was conducted for a non-dialysis dependent patient presenting with CKD [16] (Table 3).

Quality of life was assessed in eleven studies from the included trials [16, 17, 19–27] by applying the Short Form Health Survey (SF-36) and the QOL-SF 1.3 questionnaire, both of which measured quality of life in chronic renal patients. Functional capacity was measured in 12 studies from the included trials using the Six-Minute Walk Test

[15–18, 20–27] and the Shuttle Walk Test (ISWT) in one study [19].

Marchesan et al. and Fernandes et al. [18, 24] adopted the same strategy of treatment (aerobic exercise versus control with no exercise). The intervention was done during the dialysis session, and the result showed significant improvement in exercise capacity using the Six-Minute Walk Test (see Table 4), based on the weighted mean difference (95% CI) and the overall effect ($Z=3.59, p=0.003$) of the aerobic exercise vs no exercise on the Six-Minute Walk Test.

Abdelaal and Abdulaziz and Rosa et al. [15, 27] performed the same treatment protocol (aerobic exercise vs resisted exercise). The intervention was conducted during the dialysis session, and the result showed significant improvement in the exercise capacity using the Six-Minute

Table 2 Published exercise interventions in chronic kidney disease patient (June 2010–December 2020)

References	Sample	Age	Diagnosis	PEDRO SCALE	Exercise protocol	Measurement	Main results
Figueiredo et al. [19]	37	50–60	HD	8	G1 IMT at 50% P _{Imax} G2 low intensity AT G3 AT + IMT 3time /week for 24 weeks In the first 2 h of HD	MIP Shuttle Walk Test (ISWT) Lower limbs strength Kidney Disease Quality of Life (KDQOL-SF) Inflammatory biomarkers	Improved all measurement MIP Shuttle Walk Test (ISWT) Lower limbs strength Kidney Disease Quality of Life (KDQOL-SF)
Fernandes et al. [18]	39	> 18	HD	7	G1 Treatment group on cycle ergometer Attended 24 training sessions, three times a week, during the intradaylytic period. Training intensity Was between 50 and 70% of maximum heart rate G2 control group no trained	6MWT Pimax and Pemax FVC, (FEV1), (PEF)	A significant difference was observed between groups in FVC, (FEV1), (PEF), and Borg score and distance covered in the 6-minute walk test
Marchesan et al. [24]	22	20–60	HD	6	G1 (control, <i>n</i> = 11) G2 Intervention group (<i>n</i> = 11) aerobic exercise, strength training, and stretching) during HD, three times/week, for 4 months	6MWT, respiratory muscle strength (RMS) testing, chair-stand test (CST), and abdominal Strength test. The SF-36 was used to evaluate QoL	Improvement of functional capacity, respiratory muscle strength and abdominal Strength and QoL
Pellizzaro et al. [26]	39	18–70	HD	5	G1: RMT G2: PMT G3: Control no exercise 30 sessions/10 weeks In the first 2 h of HD	Pimax and PEmax Spirometry FVC 6MWT QoL questionnaire The KDQOLSF 1.3 Blood hematocrit and hemoglobin, and Serum levels of urea, creatinine, potassium, phosphorus, high sensitivity C-reactive protein (hsCRP), and albumin	Significantly improved functional capacity, QoL, P _{Imax} , P _{Emax} FVC, biochemical and inflammatory markers with RMT and PMT. Than control
de Lima et al. [17]	32	18–75	HD	5	G1: control on dialysis only G2: strength ex, (40% of 1RM) of ankle joint G3: aerobic ergometer bicycle Ex 3 day/week, in the first 2 h of HD for 8 weeks	Respiratory muscular strength, pulmonary function, functional capacity (6MWT), blood biochemistry, and quality of life (KDQOLSF 1.3)	Improvement of the maximal inspiratory pressure (MIP), number of steps achieved (NSA), and quality of life (QoL) in the trained groups

Table 2 (continued)

References	Sample	Age	Diagnosis	PEDRO SCALE	Exercise protocol	Measurement	Main results
Frith et al. [20]	41	60–70	HD	5	G1 intervention group (resistance and endurance training exercises. 4/week G2 control group: no ex	Biochemical analyses (Hemoglobin, albumin, cholesterol, C-reactive protein) Medical Outcomes Study Short Form (SF-36 questionnaire) Hospital Anxiety and Depression Scale (HADS) Sit-to-Stand-to-Sit Tests (STS) (6MWT) Timed Up and Go Test (TUG) Dialysis adequacy (Kt/V) Timed Up and Go test Six-Minute Walk Test The Medical Outcomes Study 36-Item Short-Form The Hospital Anxiety and Depression Scale (HADS)	The combined endurance-resistance training program had a beneficial effect on physical capacity and quality of life in chronic hemodialysis patients
Frith et al. [21]	53	60–80	HD	5	G1 Intervention group (listening to Holy Qur'an recitation in combination with an endurance-resistance exercise program) G2 Control group: endurance-resistance exercise program only on days 1, 3, 5, and 7 of the week /24 week dialysis on day 2,4,6	Final measurements were significantly higher in the intervention group than in the control group for all measured parameters,	
Rosa et al. [27]	52	50–70	HD	5	G1 received strength exercises in 2 sets of 15–20 repetitions, in a repetition maximum training zone regime, thrice a week for 12 weeks, during hemodialysis G2 control group received a sham-exercise with active mobilization of the arms and legs without load and progression	Body composition using dual-energy X-ray absorptiometry (DXA), Strength using handgrip dynamometry (HGS), Repeated sit-to-stand test (STT), 6-min walk test, Flexibility The SF-36 questionnaire (quality of life (QoL) were assessed at baseline and at 12 weeks	All measured parameter are significantly improved in PRT group than control except Walking capacity, HGS and QoL were not Different between the groups
Aoike et al. [16]	40	18–70	NDD-CKD	5	G1 exercise group home-based group (aerobic exercise –mild and moderate intensity) G2 center-based exercise group G3 control group no exercise 24 week	cardiopulmonary exercise test QoL using (SF-36) 6 min walk test	All cardiopulmonary parameter and functional capacity improved in both exercise groups No changes in QOL in all groups
Lazarus [23]	150	20–70	HD	5	G1 intervention group (aerobic exercise during dialysis) G2 control group (on regular care)	Kidney Disease Quality of Life- Short form (KDQOL-SF)	The education and exercise intervention had a positive effect on the physical and mental health wellbeing of patients with ESRD

Table 2 (continued)

References	Sample	Age	Diagnosis	PEDRO SCALE	Exercise protocol	Measurement	Main results
Abdelaal and Abdulaziz [15]	66	35–45	HD	5	G1 aerobic exercise training group (AETG), G2 resistance exercise training group (RETG), G3 control group (CG)	Physical performance by (6-min walk test *6MWT*) Functional balance by Borg balance scale (BBS)	Both groups have significant improvement But aerobic exercise group more higher
Jamshidpour et al. [22]	28	HD	HD	5	G1 control (no exercise) G2 exercise training group performed combined aerobic and resistance exercise training at moderate intensity (11–15/20 on the Borg scale) during hemodialysis treatment, three times a week for 8 WK	(6MWT), HR-QoL by the Short Form Health Survey (SF-36), lower limb muscle strength measured using a hand-held Digital Dynamometer	6MWT distance increased significantly in the exercise training group No significant change in QoL and in muscle power
Nilsson et al. [25]	20	20–57	HD	5	G1 HIIT G2 MICT (two times a week within 22 weeks) G3 usual care	Peak oxygen uptake (VO2peak), (6MWT), a HRQoL questionnaire	Two of the three patients increased VO2peak by 46% and 53%, respectively. Three of the five patients in the MICT group increased their VO2peak by 6%, 18% and 36%, respectively

RCT randomized control study/CKD

HD hemodialysis, G group, RMT respiratory muscle training, PMT peripheral muscle training, QoL quality of life, IRM one repetition maximum, NSA number of steps achieved, VREP virtual reality exercise program, PRT progressive resisted training, NDD-CKD non-dialysis-dependent patients with chronic kidney diseases, IMT inspiratory muscle training, P_{max} maximum inspiratory pressure, P_{emax} maximum expiratory pressure, forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), and peak expiratory flow (PEF). AT aerobic training, MIP maximum inspiratory pressure

Walk Test (see Table 4). It discussed the weighted mean difference (95% CI) and the overall effect ($Z=9.18$, $p<0.001$) of the aerobic exercise vs resisted exercise on the Six-Minute Walk Test (Table 5).

Frih et al. and Jamshidpour et al. [20, 22] adopted the same strategy of treatment (combined resisted aerobic exercise vs no exercise). The intervention was carried out during the dialysis session, and the result showed significant improvement in the exercise capacity using Six-Minute Walk Test, see Table 4, discussing the weighted mean difference (95% CI) and the overall effect ($Z=6.19$,

$p<0.001$) of the combined resisted aerobic exercise vs no exercise (Table 6).

Discussion

The prevalence of CKD has increased dramatically. CKD has been associated with many complications and a high mortality rate [28]. Functional capacity is often severely impaired in CKD patients because of the disease’s side effects and its complications [29]. Reduction in functional capacity is one

Table 3 PEDro scores for articles included in the systematic review with CKD-treated population

Author/year	PEDRO SCALE											TOT score
	1	2	3	4	5	6	7	8	9	10	11	
Figueiredo et al. [19]	1	1	1	1	0	0	1	1	1	1	1	8
Fernandes et al. [18]	1	1	1	1	0	0	1	1	0	1	1	7
Marchesan et al. [24]	1	1	0	1	0	0	0	1	1	1	1	6
Pellizzaro et al. [26]	1	1	0	1	0	0	0	1	0	1	1	5
de Lima et al. [17]	1	1	0	1	0	0	0	1	0	1	1	5
Frih et al. [20]	1	1	0	1	0	0	1	0	0	1	1	5
Frih et al. [21]	1	1	0	1	0	0	1	0	0	1	1	5
Rosa et al. [27]	1	1	0	1	0	0	0	0	1	1	1	5
Aoike et al. [16]	1	1	0	1	0	0	0	1	0	1	1	5
Lazarus [23]	1	1	0	1	0	0	0	0	1	1	1	5
Abdelaal and Abdulaziz [15]	0	1	0	1	0	0	1	1	0	1	1	5
Jamshidpour et al. [22]	1	1	0	1	0	0	1	1	0	0	1	5
Nilsson et al. [25]	0	1	1	1	0	0	1	0	1	0	0	5

Table 4 Weighted mean difference (95% CI) of effect of aerobic exercise vs no exercise on 6 min walk test

Study	Aerobic exercise G			No exercise G			Weight (%)	Std. mean difference IV, fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Marchesan et al. [24]	486.4	62.7	11	457.6	64.2	11	41	0.44 [– 0.41, 1.28]
Fernandes et al. [18]	386.9	19.38	20	325.0	59.8	19	59	1.38 [0.67, 2.09]
Total (95% CI)			31			30	100	0.99 [0.45, 1.54]
Heterogeneity: $\chi^2=2.80$, $df=1$ ($P=0.09$); $I^2=64\%$								
Test for overall effect: $Z=3.59$ ($P=0.003$)								

Table 5 Weighted mean difference (95% CI) of effect of aerobic exercise vs resisted exercise on 6-min walk test

Study	Aerobic exercise G			Resisted exercise G			Weight (%)	Std. mean difference IV, fixed, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Abdelaal and Abdulaziz [15]	425.0	21.49	20	366.86	17.47	21	97.9	58.14 [46.12, 70.16]
Rosa et al. [27]	469.42	169.19	24	526.45	126.15	28	2.1	– 57.03 [– 139.28, 25.22]
Total (95% CI)			44			49	100.0	55.73 [43.84, 67.63]
Heterogeneity: $\chi^2=7.37$, $df=1$ ($P=0.007$); $I^2=86\%$								
Test for overall effect: $Z=9.18$ ($P<0.001$)								

Table 6 Weighted mean difference (95% CI) of effect of combined resisted aerobic exercise vs no exercise on 6-min walk test

Study	Combined resisted aerobic exercise G			No exercise G			Weight (%)	Std. mean difference IV, fixed, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Frih et al. [20]	480.5	31.9	21	415.6	36.3	20	92.2	64.90 [43.94, 85.86]
Jamshidpour et al. [22]	338.9	95.6	15	291.18	97.9	13	7.8	47.78 [- 24.14, 119.70]
Total (95% CI)			36			33	100.0	63.56 [43.44, 83.68]
Heterogeneity: $\chi^2=0.20$, df = 1 ($P=0.65$); $I^2=0\%$								
Test for overall effect: Z = 6.19 ($P < 0.0001$)								

of the important complaints of dialysis patients, manifested by decreased exercise tolerance and reduction of daily life activities. Both the HD procedure and uremic myopathy are associated with muscle protein breakdown, affecting peripheral and proximal muscles with a strong impact on overall physical capacity [30].

The outcomes of the included studies showed that exercise training has a positive effect on the functional capacity and quality of life of CKD patients. Intradialytic exercise training has been shown to improve dialysis efficacy by increasing blood flow and perfusion of the muscle tissue and enlarging the surface area, which diffuses greater flux in circulating toxins and urea from the muscle to circulation and removal by dialysis [31, 32]. This is in agreement with Huang et al.'s [33] systematic review that showed that different types of exercise for more than 8 weeks can effectively improve quality of life in CKD patients on dialysis.

The study conducted by Ouzouni et al. [9] established that intra-dialytic resistance training exercise resulted in a significant improvement in physical functioning. It was shown that patients under dialysis can participate safely in a resistance training program and that there is no hemodynamic and musculoskeletal complication as a result of the exercise program. This improvement can be attributed to the functional, morphological, and neural adaptations of the skeletal muscles for resistance training. However, other studies showed a decrease in the walking capacity and have not observed any statistically significant increase in the Six-Minute Walk Test after exercise intervention [34, 35].

Two studies were conducted by Fernandes et al. and Marchesan et al. to analyze the effects of physical training (PT) using aerobic training on the physical fitness of patients undergoing HD, and revealed significant improvement in functional capacity post-treatment in the experimental group using the Six-Minute Walk Test. Further, QoL was measured by Marchesan et al. and improvement was observed in the study group [18, 24].

Studies by Abdelaal and Abdulaziz [15], and Rosa et al. [27] were conducted to analyze the effects of physical

training (PT) on the functional capacity of HD patients. They revealed significant improvement in functional capacity post-treatment in the experimental group using the Six-Minute Walk Test; however, QoL measured by Rosa et al. [27] revealed no difference between the study groups. This is in agreement with the study of Headley et al. [36] who showed a significant improvement in the distance measured with the Six-Minute Walk Test after training CKD patients.

One of the explanations for the significant gain in functional capacity was the use of a combined aerobic and strength training program. This suggests that impairment of functional capacity may be decreased by the gain of muscle strength and improved muscle atrophy, and has beneficial effects on overall work performance [37].

The studies carried out by Frih et al. [20] and Jamshidpour et al. [22] using PEDro score 5 assessed the combined resisted aerobic exercise vs. no exercise during the dialysis session and found a significant improvement in the exercise capacity using the Six-Minute Walk Test.

QoL was measured using a short form (SF-36 questionnaire). Frih et al. [20] revealed a significant improvement in the physical and mental components after 4 months of training. On the other hand, Jamshidpour et al. [22] found neither any significant changes in any of the eight generic subscales of HRQoL nor in the exercise training group or controls following an 8-week study, possibly due to the duration of the study and the characteristics of the selected patients. These results are in line with the study by Wu et al. [38], which showed that combined aerobic and resistance exercise had no significant effect on all the domains of QoL, physical or mental. This contradicts the Cochrane systematic review results by Heiwe and Jacobson [39] which concluded that regular exercise can improve QoL in CKD patients.

The only study in our investigation that used home-based versus center-based aerobic exercise in non-dialysis dependent patients with CKD (NDD-CKD) was carried out by Aoike et al. [16] using the Six-Minute Walk Test for measuring functional capacity, and QoL (SF-36) questionnaire for measuring QoL. The results of this study revealed

significant improvement in the Six-Minute Walk Test after 12 weeks, and the duration was further increased after 24 weeks in both exercise groups. No changes were found in the control group, and this improvement was maintained after 24 weeks [16]. It was also documented that aerobic exercise training with low-intensity provides efficient influences on QoL, psychological status, and physical performance in CKD patients [40].

There was limited data for NDD-CKD patients, which showed that these patients had better QoL scores than the patients on dialysis, possibly due to less impaired physical capacity and better clinical condition with fewer complications [36, 41, 42]. The findings of our systematic review are in agreement with the meta-analysis of Heiwe and Jacobsen, published in 2011 [39] and updated in 2014 [43]. They found a significant improvement in the various types of exercise for CKD patients, physical fitness, walking capacity, muscular functioning, cardiovascular function, and HRQOL, with stronger evidence for dialysis patients and aerobic exercise programs [43].

Also, our review is in agreement with the systematic review by Barcellos et al. [44] who found significant improvement in physical fitness and QoL after conducting the aerobic exercise in CKD patients under dialysis. These findings indicate that exercise may have multiple benefits for the functional capacity and QoL of non-dialysis dependent CKD patients who make up the largest part of the CKD population, however, there are still relatively few studies of exercise in this group.

Conclusion

Conducting an exercise training program for CKD patients is feasible and effective, as assessed by a statistically and clinically significant improvement in functional capacity, measured by the Six-Minute Walk Test, and QoL, measured by the QOL-SF questionnaire. Future studies are still needed to concentrate on high-quality evidence and to assess the benefits and adverse effects of exercise in patients presenting with CKD. Further, they will also be able to provide more comprehensive evidence for developing exercise programs.

Acknowledgements This research has been funded by Scientific Research Deanship at University of Ha'il—Saudi Arabia, through project number RG-191348.

Funding University of Ha'il.

Declarations

Conflict of interest The authors have no conflict of interest.

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