Received: 27 July 2023 | Accepted: 29 September 2023

DOI: 10.1111/eci.14105

NARRATIVE REVIEW

WILEY

Physical exercise in kidney disease: A commonly undervalued treatment modality

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Abstract

Background: Physical inactivity has been identified as a risk factor for multiple disorders and a strong association exists between chronic kidney disease (CKD) and a sedentary lifestyle. Even though physical activity is crucial in the development and progression of disease, the general focus of the current medical practice is the pharmacological perspective of diseases with inadequate emphasis on lifestyle intervention.

Methods: In this narrative review we explain the pathophysiological mechanisms underlying the beneficial effects of physical exercise on CKD in addition to discussing the clinical studies and trials centred on physical exercise in patients with CKD.

Results: Physical activity influences several pathophysiological mechanisms including inflammation, oxidative stress, vascular function, immune response and macromolecular metabolism. While exercise can initially induce stress responses like inflammation and oxidative stress, long-term physical activity leads to protective countermeasures and overall improved health. Trials in pre-dialysis CKD patients show that exercise can lead to reductions in body weight, inflammation markers and fasting plasma glucose. Furthermore, it improves patients' functional capacity, cardiorespiratory fitness and quality of life. The effects of exercise on kidney function have been inconsistent in these trials. In haemodialysis, peritoneal dialysis and kidney transplant patients exercise interventions improve cardiorespiratory fitness, walking capacity and quality of life. Combined training shows the best performance to increase peak oxygen uptake in haemodialysis patients. In kidney transplant recipients, exercise improves walking performance, quality of life and potentially arterial stiffness. However, exercise does not affect glucose metabolism, serum cholesterol and inflammation biomarkers. Long-term, adequately powered trials are needed to determine the long-term feasibility, and effects on quality of life and major clinical outcomes, including mortality and cardiovascular risk, in all CKD stages and particularly in kidney transplant patients, a scarcely investigated population.

Conclusion: Physical exercise plays a crucial role in ameliorating inflammation, oxidative stress, vascular function, immune response and macromolecular metabolism, and contributes significantly to the quality of life for patients with CKD, irrespective of the treatment and stage. Its direct impact on kidney function remains uncertain. Further extensive, long-term trials to conclusively determine the effect of exercise on major clinical outcomes such as mortality and cardiovascular risk remain a research priority.

KEYWORDS

cardiovascular disease, chronic kidney disease, diabetes mellitus, disease, exercise, fitness, health, inflammation

1 | INTRODUCTION

Physical inactivity has been identified as a risk factor for multiple disorders including pre-diabetes and diabetes mellitus, hypertension, dyslipidaemia, metabolic syndrome, non-alcoholic fatty liver disease, osteoporosis and osteoarthritis, cardiovascular and cerebrovascular diseases, various types of malignancies and dementia.[1] Although there is no universally accepted definition for being physically inactive, it is commonly defined as physical activity levels less than those required for optimal health status.[1] Even though physical activity has a fundamental role in the development and progression of disease status, the general focus of the current medical era is the pharmacological perspective of diseases with inadequate stress on lifestyle intervention.

Chronic kidney disease (CKD) is among the top 10 leading causes of mortality among the adult population globally affecting approximately 15% of the adult population in the United States and more than 500 million individuals globally.[2] Irrespective of the underlying aetiology, CKD imposes a high disease burden with an estimated 35.8 million disease-adjusted life years in 2017.[3] Epidemiological studies indicate a strong association between CKD and sedentary life by the demonstration of more than 40% of CKD patients not exercising at all.[4]

In this narrative review, we delineate the pathophysiological mechanisms underlying the beneficial effects of physical exercise on CKD, then we discuss the clinical studies and trials centred on physical exercise in patients with CKD.

2 | THE PATHOPHYSIOLOGICAL PERSPECTIVE

Physical inactivity has been identified as a risk factor for various conditions while multiple hypotheses regarding the underlying pathophysiological role of physical exercise in the development and progression of disease status have been postulated (Figure 1). Evidence derived from multiple studies suggest that exercise leads to favourable effects on inflammation, metabolism and cardiovascular health in individuals with kidney disease.[5]

2.1 | Inflammation

The effects of exercise on inflammatory biomarkers are widely being evaluated in pre-clinical and clinical studies (Box 1). Serum interleukin (IL)-6 levels are upregulated following physical exercise by the duration and intensity of exercise.[6–8] Moderate-level physical exercise has been shown to result in a 16-fold increase in IL-6 mRNA levels in human skeletal muscle cells and a 20-fold increase in serum IL-6 levels while such changes may be attenuated via antioxidant agents including vitamin C and E.[9] Moreover, elderly individuals show an amplified IL-6 release in response to exercise.[10] Even though IL-6 has a wide range of pro-inflammatory activity in the immune system including the activation of humoral and cellular immunity cells and secretion of acute phase reactants including C-reactive protein (CRP), IL-6 also has considerable anti-inflammatory properties.[11–13] The monocytes/macrophage-derived IL-6 in response to the nuclear factor-kappa B signalling pathway has a wide range of pro-inflammatory roles in humans while muscle-contraction derived IL-6 in response to the calcium/nuclear factor of activated T cells and glycogen/p38 mitogen-activated protein kinase pathways has anti-inflammatory roles.[14] Such anti-inflammatory properties of physical exercise have been validated in a model of 'low-grade inflammation' in which the immune response in healthy subjects to the administration of low doses of Escherichia coli endotoxin is evaluated.[11] The two-to-three-fold increase in serum tumour necrosis

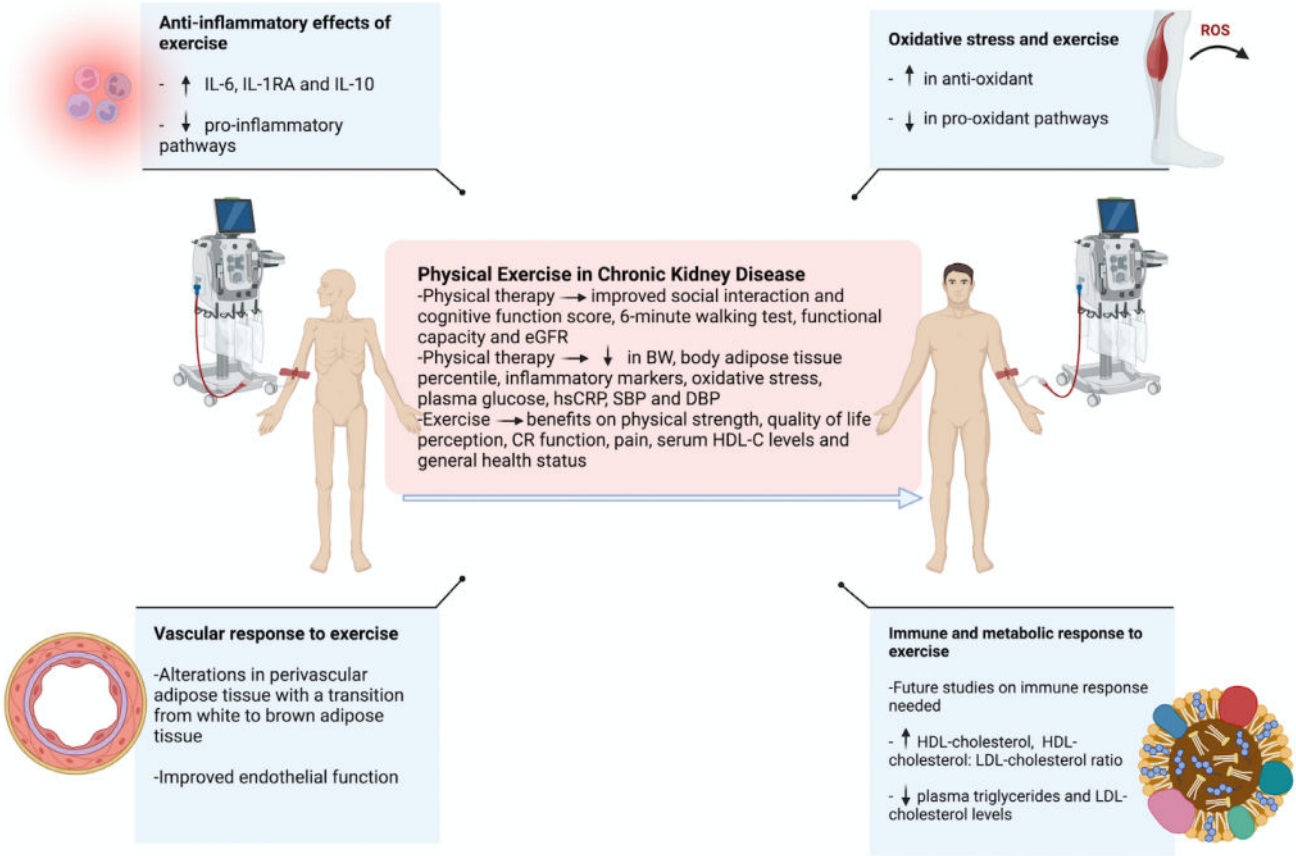

FIGURE 1 The effects of physical exercise on inflammation, oxidative stress, cellular metabolism and vascular functions in CKD patients. BW, body weight; CR, cardiorespiratory; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; IL, interleukin; IL-1RA, interleukin-1 receptor antagonist; LDL, low-density lipoprotein cholesterol; ROS, reactive oxygen species; SBP, systolic blood pressure; TNF-α, tumour necrosis factor alpha.

factor-alpha (TNF-a) levels in response to the administration of endotoxin observed in resting participants is attenuated in subjects following 3 h of ergometer cycling exercise.[11] Mimicking such attenuation via the administration of continuous IL-6 infusion illustrates the central pathophysiological role of IL-6 in a physical exercise-mediated anti-inflammatory state.[11]

Elevated serum muscle contraction-derived IL-6 levels lead to the upregulation of soluble TNF-α receptors, which behave as decoy receptors.[15] Moreover, two major anti-inflammatory molecules, namely IL-1 receptor antagonist and IL-10, that inhibit the activity and production of IL-1β, TNF-α, macrophage inflammatory protein-alpha and IL-8 decrease significantly following physical exercise.[16,17] The pathophysiological role of IL-6 following physical exercise is not limited to such direct effects. Elevated serum IL-6 levels have been proposed to induce pancreatic beta-cell proliferation and enhance peripheral glucose uptake, therefore a decline in peripheral insulin resistance which is a factor involved in long-term low-grade pro-inflammatory status.[18]

IL-1 inhibition has been suggested to ameliorate the functioning of the vascular endothelial without changes in large elastic artery stiffness in individuals with CKD.[19] Furthermore, it has been shown to lead to a decrease in systemic inflammation as well as oxidative stress in the vasculature.[19] The levels of IL-1β in kidney disease patients following exercise have also been investigated. One study evaluated the effect of exercise with virtual reality while undergoing haemodialysis on plasma cytokine levels including IL-1β.[20] The authors showed a significant decrease in IL-1β after undergoing low-intensity exercise via virtual reality in the study population and a significant increase in IL-1β levels in the control group who had not exercised.[20] Further studies are needed to better understand the changes in interleukin levels following exercise in kidney disease patients. Given that uraemia is linked with a dysfunctional immune system

BOX 1 Exercise and inflammation: The changes in inflammatory biomarkers following exercise.

The effects of exercise on inflammatory biomarkers are widely being evaluated in pre-clinical and clinical studies:

1. Serum interleukin (IL)-6 levels are upregulated following physical exercise by the duration and intensity of exercise.
2. Two major anti-inflammatory molecules, namely IL-1 receptor antagonist and IL-10 decrease significantly following physical exercise.
3. IL-1β levels potentially decrease during exercise; although C-reactive protein (CRP) levels increase slightly following physical exercise, serum levels of such biomarkers are significantly higher in physically inactive individuals.
4. Two myokines, namely growth differentiation factor 15 (GDF15) and IL-15, have been proposed in the pathophysiological mechanisms underlying the anti-inflammatory state of physical exercise.

There is a clear need for future pre-clinical and clinical studies investigating the effects of physical exercise on inflammation and the immune system in human subjects for a better understanding of the issue.

resulting in both an immunosuppressive environment and an continuous overactivating immune system at the cellular level causing chronic inflammation, elevated levels of exercise can contribute to the reduction of chronic inflammatory markers in CKD, dialysis and transplant patients.[5]

Although CRP levels increase slightly following physical exercise, serum levels of such biomarkers are significantly higher in physically inactive individuals compared to physically active individuals, indicating the distinction between acute and chronic responses to exercise.[21,22]

Two other myokines, namely growth differentiation factor 15 (GDF15) and IL-15, have been proposed in the pathophysiological mechanisms underlying the anti-inflammatory state of physical exercise. GDF-15, a member of the tumour growth factor (TGF)-β superfamily, is upregulated by exercise. This protein decreases appetite and has anti-inflammatory actions that may prevent acute kidney injury and CKD in mice, at least in part through upregulation of the antiaging and anti-inflammatory protein of kidney origin, Klotho.[23,24] IL-15 levels have been shown to increase following weeks of running exercise among mice subjects which appears to be protective against abdominal obesity.[25] Nevertheless, it is yet unclear whether such anti-inflammatory properties of those myokines are also valid in human subjects. There is a clear need for future pre-clinical and clinical studies investigating the effects of physical exercise on inflammation and the immune system in human subjects for a better understanding of the issue.

2.2 | Oxidative stress

The association between physical exercise and oxidative stress has been evaluated by multiple studies over the decades while the first landmark study demonstrating an association between exercise and increased oxidative stress has been published in 1978. According to that study participants performing 60 min of endurance exercise at 50% of VO_2 max exhales higher levels of pentanes which is a biomarker of lipid peroxidation which is reversible with vitamin E supplementation.[26] Later studies conducted by the use of electron spin resonance have indicated the origin of such oxidative stress as contracting muscle fibres.[27,28] Contracting skeletal muscle fibres have been shown to release high amounts of superoxide and hydroxyl radicals.[29,30] The major intracellular site for the formation of reactive oxygen species and therefore oxidative stress appears to be mitochondria.[31,32] Oxygen radicals formed during physical exercise are involved in muscular fatigue, limitation of maximum muscular force, cellular damage, intercellular signalling and adaptive muscle and whole-body responses.[29,33] The adaptive response to oxidative stress during exercise involves the upregulation of antioxidant pathways and enzymes and the downregulation of pro-oxidative pathways and enzymes such as citrate synthase and malate dehydrogenase.[34–36] Multiple studies have illustrated that exercise training has led to upregulation of various antioxidant mechanisms in skeletal and cardiac muscle cells that protect against oxidative stress which is dependent on the duration and intensity of physical exercise.[37–39] Additionally, cellular and tissue damage in response to reactive oxygen species upregulates tissue repair mechanisms and tissue hypertrophy/hyperplasia, depending on the tissue type. Upregulation of superoxide dismutase-2 in cardiomyocytes[40,41] is critical for the cardioprotective effects of physical exercise. To conclude, physical exercise leads to the formation and release of high amounts of reactive oxygen species and therefore oxidative stress, though, long-term physical exercise training leads to counter-regulatory mechanisms protecting against such stress.

2.2.1 | Vascular function

Living an inactive and sedentary life has been associated with worse cardiovascular outcomes and mortality in kidney disease patients both dependant on dialysis and those who are not, with ameliorations in outcomes in subjects being more active.[5,42–44]

Physical exercise has considerable effects on vascular function both at acute and chronic stages through various mechanisms. The beneficial effects of exercise on vascular health include improvement in serum lipid profile and blood pressure, nonetheless, it is not limited to such alterations. Early studies have demonstrated that physical exercise results in a considerable increase in peak reactive hyperaemic blood flow which is mostly attributable to the increase in the diameter of resistance vasculatures, namely large arterioles, rather than an increase in vessel numbers.[45,46] The upregulation of shear stress-mediated nitric oxide production in response to physical exercise is the major pathophysiological mechanism underlying such improvement in vascular functions.[47] Additionally, physical exercise decreases total body and perivascular adipose tissue and M1-type macrophages within perivascular adipose tissue.[48] Such changes are secondary to decreased expression of inflammatory cell adhesion molecules—intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1)—a phenotype switch from M1 to M2 macrophages, and mobilization of regulatory T-cells.[48,49] Increased adiponectin expression, nitric oxide bioavailability and upregulation of adenosine monophosphate-activated protein kinase (AMPK) improve endothelial function.[50] Perivascular adipose tissue comprises white and brown adipose tissue cells, innervated by the autonomic nervous system.[51] In response to exercise, increased sympathetic tone and certain myokines, including irisin, fibroblast growth factor-21 (FGF-21), PR/SET domain 16 (PRDM16) and meteorin-like (metrnl), promote a transition from white-to-brown adipose tissue in rodents studies.[52–54] However, such a white-to-brown adipose tissue transformation has not been confirmed in human subjects.[55] Moreover, physical exercise training results in an increase in the cross-sectional area of conduit arteries and muscular capillary network.[56]

There are a number pathophysiological mechanisms resulting in an elevated risk of cardiovascular disease in kidney disease patients and studies suggest that elevated levels of exercise and physical activity can have a beneficial effect on these patients.[5]

2.3 | Immune response

Long-term physical exercise has been shown to have anti-inflammatory effects as shown by multiple pre-clinical and clinical studies, though, the acute effects of physical exercise may potentially create an 'open-window' period in which immune response to internal and external stimuli is impaired.[57] Such an 'open-window' period hypothesis is based on findings from multiple studies demonstrating the decline in the immune response. During exercise, a decline in the expression of vascular adhesion molecules results in lower recruitment of leucocytes and higher neutrophils, monocytes and lymphocytes, including CD4 or CD8-positive T cells.[58] In contrast to such an increase, serum lymphocyte counts considerably decline at post 1–2 h of physical exercise; however, it is unclear whether such change is an indicator of immunosuppressive status or active surveillance for external stimuli is unclear.[57] Antibody responses, proliferative responses to mitogens and hypersensitivity reactions considerably diminish during exercise. Secretory immunoglobulin A, which is critical in the mucosal immune defence, decreases after physical exercise.[59,60]

Furthermore, intradialytic exercise was suggested to ameliorate the functioning of the nuclear factor erythroid-2-related factor 2 (NRF2) molecule and its associated pathways in mononuclear cells located in the peripheral bloodstream.[5,61] NRF2 was shown to be an important regulator responsible for balancing pro-oxidative and antioxidative defence mechanisms as well as playing a central role in vascular aging and calcification and cellular senescence.[62] Therefore, nuclear-factor Kappa B signalling and resultant cytokine synthesis responsible inflammation has been suggested to be impaired.[5]

On the other hand, moderate-intensity exercise improves neutrophil adherence, chemotaxis, phagocytosis, oxidative burst and degranulation, whereas high-intensity exercise depresses such functions, except leucocyte degranulation and chemotaxis, which remain unchanged.[63] However, most studies are pre-clinical. Detailed studies addressing physical exercise's short-term and long-term impact on the immune system are needed, given the large differences between rodent and human immune responses.

2.4 | Metabolism

Carbohydrates, predominantly glucose, are the major energy source during short-term intense physical activity. At the same time, lipids are the main source during prolonged exercise periods or low-to-moderate-intensity physical exercises.[64] Trained subjects can use higher proportions of lipids during physical exercise than non-trained counterparts and faster normalization of serum levels of lipid metabolites after the exercise.[65,66]

Physical exercise has anti-atherogenic effects. Three to five days per week of moderate-intensity training for more than 6 months results in increased high-density lipoprotein (HDL)-cholesterol and HDL-cholesterol: low-density lipoprotein (LDL)-cholesterol ratio and in decreased plasma triglycerides and LDL-cholesterol levels.[67,68] These changes are observed in healthy subjects and patients with ischaemic heart disease, diabetes mellitus or CKD.[69] Moderate-intensity exercise increases ApoA1 levels and decreases ApoB levels.[70,71]

CKD has been associated with premature and accelerated aging as well as muscle wasting, frailty, vascular disease and systemic inflammation.[62] Initial studies have suggested that myostatin levels in the serum are elevated with increasing age, especially highest in physically frail elderly females, and are inversely correlated with the mass of skeletal muscle.[72,73] However, further studies have shown contradicting findings and have failed to report differences in myostatin levels based on age.[73–75] Further studies are needed to understand this association. Nevertheless, as the kidneys progressively fail sarcopenia becomes more prevalent and is related to increased morbidity and mortality.[76] In one study, the impact of 12 months of exercise on myostatin which negatively regulates muscle growth, muscle mass and sarcopenia has been evaluated.[76] Among 151 non-dialysis kidney disease patients randomly divided into strength or balance together with endurance training, sarcopenia prevalence was unaffected, leg and whole-body lean mass was elevated in a significant manner in the balance population and showed no change in the strength population.[76] In both populations whole fat mass was lowered and this change was significant. Furthermore, in both of the study populations, levels of myostatin in the plasma were significantly elevated and a significant difference was observed in the strength population.[76] Furthermore, myostatin levels were initially in parallel with muscle mass, however this association gradually declined in the follow-up period of 12 months.[76] This study suggests that exercise is important to help preserve muscle mass and contribute to the prevention of sarcopenia in these patients.[76]

Overall, kidney disease results in dysfunction of multiple systems and interventions focusing on increasing physical activity and exercise may be beneficial to these patients by targeting the aforementioned pathophysiological mechanisms.

3 | CLINICAL STUDIES AND TRIALS ON PHYSICAL EXERCISE IN THE CKD POPULATION

This part of the review is based on recent systematic reviews and clinical trials in CKD patients (also included in some systematic reviews) selected for their clinical relevance and/or because posterior to the systematic reviews. We separately focus on studies in pre-dialysis CKD patients, haemodialysis and peritoneal dialysis patients and kidney transplant patients.

3.1 | Physical exercise in pre-dialysis CKD patients

Several clinical studies investigated the efficacy of various physical exercise training programs in pre-dialysis CKD patients (Table 1). We hereby comment on two reasonably large trials that produced results of particular clinical relevance because the target population (overweight and obesity) in some detail to then discuss two recent meta-analyses.

The first trial, including 111 overweight or obese CKD patients with a 4-month follow-up period, demonstrated that physical therapy alone or in combination with caloric restriction associates with a decline in body weight and body adipose tissue and a reduction in the circulating levels of biomarkers of inflammation and oxidative stress such as serum IL-6 levels and F2-isoprostane levels.[77] The 111 patients were subject to randomization for caloric restriction and aerobic exercise, only caloric restriction, aerobic exercise alone, or usual care. The combined group had a lowering of body weight and fat percentage in a statistical manner compared to the usual care group. In addition caloric restriction also led to this fall significantly; however, this was not seen in the exercise group. The combination as well as the independent interventions resulted in falls in F2-isoprostane and IL-6 levels significantly. However none of the groups had changes that were significant in urine albumin-to-creatinine ratio, VO_2 peak and renal function.[77] The second, published after the most recent meta-analysis was a 3-year trial in 160 stage G3-4 CKD patients testing an articulated lifestyle intervention supervised by a multidisciplinary team, including a nephrologist, nurse practitioner, exercise physiologist, dietitian, diabetes educator, psychologist and social worker. The exercise training component of the intervention consisted of a 2-month personalized, gym-based exercise program which was then continued at home for 34 months.[78] The intervention increased the proportion of patients meeting the physical activity guideline target of 500 MET min/week (29% at baseline and 63% at 3 years). At 12 months, both VO_2 peak (the maximal volume of oxygen uptake) and METs (metabolic equivalent of task) increased significantly in the lifestyle intervention group by 9.7% and 30%, respectively, but did not change in the usual care group. VO_2 peak declined to near baseline levels,

TABLE 1 The studies investigating the effects of physical exercise in non-dialytic chronic kidney disease patients.

Study	Design and follow-up	Results and outcome
Beetham et al. (2019)[92]	Randomized pilot study Follow-up: 12 weeks 14 non-dialysis dependent stage 3–4 CKD patients were randomized to HIIT ($n=9$, 80%–95% PHR) or MICT ($n=5$, 65% PHR).	• No adverse events attributable to exercise training. • Significant time effect for exercise capacity (HIIT = +0.8 ± 1.2; MICT = +1.3 ± 1.6 METs; $p=.01$). • Muscle protein synthesis (HIIT = +0.6 ± 1.1; MICT = +1.4 ± 1.7 au; $p=.04$). • No significant group × time effects for any outcomes.
Hellberg et al. (2019)[93]	Randomized control trial Follow-up: 12 months 151 patients (mGFR: 22 ± 8 mL/min per 1.73 m^2; age 65 ± 14 years) randomized to either balance or strength training.	• There were no treatment differences for any of the primary outcomes measuring physical performance. • The strength and balance groups showed significantly increased effect sizes after 12 months for the following: walking (31 m and 24 m, $p<.001$), the 30-second sit-to-stand test (both: 1 time, $p<.001$), quadriceps strength (right/left: strength 1.2/0.8 kg*m, $p<.003$; balance 0.6/0.9, $p<.01$), functional reach (both: 2 cm, $p<.01$) and fine motor skills (open/closed eyes, right/left, both: between 0.3 and 4 s faster, $p<.05$). • After 12 months, there was a significant treatment difference for albuminuria ($p<.02$), which decreased by 33% in the strength group.
Kirkman et al. (2019)[94]	Randomized controlled trial Follow-up: 12 weeks 36 Nondialysis patients with CKD (means ± SE, age: 58 ± 2 years, eGFR: 44 ± 2) were allocated to an EXT ($n=18$) or control ($n=18$).	• Microvascular function improved after EXT (*week 0* vs. *week 12*, EXT: 87 ± 2% vs. 91 ± 2% and CON: 86 ± 2% vs. 84 ± 3%, $p=.03$). • Brachial artery flow-mediated dilation was maintained after EXT (EXT: 2.6 ± 0.4% vs. 3.8 ± 0.8% and CON: 3.5 ± 0.6% vs. 2.3 ± 0.4%, $p=.02$). • Aerobic exercise improved microvascular function and maintained conduit artery function and should be considered as an adjunct therapy to reduce CVD risk in CKD.
Nixon et al. (2021)[95]	A mixed-methods pilot randomized controlled trial Follow-up: 12-week 35 (16%; 95% CI 12, 22) participants were recruited. 6 were categorized as robust and withdrawn prior to randomization. 15 participants were randomized to exercise and 14 to usual care. 11 (73%; 95% CI 45, 91) participants completed ≥2 exercise sessions/week. 21 Retained participants completed all outcome measures. 8 participants were withdrawn. 15 participated in interviews.	• The adjusted mean group difference in walking speed and SPPB between exercise and usual care groups were: 0.01 metres/second (95% CI −0.07, 0.10) and 0.5 (95% CI −0.9, 1.8), respectively. • The adjusted mean group difference in FESI, POS-S RENAL, SF-12 PCS and SF-12 MCS were: 3.4 (95% CI −3.5, 10.3), −1.4 (95% CI −6.6, 3.7), −3.9 (95% CI −9.3, 1.5) and 0.2 (95% CI −6.2, 6.6), respectively. • Activities of daily living has been evaluated with the Barthel Index questionnaire, and results indicate median Barthel Index scores for the usual care group at baseline and follow-up were 95 (IQR 5; 95% CI 95, 100) and 95 (IQR 9; 95% CI 90, 100), respectively. The median Barthel Index scores for the exercise group at baseline and follow-up were 100 (IQR 8; 95% CI 90, 100) and 100 (IQR 8; 95% CI 90, 100), respectively.
Böhm et al. (2022)[96]	Observational study Median follow-up of 56 months Self-reported physical activity with renal and CV outcomes in high-risk patients aged ≥55 years.	• Physical activity was inversely associated with renal outcomes and CV outcomes. • Moderate activity (at least 2 times/week to every day) was associated with lower risk of renal outcomes and lower incidence of new albuminuria ($p<.0001$ for both) compared to lower exercise levels. • Similar results were observed for those with and without diabetes without interaction for renal outcomes ($p=.097$–.27). • Physical activity was associated with reduced eGFR decline with a moderate association between activity and diabetes status ($p=.05$).

(Continues)

TABLE 1 (Continued)

Study	Design and follow-up	Results and outcome
Weiner et al. (2023)[97]	Multicentre, parallel group, randomized control trial Follow-up: 12 months 99 participants, the mean age was 68 years, 62% were African American, and the mean eGFR was 33 mL/min/1.73 m^2; 59% had diabetes, and 29% had coronary artery disease. Among those randomized to exercise, 59% of exercise sessions were attended in the initial 6 months.	• Exercise was well tolerated without excess occurrence of adverse events. • At 6 months, aerobic capacity was higher among exercise participants (17.9 ± 5.5 vs. 15.9 ± 7.0 mL/kg/min, $p = .03$), but the differences were not sustained at 12 months. • The 6-minute walk distance improved more in the exercise group (adjusted difference: 98 feet [$p = .02$; $p = .03$ for treatment-by-time interaction]). • The exercise group had greater improvements on the Timed Up and Go Test ($p = .04$) but not the Short Physical Performance Battery ($p = .8$).

Abbreviations: AVF, arteriovenous fistula; BFR, blood flow restriction; BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; EXT, exercise training; HD, haemodialysis; HGS, handgrip strength; HIIT, high-intensity interval training; HRQOL, Health-related quality of life; IDEX, intradialytic exercise; IQR, interquartile range; K, Potassium; KT, kidney transplant; MET, exercise capacity; mGFR, measured glomerular filtration rate; MICT, moderate-intensity continuous training; NA, not applicable; NYHA, New York Heart Association; PD, peritoneal dialysis; PHR, peak heart rate; RPE, rating of perceived exertion; RR, renal rehabilitation; RWMAs, regional wall motion abnormalities; SD, standard deviation; SF-36, Short Form 36 Health Survey questionnaire; wks, weeks.

whereas METs remained elevated in the lifestyle intervention group at 24 and 36 months. After 3 years, the distance covered in the 6-minute walk distance and the get-up-and-go test time improved in the intervention group but not in the control group.

The most recent meta-analysis, published in 2020,[79] reviewed randomized trials performed between 2007 and 2018 on physical exercise in CKD patients reporting the effect of exercise on functional capacity, quality of life and the progression of kidney disease. Overall, among the 927 CKD patients (21 trials) included in this meta-analysis, no differences were found in the glomerular filtration rate or proteinuria between the intervention and control groups. Favourable effects of exercise were registered on VO_2, functional capacity, upper limb strength and haemoglobin. Furthermore, in the same meta-analysis, an improvement in the quality of life (by the KDQOL-36 or the SF-36 instruments) was registered.[79] The results of this meta-analysis in part contrast with those of a previous one including 421 patients (13 trials) in the same population. Indeed, in this meta-analysis exercise increased the eGFR, decreased systolic and diastolic BP pressure and the BMI (68). A larger meta-analysis by Gaiqin Pei et al.,[80] included 9 trials in 321 pre-dialysis CKD patients (160 in the exercise arms and 161 in the control arms) and 22 trials in 925 dialysis patients (443 in the exercise arms and 482 in the control arms). The most applied aerobic exercise program in these trials was a moderate intensity (in 15 trials), three times/week frequency (in 22 trials), 30 min duration (in 9 trials) and 3-months follow-up (12 out of 31 trials). Both in pre-dialysis and dialysis patients, significant improvements were observed in the exercise groups as compared to control groups in VO_2 peak, exercise duration, HDL-cholesterol and in three dimensions of quality of life (pain, physical role, general health). No subgroup differences were noted in these outcomes when studies were divided based on exercise training intensity, dialysis treatment or the intervention length.

Trials investigating the health benefits of physical exercise in CKD patients generally included a low number of participants, a relatively short clinical trial follow-up period, various aetiologies of renal failure and differences in the baseline demographic parameters of the participants. Relatively short follow-up periods (3-to-6 months) may not be adequate to capture the effects of exercise on renal function. Furthermore, low study power might have prevented potentially clinically significant outcomes to reach statistical significance. Larger and better designed clinical trials with long-term follow-up are still needed for understanding the effects of physical exercise among pre-dialysis CKD patients.

3.2 | Physical exercise in haemodialysis and peritoneal dialysis patients

The vast majority of physical exercise trials performed so far tested interventions performed during the haemodialysis session and consisting either in aerobic exercise (cycling or walking) or resistance training of some muscular groups against elastic bands or a combination thereof (Table 2). These in-centre programs allow effective, supervised exercise training. On the other hand, promoting therapeutic programs embedded in the actual familial and social context of individual patients, like the home-based

TABLE 2 The studies investigating the effects of physical exercise in haemodialysis patients.

Study	Design and follow-up	Results and outcome
Jeong et al. (2018)[98]	Randomized cross-over study Total $n=12$ Groups: (1) without exercise (control); (2) with 30 min of IDEX performed in the first hour of treatment; (3) with 30 min of IDEX in the third hour of treatment.	• IDEX during first or third hour did not exacerbate haemodynamic instability during treatment regardless of patient's hydrations status. • While there were transient increases in stroke volume, cardiac output, and heart rate during IDEX, intradialytic changes in brachial and aortic blood pressure, cardiac haemodynamics and autonomic function were similar on days with and without IDEX.
Jeong et al. (2019)[99]	Randomized controlled trial Follow-up: 12 months 138 HD patients (average age 58 years) were assigned to control, intradialytic protein or protein plus exercise groups The protein and protein plus exercise groups consumed an oral protein supplement (30 grams of whey) 3 days/week during dialysis $n=44$ control, $n=45$ protein, $n=49$ protein + EXT 117 and 101 patients completed testing at 6 and 12 months.	• No significant differences between groups in shuttle walk test performance from baseline to 12 months. • Trends for improvements in some secondary measures of physical function and strength in the protein and protein plus exercise groups at 6 or 12 months were observed, but these did not reach statistical significance.
Penny et al. (2019)[100]	Single-centre cross-sectional exploratory study Adults on chronic HD participating in a clinical IDEX program 19 HD patients Mean age 57.2 ± 11.8 years, Median dialysis vintage 3.8 years Control visit ($n=19$) Exposure visit ($n=19$).	• Mean number of RWMAs during the control visit was 4.5 ± 2.6, falling to 3.6 ± 2.7 when incorporating IDE (a reduction of −0.95 ± 2.9; $p=.17$). • At peak HD stress, the mean number of RWMAs was 5.8 ± 2.7 in the control visit versus 4.0 ± 1.8 during the exposure visit (a reduction of −1.8 ± 2.8; $p=.01$).
Segura-Orti et al. (2019)[101]	Randomized controlled trial 3 sessions per week Follow-up: 20 weeks 18 dialysis patients who participated in a 16-week intradialysis Combined exercise vs. virtual reality exercise.	• Physical function improved in both groups. • By the end of the 20 wks, function improved as measured through the sit-to-stand-to-sit tests 10 and 60, gait speed, one-leg heel-rise left leg, and the 6-min walk test.
Lin et al. 2021[102]	Randomized controlled trial Follow-up: 12 weeks 64 HD patients were recruited using stratified random sampling. Participants were randomized into an experimental group (EG, $n=32$) or a control group (CG, $n=32$). The EG received a 12 week intradialytic exercise program while the CG maintained their usual lifestyles.	• The results indicated no differences in the dialytic parameters from the baseline between both groups. However, the EG had increased health-related quality of life ($\beta=22.6$, $p<.001$) and reduced depression status ($\beta=-7.5$, $p=.02$) at 12 weeks compared to the CG. Therefore, a 12-week intradialytic exercise regime is safe and effective in improving health-related quality of life and reducing depression status for HD patients.
Perez-dominguez et al. (2021)[103]	Randomized controlled trial Follow-up: 16 weeks Referred sample of 71 patients that suffered end-stage CKD who underwent HD for at least 3 months and had a medical stable condition. 36 participants performed for 16 weeks an intradialytic exercise program lead by the nursing staff of the HD unit and 35 a home-based program supervised by physical therapists of the hospital.	• Nurse-led and home-based exercise interventions produce beneficial effects involving physical function, activity levels and health-related quality of life in patients undergoing HD.

(Continues)

TABLE 2 (Continued)

Study	Design and follow-up	Results and outcome
Silva et al. (2021)[104]	A randomized clinical trial Follow-up: 8 weeks Total of 26 patients with CKD were randomized to the BFR experimental group (EG, $n=12$) and to the non-BFR control group (CG, $n=14$) prior to AVF and underwent isometric exercises for the flexor muscles of the fingers and elbow where the AVF will be performed.	• There were no differences at the end of eight weeks of training between the experimental and control groups [$F_{(1.23)}=0.03$, $p=.96$] regarding the HGS and the forearm circumference [$F_{(1.23)}=0.90$, $p=.76$], however muscle strength [$F_{(1.23)}=189.84$, $p<.001$] and forearm circumference [$F_{(1.23)}=540.90$, $p<.001$] improved between baseline and the results at the end of the program.
Yabe et al. (2021)[105]	Randomized controlled trial Follow-up: 6 months 101 patients who were randomly assigned to intradialytic exercise ($n=51$) or usual care ($n=50$) groups.	• There were statistically significant improvements in Short Physical Performance Battery score (effect size, 0.57; 95% confidence interval, 0.15–1.95) in the exercise group relative to the control group. • There were no statistically significant differences in lower extremity muscle strength or in the 10-m walking speed between the two groups.

Abbreviations: AVF, arteriovenous fistula; BFR, blood flow restriction; BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; EXT, exercise training; HD, haemodialysis; HGS, handgrip strength; HIIT, high-intensity interval training; HRQOL, health-related quality of life; IDEX, intradialytic exercise; IQR, interquartile range; K, potassium; KT, kidney transplant; MET, exercise capacity; MICT, moderate-intensity continuous training; NA, not applicable; NYHA, New York Heart Association; PD, peritoneal dialysis; PHR, peak heart rate; RR, renal rehabilitation; RWMAs, regional wall motion abnormalities; SD, standard deviation; SF-36, Short Form 36 Health Survey questionnaire; wks, weeks.

exercise programs, is an important opportunity for expanding the application of these programs and for patient's empowerment. The walking capacity encompasses cardiorespiratory and muscle endurance, and muscle strength as well as balance and coordination, which is fundamental in daily living in patients with chronic disease and in the elderly.[81] In a net-work meta-analysis by Ferrari et al., published in April 2023 including 39 trials and 3326 haemodialysis patients, only 10 trials were based on home-based training programs.[82] The most analysed outcome was 6-minute walking test (6MWT) (39 studies) followed by systolic and diastolic blood pressure (22 studies) Kt/V (21 studies), VO_2 peak (19 studies), C-reactive protein (15 studies), quality of life for SF-36 physical functioning (11 studies) and SF-36 mental functioning (8 studies).

This analysis showed that combined training (see above) either during haemodialysis (20 trials) or at home (19 trials), was the intervention with the best performance to increase VO_2 peak [mean difference (MD) = 3.94 mL/kg/min; 95% Bayesian confidence interval ($_B$CI), 2.38–5.76] and to reduce diastolic blood pressure (−5.19 mmHg; 95% $_B$CI, −9.35 to −0.96) compared to the usual care group. Inspiratory muscle training was the intervention that most improved the 6MWT distance (70.97 m; 95% $_B$CI, 18.09–129.87) but this intervention was applied in just three studies that allocated only a limited number patient to this intervention ($n=65$) or to control ($n=65$) treatments. C-reactive protein decreased in resistance training (MD = −2.6 mg/L; 95% CrI, −4.97 to −0.33) and aerobic training (MD = −1.4 mg/L; 95% $_B$CI, −3.15 to −0.06). Kt/V improved in aerobic training (MD = 0.11; 95% $_B$CI, 0.02–0.18), and SF-36 physical functioning outcomes improved in resistance training (MD = 10.66 points; 95% $_B$Cl, 1.91–20.22). All intradialytic exercise modalities were of similar benefit to the corresponding home-based ones in improving the outcomes that could be face to face compared. Interventions lasting over 12 weeks improved functional capacity more than shorter interventions. Furthermore, moderate or moderate-to-vigorous intensity training improved functional capacity, whereas mild- or mild-to-moderate-intensity training did not. Thus, both intradialytic training and home-based training improved selected outcomes in haemodialysis patients, with no evidence of the superiority of either intervention over the other.

Another recent systematic review by Battaglia et al.,[83] restricting the analysis on home-based exercise interventions in haemodialysis ($N=691$) or peritoneal dialysis ($n=100$) patients registered an improvement of walking speed in the 6MWT (nine trials; pooled weighted mean differences (WMD): 33.7 m, 95% confidence interval (CI) 22.8–44.5; $p<.001$) and in aerobic capacity as assessed by the VO_2 peak [three trials; pooled WMD: 2.04 mL/kg/min, 95% CI 0.25–3.83; $p=.03$]. These interventions were also associated with improved QoL, as assessed by the Short Form (36) Health (SF-36) score.

Even though evidence accrued so far has not raised safety issues and showed a positive impact of physical exercise programs on physical performance measures, trials with a longer follow-up need to be done to assess the safety, adherence, long-term feasibility and effects on QoL and major clinical outcomes, including mortality and the

risk of cardiovascular events, of intra-dialysis and home-based exercise programs in dialysis patients.

Until now only three trials, two of whom uncontrolled, allotting peritoneal dialysis patients to exercise (43 patients) or control (23 patients) groups were captured in a 2018 systematic review by Thangarasa et al.[84] In these trials there was a tendency for a beneficial effect of physical exercise for some of the outcome measures collected in these trials, including QoL, VO_2 and blood pressure. No new trials were published after this systematic review. Peritoneal dialysis is a treatment modality applied in about 10% of kidney failure patients worldwide.[85] Therefore, trials testing the effects of physical exercise in this population constitutes a research priority. We summarize the studies investigating the effects of physical exercise in peritoneal dialysis patients in Table 3.

TABLE 3 The studies investigating the effects of physical exercise in peritoneal dialysis patients.

Study	Design and follow-up	Results and outcome
Aramrussameekul et al. (2019)[106]	A pretest-posttest design Follow-up: 12 weeks All participants were asked to perform home-based exercise 3 times per week for 12 wks Thirty patients (16 males and 14 females) on CAPD Mean age was 51.6 years (SD ± 11.8) and mean duration of CAPD was 21.5 months (SD ± 19.1).	• When comparing data between the baseline and at the end of the fourth week, systolic and diastolic BP declined significantly ($p < .05$). • Hand, leg and back muscle strength increased; and the SF-36 scores of social functioning, bodily pain, emotional role functioning, and vitality and the total score, increased significantly ($p = .030$, $p = .009$, $p = .001$, $p = .000$, $p = .003$, respectively).
Greenwood et al. (2019)[107]	Observational Retrospective longitudinal study 757 patients (male 54%) (242 haemodialysis patients, 221 kidney transplant recipients, 43 PD patients, 251 non-dialysis CKD patients) were referred for RR 193 events (136 deaths) during the follow-up occurred Age in years mean (SD) = 56.11 (±12.38).	• A total of 43% of referrals were classified as 'completers', and time to event was significantly greater when compared with 'non-completers' ($p = .009$). • Responding to RR was associated with improved event-free survival time ($p = .02$) with Kaplan–Meier analyses and log rank test. • 'Non-completers' of RR had a 1.6-fold [hazard ratio = 1.6; 95% confidence interval (CI) 1.00–2.58] greater risk of a combined event ($p = 0.048$). • 'Improvers' had a 40% (hazard ratio = 0.6; 95% CI 0.36–0.98) independent lower risk of a combined event ($p = .041$).
Uchiyama et al. (2019)[108]	Randomized control trial Follow-up: 12 weeks 47 PD patients were randomly assigned to exercise ($n = 24$) and usual care ($n = 23$) groups Care group age (years) mean ± SD = 63.2 ± 9.5 Exercise group age (years) mean ± SD = 64.9 ± 9.2.	• The distance in incremental shuttle walking test significantly improved in the exercise group compared with the usual care group ($p = .02$). • Among the HRQOL subscales assessed using the Kidney Disease Quality of Life-Short Form questionnaire, kidney disease component summary ($p = .03$), physical role functioning ($p = .01$), emotional role functioning ($p < .01$), and role/social component summary ($p < .01$) significantly improved in the exercise group.
Bennett et al. (2020)[109]	Parallel randomized controlled feasibility study Follow-up: 12 weeks PD patients are randomly assigned to the intervention (exercise; $n = 18$) or control (nonexercise; $n = 18$) group. 10 patients discontinued the study (5 in each arm), resulting in 26 (72%) patients, 13 in each arm, completing the study 10 of 13 (77%) intervention patients were adherent to the exercise program.	• A difference between the treatment groups for the timed-up-and-go test ($p = .04$) and appetite ($p = .04$). • No serious adverse events caused by the exercise program were reported.

Abbreviations: AVF, arteriovenous fistula; BFR, blood flow restriction; BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; EXT, exercise training; HD, haemodialysis; HGS, handgrip strength; HIIT, high-intensity interval training; HRQOL, health-related quality of life; IDEX, intradialytic exercise; IQR, interquartile range; K, potassium; KT, kidney transplant; MET, exercise capacity; MICT, moderate-intensity continuous training; NA, not applicable; NYHA, New York Heart Association; PD, peritoneal dialysis; PHR, peak heart rate; RR, renal rehabilitation; RWMAs, regional wall motion abnormalities; SD, standard deviation; SF-36, Short Form 36 Health Survey questionnaire; wks: weeks.

3.3 | Physical exercise in kidney transplant patients

In kidney transplant patients, low physical activity is associated with higher risk for all-cause and cardiovascular death.[86,87] Physical activity levels in this population is lower than in similar-aged patients with rheumatoid arthritis and osteoarthritis.[87] The studies investigating the effects of physical exercise in kidney transplant patients are shown in Table 4.

In a systematic review by De Smet and Van Craenenbroeck published in 2021 these authors identified 17 randomized trials testing physical exercise interventions in kidney transplant recipients.[88] Twelve trials lasted less than 1 year. Three of these studies focused on walking performance (6MWT). An improvement in the 6MWT after a resistance training intervention, with or without a parallel aerobic training intervention was registered in these trials. In the majority of short-term trials including information on QoL (five out six trials) exercise improved some indices of health-related quality of life irrespective of the type of training or the time after transplantation. In short-term trials, exercise failed to modify glucose metabolism biomarkers (serum glucose, HOMA index), serum cholesterol, inflammation biomarkers (CRP, TNF-alpha and other cytokines). Overall, exercise did not impact BP

TABLE 4 The studies investigating the effects of physical exercise in kidney transplant patients.

Study	Design and follow-up	Results and outcome
Henggeler et al. (2018)[110]	Single-blind, randomized control trial Total of 37 participants were randomized to intensive intervention ($n=19$; individualized nutrition and exercise counselling) or standard care ($n=18$; guideline based 4 dietitian visits).	• Weight increased between baseline, 6 and 12 months (mean ± SD = 78.0 ± 13.7, 79.6 ± 13.0 kg, 81.6 ± 12.9 kg; mean change 4.6% $p<.001$), 82.2 ± 13.4 kg (standard); difference in adjusted means 0.4 kg (95% confidence interval: −2.2 to 3.0 kg); analysis of covariance $p=.7$. • Across the whole cohort, total body protein and physical function (gait speed, sit to stand, grip strength, physical activity, and quality of life) improved. • However, adverse changes were seen for total body fat, HbA1c, and fasting glucose across the cohort.
Roi et al. (2018)[111]	Non-randomized clinical trial Follow-up: 12 months 99 KT recipients were assigned to interventional exercise (Group A, $n=52$) and a usual care (Group B, $n=47$).	• Group A significantly increased maximum workload (+13 W, $p=.0003$), VO_2 peak (+3.1 mL/kg per minute, $p=.0099$), muscular strength in plantar flexor (+12 kg, $p=.0368$), height in the countermovement jump (+1.9 cm, $p=.0293$) and decreased in BMI (−0.5 kg/m^2, $p=.0013$). • HRQOL significantly improved in physical function ($p=.0019$), physical-role limitations ($p=.0321$) and social functioning scales ($p=.0346$). No improvements were found in Group B.
McAdams-Demarco et al. (2019)[112]	Single-arm intervention trial Follow-up: >10 weeks 18 KT candidates were in prehabilitation (75% of enrolled; 17% of eligible) Control = 25.	• By 2 months of prehabilitation, participants improved their physical activity by 64% ($p=.004$) based on accelerometry. • Among 5 prehabilitation participants who received KT during the study, length of stay was shorter than for age-, sex- and race-matched control (5 vs. 10 days; RR = 0.69; 95% CI: 0.50–0.94; $p=.02$).
Serper et al. (2020)[113]	Randomized, controlled trial 61 KT recipients were randomized within 24 months of transplant to: (i) control, (ii) accelerometer or (iii) intervention: accelerometer paired with financial incentives and health engagement questions to increase steps by 15% from baseline every 2 weeks.	• At 3 months, there were no significant differences in weight change across the three arms. • The intervention arm was more likely to achieve ≥7000 steps compared to control with device (OR 1.99, 95% CI: 1.03–3.87).

Abbreviations: AVF, arteriovenous fistula; BFR, blood flow restriction; BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; EXT, exercise training; HD, haemodialysis; HGS, handgrip strength; HIIT, high-intensity interval training; HRQOL, health-related quality of life; IDEX, intradialytic exercise; IQR, interquartile range; K, Potassium; KT, kidney transplant; MET, exercise capacity; MICT, moderate-intensity continuous training; NA, not applicable; NYHA, New York Heart Association; PD, peritoneal dialysis; PHR, peak heart rate; RR, renal rehabilitation; RWMAs, regional wall motion abnormalities; SD, standard deviation; SF-36, Short Form 36 Health Survey questionnaire; wks, weeks.

but improved autonomic control of the heart in the two studies that reported information on this issue. Exercise did not impact graft function and was generally safe in the same trials.

Among long-term (>1 year) trials only two out four trials had sufficient power and scientific quality to produce meaningful clinical information. In the first, a randomized trial by Painter et al.,[89] a home-based aerobic exercise significantly improved ($p = .016$) the prespecified main outcome measure (VO_2 peak) vs. usual care in 167 patients over 11 months follow. The SF-36 Health Status Questionnaire self-reported functioning tended ($p = .06$) to improve alongside in the same trial. No significant effect of exercise was seen on graft function (creatinine levels). In the second, a trial by O'Connor,[90] comparing the long-term (1 year) effects of 3 months aerobic training intervention vs. resistance training and vs. usual care in 60 kidney transplant patients. Forty-two participants completed the trial (aerobic training = 12, resistance training = 10 and usual care = 20). In an analysis adjusting (covariance analysis) for baseline values, age, and time on dialysis pre-transplantation, a significant mean between-group difference in pulse wave velocity of −1.30 m/sec (95% CI −2.44 to −0.17, $p = .03$) between resistance training and usual care groups was evident at 1 year (i.e. 9 months after the end of the intervention). Similarly, in the comparing the aerobic training and usual care groups, there was a mean difference of −1.05 m/sec (95% CI −2.11 to 0.017) of borderline significance ($p = .05$). At 1 year, VO_2 peak was by 2.2 mL/kg/min higher (95% CI 0.37–4.03, $p = .02$) in aerobic training group than in the usual care group while the same parameter in the resistance training group did not differ from that in the usual care group ($p = .40$). No effect of the interventions was registered in body weight or blood pressure.

Both in Painter's and in O'Connor's trials, exercise programs did not impact mortality, graft health and major cardiovascular events in the first year after transplantation. No data regarding the effect of exercise training on the risk of malignancy and infections were reported in these and two additional long-term trials of suboptimal scientific quality (not discussed here). Overall, high-quality trials with long-term follow-up assessments of clinical outcomes—including the core SONG transplantation outcomes,[91] that is, graft health, cardiovascular disease, cancer, infection, life participation and mortality—are eagerly awaited in kidney transplant patients.

No trial testing exercise interventions was published after the systematic review by De Smet and Van Craenenbroeck. Overall, this systematic review produced indirect evidence pointing to the absence of exercise-induced effects on mortality, graft health and major CV events in the first year after transplantation. Arterial stiffness, a surrogate marker of CV disease, improves after training. No data exist regarding the effect of exercise training on the incidence of malignancy and infections in KTRs. Only one study reports on the formal outcome of life participation (i.e. employment rate). Therefore, high-quality RCTs with long-term follow-up assessments of core outcomes are eagerly awaited.

4 | CONCLUSION AND PERSPECTIVES

In the current medical era where the pharmacological perspective of diseases is the major focus without sufficient emphasis on lifestyle interventions, the potential of physical exercise to enhance the lives of CKD patients is significant and this has allowed exercise to become an important component in the management of this patient population. Reductions in inflammation, body weight and fasting glucose levels, along with improved functional capacity and quality of life have been shown as the major beneficial effects of exercise in patients with kidney disease. However, the role of exercise on kidney function itself is still unclear and inconsistent. In the context of haemodialysis, peritoneal dialysis and kidney transplant patients, the potential benefits of exercise, such as increased cardiorespiratory fitness, walking capacity and possibly reduced arterial stiffness, are encouraging. Yet, its effects on metabolic and inflammation biomarkers remain inconclusive. There is a clear need for comprehensive, long-term trials with large sample sizes to definitively determine the safety, adherence, feasibility and impact of exercise on the quality of life and crucial clinical outcomes such as mortality, the risk of cardiovascular events as well as graft health and the incidence of malignancy and infections in kidney transplant recipients.

AUTHOR CONTRIBUTIONS

Contributed substantially to the conception or design of the work: Mehmet Kanbay, Abdullah B. Yildiz, Sidar Copur and Cem Tanriover. Drafted the manuscript: Sidar Copur, Abdullah B. Yildiz and Cem Tanriover. Revision of the manuscript for important intellectual content: Mehmet Kanbay, Francesca Mallamaci and Carmine Zoccali.

ACKNOWLEDGEMENTS

The figure of this review is crafted with the use of app.biorender.com.

FUNDING INFORMATION

This study was not funded by any grant.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

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How to cite this article: Kanbay M, Copur S, Yildiz AB, Tanriover C, Mallamaci F, Zoccali C. Physical exercise in kidney disease: A commonly undervalued treatment modality. *Eur J Clin Invest*. 2024;54:e14105. doi:10.1111/eci.14105