REVIEW ARTICLE

Physical Activity and Exercise in Patients With Coexisting Chronic Kidney Disease and Peripheral Artery Disease: Time to Bridge the Gap?

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Chronic kidney disease (CKD) and peripheral artery disease (PAD) are highly prevalent conditions associated with morbidity, mortality, and health-care costs, particularly when they coexist. Despite advances in pharmacological and interventional therapies, patients with both CKD and PAD have rapid functional decline, higher hospitalization rates, and poor cardiovascular outcomes. In populations with either CKD or PAD alone, exercise training has been shown to improve cardiorespiratory fitness, muscle strength, physical function, and quality of life and is strongly recommended in the guidelines. However, evidence for exercise training in patients with overlapping CKD and PAD remains limited with no randomized controlled trials and only a single observational cohort, suggesting potential benefits of home-based walking programs on renal and cardiovascular outcomes. This narrative review examines the potential benefits of exercise training as a nonpharmacological approach to addressing this therapeutic gap. An ongoing randomized controlled trial, EXACT-CKD–PAD, is expected to provide more definitive evidence in this high-risk population, although further studies will be required to define long-term clinical impact and optimal implementation strategies.

Keywords: exercise training; home-based; cardiorespiratory fitness; muscle strength; QoL

Introduction

CHRONIC KIDNEY DISEASE (CKD) and peripheral artery disease (PAD) are two highly prevalent noncommunicable diseases that contribute substantially to global morbidity, mortality, and health-care costs.

CKD is a progressive and irreversible condition,[1] defined as a decrease in estimated glomerular filtration rate (eGFR < 60 mL/minute/1.73 m^2) or evidence of kidney damage such as proteinuria, hematuria, or abnormalities on renal imaging or biopsy, persisting for at least 3 months.[2] In 2017, CKD affected an estimated 9.1% of the global population, nearly 700 million cases,[3] although early stages often remained undiagnosed. In Italy, the prevalence was 6.3% in 2014, with early stages (G1-G2) predominating.[4]

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CKD also imposes a considerable financial burden. In the United States, Medicare expenditures for CKD in patients over 65 years reached $76.8 billion in 2021, despite a prevalence of only 13.5% in this population.[5] The etiology of CKD is multifactorial,[6,7] with hypertension and type 2 diabetes mellitus accounting for around 40% of cases, followed by glomerulonephritis and autosomal dominant polycystic kidney disease.[8,9] In some patients, however, the cause remains uncertain.[10]

Beyond kidney-specific consequences, CKD is a cardiovascular disease multiplier and is projected to become the fifth leading cause of death worldwide by 2040.[11] Despite this burden, awareness remains limited,[12-15] and referral to nephrology is often delayed until advanced stages, when CKD complications such as anemia, electrolyte disturbances, and bone metabolism disorders are already established.

PAD, in turn, is a common atherosclerotic disorder of the peripheral arteries, most frequently affecting the lower extremities.[16] In 2019, approximately 113 million adults aged ≥40 years were estimated to be affected worldwide, with prevalence increasing with age and higher rates observed in women.[17] The prevalence of PAD is increased in CKD patients, particularly in those with more advanced CKD stages. Although revascularization strategies are generally suitable for CKD patients in a similar fashion to non-CKD patients, few CKD patients undergo these procedures. Notably, while revascularization improves prognosis in PAD patients regardless of baseline eGFR,[18] CKD patients who undergo revascularization are at higher risk of amputations, mortality, reintervention, and perioperative complications.[18]

The disease arises from the progressive accumulation of atherosclerotic plaques, narrowing of arterial lumina, and impaired perfusion of limb muscles. Early in the course, compensatory dilation maintains flow; but once maximal dilation is exceeded, functional obstruction leads to ischemia.[19,20] The clinical manifestations range from intermittent claudication (i.e., pain, fatigue, or discomfort in the calves relieved by rest) to chronic limb-threatening ischemia and acute limb ischemia, as outlined in the 2024 European Society of Cardiology (ESC) guidelines.[21] Anatomical classifications such as Rutherford and Trans-Atlantic Inter-Society Consensus further refine disease staging and inform treatment strategies.[22,23] Some studies have also shown that metalloproteinases (MMPs) are involved in the onset of CKD and, concomitantly, in the development of aortic aneurysms. Notably, elevated MMPs are observed in both CKD and peripheral vascular disease.[24] A possible pathogenic link between these conditions may involve enhanced production of transforming growth factor-β. This, in turn, worsens vascular calcifications, atherosclerosis, and the development of proteinuria in patients with increased MMP levels.[25]

Patients with PAD face markedly increased risks of major adverse cardiac events, cerebrovascular risk, and major adverse limb events.[21] PAD frequently coexists with atherosclerotic disease in other vascular beds, such as the coronary, carotid, and renal arteries,[26] and is strongly associated with CKD.[23] The prevalence of multi-territory disease rises with age, from 0.04% in the 40-50-year age group to 3.6% in those aged 81-90 years.[27]

The intersection of CKD and PAD is clinically significant. Up to one-quarter of patients with CKD are also affected by PAD,[28] and this overlap confers a particularly poor prognosis, with amplified risks of cardiovascular events, functional decline, and premature mortality. Despite pharmacological and interventional advances, residual risk in this population remains high.

In recent decades, lifestyle-based strategies, particularly physical activity and structured exercise programs, have been recognized as effective, first-line interventions in the management of both CKD and PAD. Exercise has consistently been shown to improve mobility, cardiorespiratory fitness, muscle strength, and quality of life (QoL) while also influencing renal and cardiovascular outcomes in patients with CKD or PAD individually. However, evidence regarding patients with overlapping CKD and PAD remains limited.

Against this background, the present narrative review aims to explore the benefits of physical activity and exercise programs as feasible and practical strategies to bridge therapeutic gaps in patients with overlapping CKD and PAD, focusing on current evidence and future directions.

Methods

We searched PubMed, Scopus, and Web of Science for articles published from database inception to October 31, 2025, using combinations of the following keywords and MeSH terms: “chronic kidney disease,” “CKD,” “renal failure,” “peripheral artery disease,” “PAD,” “intermittent claudication,” “exercise,” “physical activity,” “rehabilitation,” “home-based,” “supervised exercise,” and “walking program”. Search strategies were adapted for each database. No language restrictions were applied.

We included randomized controlled trials (RCTs), prospective and retrospective observational studies, systematic reviews, meta-analyses, evidence-based clinical practice guidelines, case reports, and small case series. The main topics of interest were: (1) exercise or physical activity in CKD not on dialysis; (2) exercise or physical activity in asymptomatic and symptomatic PAD; and (3) exercise-based interventions in patients with concomitant CKD and PAD. In addition, we manually screened the reference lists of key articles and recent international guidelines (e.g., Kidney Disease Improving Global Outcomes [KDIGO], European Society for Vascular Surgery, ESC, and American Heart Association/American College of Cardiology

[AHA/ACC]) to identify further relevant publications. When multiple studies addressed the same clinical question, we prioritized high-quality and more recent evidence. We excluded studies conducted in (1) the pediatric population (<18 years of age), (2) in patients on dialysis, and (3) kidney transplant recipients.

Physical Activity and Exercise in CKD Not on Dialysis

Physical inactivity is a common and clinically relevant feature in patients with CKD, with many individuals becoming completely sedentary as CKD progresses.[29]

This physical inactivity is strongly associated with muscle wasting,[30] impaired physical function, reduced cardiorespiratory fitness, and adverse clinical outcomes across all CKD stages, particularly in advanced disease (stages G4 and G5).[31] Beyond musculoskeletal decline, sedentary behavior contributes to progressive cardiovascular and vascular deconditioning,[32] as well as increased fatigue, depressive symptoms, and disability.[33] Within this framework, physical activity and exercise are increasingly recognized as effective nonpharmacological interventions for CKD.[34,35] As such, physical activity and exercise are considered a central component of comprehensive CKD management.[36]

Evidence

Observational and interventional studies consistently demonstrate that regular physical activity has nephroprotective effects, mainly by improving cardiovascular and hemodynamic parameters such as blood pressure, cardiac output, and vascular tone[14] (Table 1). Exercise also has demonstrated benefits on CKD-related complications, including insulin resistance, dyslipidemia, systemic inflammation, sarcopenia, anemia, and CKD-mineral bone disorders.[37,38]

By inducing favorable physiological adaptations, exercise disrupts the "vicious cycle" of sedentary behavior and deconditioning, ultimately enhancing overall well-being.[29]

Despite these encouraging findings, the evidence is inconclusive.[39] While numerous small-scale observational and interventional studies support exercise in CKD, large RCTs with long-term follow-up remain scarce,[40–42] particularly among patients not on dialysis. Most available studies are underpowered to assess hard clinical end points such as hospitalization, CKD progression, and mortality. Moreover, the impact of exercise may vary across CKD stages and comorbid conditions, complicating the interpretation of pooled data.[43]

More recently, an umbrella review of meta-analyses by Neves et al. (2025), including 44 meta-analyses (35,432 patients in predialysis, peritoneal dialysis, and hemodialysis), analyzed the impact of different exercise modalities on several CKD-related outcomes.[44]

The authors found aerobic and combined exercise training particularly effective in improving cardiorespiratory capacity (main effect: 2.1, 95% confidence interval [CI]: 0.8–3.4, and main effect: 3.4; 95% CI: 2.4–4.6, respectively). Combined exercise training also yielded consistent benefits in psychosocial domains (main effect: −7.3; 95% CI: −9.31 to −53). Functional performance improved across nearly all exercise modalities, except for isometric training, which showed specific benefit for vascular access maturation (main effect: 0.84; 95% CI: 0.5–1.2).[45]

Furthermore, a 2024 consensus statement from the Italian Society of Nephrology's Working Group on Physical Exercise summarized the clinical evidence into 16 key points, highlighting consistent benefits of physical activity on physical performance, cardiometabolic health, neuromuscular strength, cognitive function, and QoL.[46] Notably, two statements specifically address the interaction between diet and exercise. First, a low-protein diet, recommended in the conservative management of CKD, does not impair muscle mass provided that energy intake is adequate.[46] Therefore, an low-protein diet does not appear to limit the favorable effects of exercise training on muscle ultrastructural, metabolic, and morpho-functional adaptations. On the contrary, it may exert beneficial effects on CKD-associated metabolic acidosis and insulin resistance, thereby reducing their pro-catabolic impact on protein metabolism.[47] Second, protein supplementation combined with resistance exercise training is likely to stimulate protein synthesis by activating the pAkt and mTOR pathways, whereas aerobic exercise training and adequate energy intake mainly improve mitochondrial and energy metabolism, contributing to a reduction in protein degradation.[46] Altogether, these data suggest that exercise training in CKD should be planned in conjunction with individualized dietary prescriptions, in order to optimize protein–energy intake and support muscle maintenance while preserving nephroprotection.

Overall, the available data provide a moderate degree of certainty that exercise improves surrogate outcomes such as physical performance, cardiorespiratory fitness, and QoL in CKD not on dialysis. By contrast, because of the small sample sizes, short follow-up, and heterogeneity of studies, the strength of the evidence for an effect on hard clinical outcomes such as CKD progression, hospitalizations, or mortality remains low (Table 2).

Barriers and Facilitators

Despite a growing body of evidence, the implementation of structured exercise programs in CKD care is poor.[50]

Barriers occur at four main levels: (1) physician-related barriers (e.g., uncertainty regarding safe exercise prescriptions, limited training in exercise physiology, and lack of integration into standard care pathways); (2) disease-related barriers (e.g., cardiovascular comorbidities, anemia, and musculoskeletal impairments); (3) patient-related barriers (e.g., low motivation, fear of adverse events, fatigue, and psychosocial factors); and (4) health-care

Table 1. Main Characteristics of Studies Assessing the Effect of Physical Activity and Exercise in Patients With CKD and PAD

Population	Study Designs	Sample Size and Follow-Up	Risk of Bias
CKD not on dialysis	Interventional trials (often single-center) Mix of RCTs and nonrandomized trials Prospective/retrospective cohorts	Sample size: small Short-term follow-up: adequate Long-term follow-up: limited	Selection of fitter, motivated, ambulatory patients Heterogeneity in CKD stage, comorbidities, and exercise protocols Variable outcome measures Limited adjustment for changes in therapy and baseline activity
PAD (asymptomatic and symptomatic)	Multiple RCTs (supervised vs. home-based vs. usual care) Observational cohorts Registry data	Sample size: adequate Short-term follow-up: adequate Long-term follow-up: adequate	Variability in program structure, intensity, and supervision Difference in adherence between groups Selective inclusion criteria (i.e., patients able to walk) Residual confounding from comorbidities
CKD + PAD (overlap)	Observational cohorts Single-center nonrandomized home-based walking study	Sample sizes: small Short-term follow-up: limited Long-term follow-up: limited	Marked selection bias (fitter, closely monitored patients) Absence of randomization Limited control for changes in medications, revascularization procedures, and comorbidities Possible survival bias Nonstandardized outcome definitions

CKD, chronic kidney disease; PAD, peripheral artery disease; RCT, randomized controlled trial.

system–related barriers (e.g., lack of structured referrals and reimbursement).[51,52] Survey-based data confirm the under-prescribing of exercise therapy; structured programs are available to CKD patients in only 42-81% of centers across Italy, Spain, Canada, New Zealand, and Australia,[46,53,54] and it is unclear how robust many of these programs are.

On the other hand, facilitators for successful implementation include (1) the proactive role of nephrologists in prescribing physical activity; (2) the integration of multidisciplinary teams (e.g., physiotherapists, kinesiologists, and psychologists); (3) the tailoring of exercise protocols to individual cardiovascular tolerance and baseline physical function for ensuring safety and adherence; and (4) the use of novel technologies (e.g., telemonitoring and digital coaching platforms), to expand access, reduce logistical barriers, and provide continuous feedback for patients and clinicians.[46] Together, these facilitators highlight the importance of a system-level approach in embedding exercise into CKD management, shifting from sporadic to structured, evidence-based interventions.[55]

Physical Activity and Exercise in PAD

Patients with symptomatic peripheral arterial disease, who typically report exertional leg symptoms such as pain, burning, cramping, or weakness during ambulation, have a more rapid decline in ambulatory function over time compared with individuals without PAD.[56] The disease severity correlates strongly with the functional decline, as patients with lower ankle–brachial index values demonstrate steeper reductions in walking capacity.[57] Notably, even individuals with asymptomatic PAD, those who do not report exertional leg symptoms, commonly display impaired lower extremity function.[58]

Within this framework, exercise and physical activity serve as safe, noninvasive, and cost-effective therapeutic strategies to counteract functional decline. Exercise training can be implemented as a stand-alone intervention or integrated into stepwise care models alongside pharmacological therapy, endovascular procedures, or surgical revascularization.[16]

Evidence

A substantial body of research supports exercise training as a cornerstone therapy[59] in the management of PAD (Table 1). McDermott et al. evaluated 260 individuals with PAD and 110 without PAD using the 6-minute walk test (6MWT) at baseline and at a 2-year follow-up. They observed a functional decline in walking ability based on disease severity: 38.5% of patients with an ankle-brachial index (ABI) < 0.50 were unable to complete 6MWT, 19.2% with an ABI of 0.50-0.70, 6.2% with an ABI of 0.71-0.89, and 1.7% with a normal ABI of 0.90-1.40.[60]

Traditionally, exercise therapy has relied on supervised intermittent walking regimens, where patients walk until experiencing moderate to severe claudication pain,

Table 2. Summary of Physical Activity and Exercise Recommendations Based on Available Evidence in the Population With CKD and PAD

Population	Recommendation	Main Benefits	Evidence	Barriers
CKD not on dialysis	Aerobic physical activity 150-300 min/wk, moderate or 75-150 min vigorous Combined exercise (aerobic + strength) 2-3 × /week	↑ Cardiorespiratory fitness ↑ Physical performance ↓ Blood pressure ↓ Inflammation ↑ QoL ↓ CKD complications (?)	KDIGO 2024[1] Italian Consensus Statements 2024[46]	Under-prescribing Poor integration in care pathways Need to tailor due to comorbidities
Asymptomatic PAD	Aerobic physical activity 150-300 min/wk (moderate) or 75-150 (vigorous)	↓ Functional decline ↓ Risk factors	ESVS 2024[23] ESC 2024[21]	Lack of RCTs Variable adherence
Symptomatic PAD (claudication)	SET (class I A) Structured home-based exercise (class II A)	↑ Max walking distance & 6-min walk test ↑ QoL ↓ Disability	ESVS 2024[23] ESC 2024[21] AHA/ACC 2024[16]	Limited access to SET Low physician referral Logistical barriers
CKD + PAD (overlap)	Pain-free interval walking home-based exercise (e.g., 2 × 10 min daily: 1-min walking/1-min rest) SET if available	↑ 6MWT/walking distance ↓ CKD progression (?) ↓ Hospitalizations and revascularizations	Observational data[48] EXACT RCT[49]	Under-diagnosis Frailty/sarcopenia Need to integrate renal-vascular assessment

6MWT, 6-minute walk test; CKD, chronic kidney disease; ESVS, European Society for Vascular Surgery; PAD, peripheral artery disease; QoL: quality of life; RCT: randomized controlled trials; SET: supervised exercise training.

followed by short rest intervals.[61] In addition, home-based walking training has been researched and validated, with favorable effects on both hemodynamics and exercise capacity.[62-66] Indeed, a systematic review has broadened the therapeutic landscape, demonstrating that alternative modalities, including cycling, lower extremity resistance training, upper arm ergometry, Nordic walking, and multimodal programs, can yield benefits comparable to those of supervised treadmill walking. Such findings highlight the importance of tailoring exercise prescriptions to patient preferences and feasibility, especially when supervised exercise training (SET) is not accessible.[67]

Long-term data reinforce the protective role of exercise. In observational studies, PAD patients who completed a home-based program of low-intensity walking showed reduced mortality rates and improved long-term clinical outcomes compared to controls.[68,69]

In line with this, the 2024 European Society for Vascular Surgery (ESVS) guidelines[23] strongly recommend supervised exercise (class I, level A) or structured home-based exercise (class IIa, level A) to improve maximum walking distance, health-related QoL, and self-reported functional impairment in symptomatic PAD patients. Meanwhile, aerobic physical activity (class I, level A) for at least 150-300 minutes a week (moderate intensity) or 75-150 minutes (vigorous intensity) is recommended as part of the preventive management in asymptomatic PAD patients.[23] Taken together, these studies support a high degree of certainty that supervised and structured home-based exercise programs improve walking performance and health-related QoLin patients with symptomatic PAD. In contrast, the evidence is less robust and more heterogeneous regarding direct effects on major cardiovascular events, limb outcomes, or mortality, so the overall strength of the evidence for these end points should be considered low to moderate.

However, exercise therapy in PAD remains limited due to gaps in patient and provider awareness, restricted accessibility and affordability of programs, and a scarcity of effective, community-based interventions. Current guidelines emphasize the need for further research and systemic solutions to overcome these barriers and enhance implementation[23,70] (Table 2).

Barriers and Facilitators

For asymptomatic patients, practice is inconsistent due to the lack of trial data directly addressing this subgroup. Among patients with symptomatic PAD, only a minority undergo structured SET, even though it is safe and effective. Barriers to widespread adoption include limited program availability, insufficient physician referrals, low health literacy, lack of motivation, exercise-limiting comorbidities, and discomfort related to claudication. Practical barriers such as travel distance, transportation costs, and time commitments further hinder adherence, particularly for patients outside major urban centers.[71]

Addressing these challenges requires systemic solutions. Expanding the workforce of physiotherapists and clinical kinesiologists specialized in PAD treatment, improving referral pathways, and ensuring reimbursement for SET are critical facilitators. Moreover, community-based and

home-based programs, potentially supported by digital health technologies, offer pragmatic alternatives to hospital-based SET. Establishing integrated care networks that align health-care providers, patients, and policymakers will be essential to bridging the gap between evidence and clinical practice, thereby maximizing the population-level impact of exercise interventions.[72-74]

Physical Activity and Exercise in Overlapping CKD-PAD

Epidemiology

In the United States, 24.9% of patients with CKD also have PAD, with incidence increasing in more advanced CKD stages.[18] Hospitalized patients with CKD and PAD have increased health-care demands, longer hospital stays, and higher costs.[28] A large cohort study further indicated that CKD patients with PAD had elevated risks of mortality and limb complications.[75]

Patients with end-stage renal disease are at particularly high risk. When PAD is present, susceptibility to cardiovascular events and amputations increases substantially compared with individuals without CKD or PAD.[76]

Pathophysiology

The interplay between CKD and PAD risk has been extensively investigated, as both conditions share several pathophysiological mechanisms and risk factors. Traditional cardiovascular risk factors, including diabetes mellitus, hypertension, dyslipidemia, obesity, advanced age, and smoking, are highly prevalent among individuals with CKD and contribute directly to PAD development.[77] Beyond these shared risk factors, CKD independently increases PAD risk and PAD-related complications through several mechanisms such as increased oxidative stress, endothelial dysfunction, pro-inflammatory cytokine production, volume overload, and accumulation of uremic toxins.[78]

A collaborative meta-analysis of individual participant data demonstrated that, compared with an eGFR of 95 mL/min per 1.73m^2, adjusted hazard ratios (HRs) for incident PAD were 1.22 (95% CI: 1.14-1.30) at an eGFR of 45 mL/minute per 1.73m^2 and 2.06 (95% CI: 1.70-2.48) at an eGFR of 15 mL/minute per 1.73m^2.[79]

Similarly, urine albumin to creatinine ratio, a marker of endothelial dysfunction and renal injury,[80] independently predicts PAD risk beyond traditional cardiovascular factors.[81]

In patients with CKD, PAD is often characterized not only by intimal atherosclerosis but also by pronounced medial arterial calcification. Perticone et al. found a significant inverse correlation between alkaline phosphate and endothelium-dependent vasodilation, mediated by fibroblast growth factor-23,[82] a marker of vascular calcification in CKD-mineral bone disease.[74] The presence of concomitant PAD and CKD[76] drives the patients to a higher cardiovascular risk, onset of a more severe stage of PAD, such as chronic limb ischemia, and worse surgical outcomes as a higher rate of reinterventions and amputations.[73,83,84] In addition, patients with PAD may be at increased risk of worsening kidney function because of several factors, including arterial stiffness, markers associated with early CKD development, metabolic factors, and contrast-induced nephropathy related to endovascular procedures.[83,85] Finally, CKD and PAD promote sarcopenia, increase hospitalization rates, impair functional status, and worsen disability, resulting in a particularly vulnerable patient subgroup. Taken together, these mechanisms provide a plausible biological basis for the benefits of physical activity in patients with overlapping CKD and PAD. In this context, exercise and appropriate protein–energy intake may help mitigate endothelial dysfunction, inflammation, and sarcopenia, which are key mediators of adverse outcomes when CKD and PAD coexist.

Evidence

Patients with overlapping CKD and PAD are a frail subgroup, often characterized by physical inactivity, accelerated sarcopenia, and progressive functional decline. Sedentary behavior perpetuates a vicious cycle of deconditioning, loss of independence, and increased risk of adverse outcomes. Given the shared pathophysiological mechanisms of CKD and PAD, physical activity and structured exercise interventions represent a promising therapeutic strategy to improve mobility, exercise tolerance, QoL, and adverse clinical outcomes, as demonstrated in each condition individually (see above) (Fig. 1).

Despite the overlap between PAD and CKD, high-quality evidence specifically supporting physical activity and exercise interventions in patients with both conditions remains limited (Table 1). The most notable data come from a retrospective observational study of 66 patients with CKD stages III-IV and PAD (Rutherford class I-III) who undertook a 6-month, pain-free, home-based walking program. After 5 years, the exercise group showed significantly slower CKD progression (serum creatinine: 2.35 ± 0.32 to 2.71 ± 0.39 mg/dL) compared with the control group (serum creatinine: 2.30 ± 0.31 to 4.22 ± 0.42 mg/dL; $P = .002$). No patients in the exercise group required dialysis, whereas five patients in the control group did ($P = .025$). Moreover, exercise participants had lower risks of peripheral revascularization (HR = 2.59; $P = .027$) and hospitalizations (HR = 1.77; $P = .031$).[48] These findings cannot establish causality due to the nonrandomized study design and small sample size. In this overlap population, the current findings should be regarded as hypothesis-generating, and the strength of the evidence for any causal effect of exercise on renal outcomes, hospitalizations, or limb events in CKD–PAD patients is very low (Table 2).

Barriers and Facilitators

Despite the overlapping mechanisms, clinical research and care pathways for CKD and PAD often remain

fragmented, leading to missed opportunities for integrated management.

One major barrier is the lack of systematic identification of patients with both conditions. In clinical practice, PAD is frequently underdiagnosed in CKD patients, as frailty and sarcopenia can mask early symptoms, delaying identification until advanced PAD stages.[86] Conversely, PAD patients are not consistently screened for CKD or albuminuria, despite their prognostic relevance and the opportunity for earlier nephrological referral. Comprehensive vascular–renal assessments could bridge this diagnostic gap and facilitate timely interventions.

Another barrier is the limited translation of exercise strategies across these populations. While home-based, pain-free walking programs are safe and effective in PAD patients,[60,62-64] their applicability in those with concomitant CKD and PAD remains untested. This represents a missed opportunity, as walking programs address shared mechanisms such as endothelial dysfunction, inflammation, and sarcopenia. Pragmatic integrated RCTs are urgently needed to evaluate whether exercise can benefit this high-risk group synergistically.

A promising step forward is the EXrcise ACTivity (EXACT) CKD–PAD trial protocol,[49] the first multicenter, single-blind, parallel-group RCT designed for patients with stages III-IV CKD and claudicating PAD. Approximately 130 participants will be randomized into (1) a home-based walking interval intervention (two 10-minute daily sessions alternating 1 minute of walking with 1 minute of rest, at a progressively prescribed pace using a metronome) or (2) a control group receiving standard nephrological care and nutritional advice only. The primary outcome is distance covered in the 6MWT, while secondary outcomes include QoL, muscle strength, body composition, peripheral perfusion, renal function, and hospitalization rates at 12 months. Recruitment is ongoing, with completion anticipated in 2026. This trial may represent a milestone in establishing integrated exercise-based care strategies for the CKD–PAD population (Fig. 2).

EXACT CKD–PAD is explicitly designed to address several current gaps: (1) by focusing on a home-based intervention rather than supervised center-based exercise, it tests a model that is more feasible for patients who face travel and access barriers; (2) its pragmatic inclusion of older,

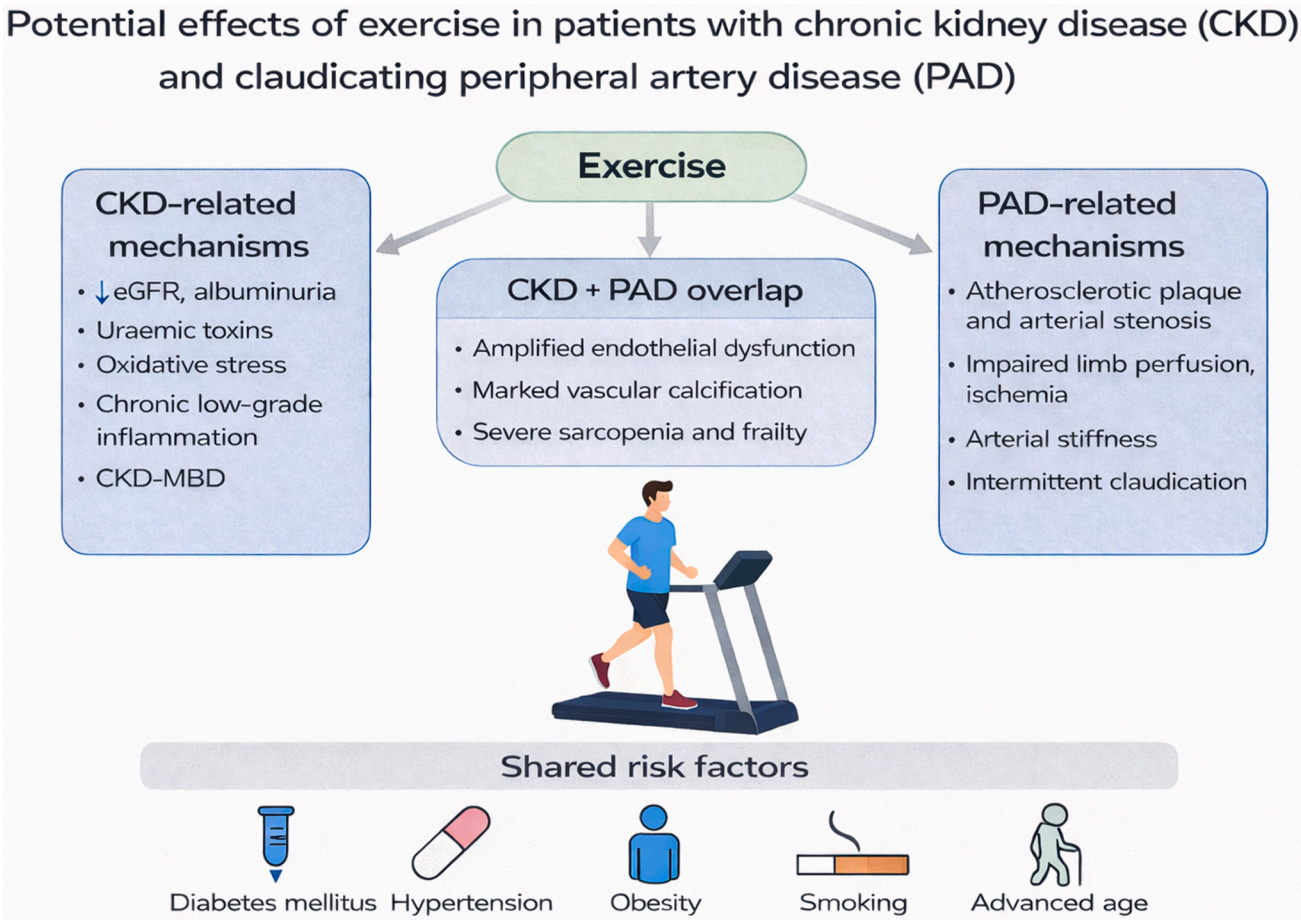

Figure 1. Potential effects of exercise in patients with CKD and claudicating PAD. CKD, chronic kidney disease; PAD, peripheral artery disease.

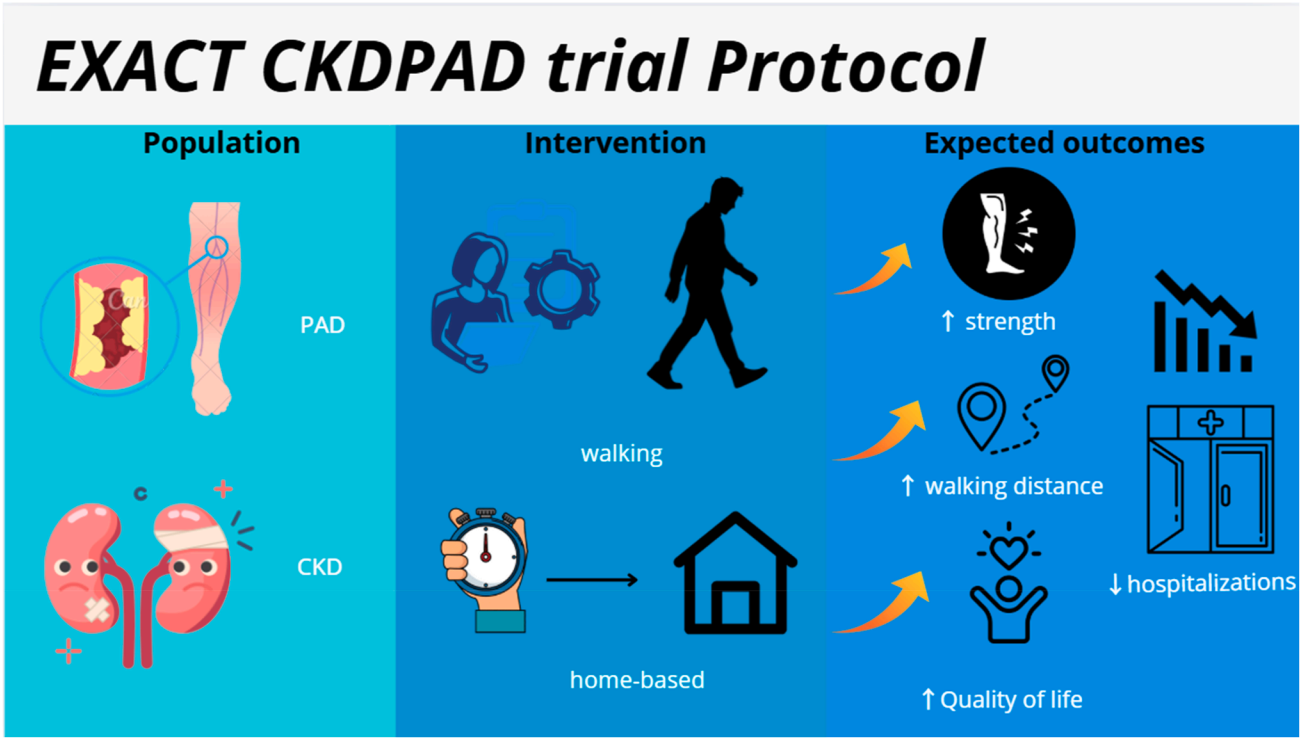

Figure 2. Schematic summary of ongoing EXACT CKD–PAD trial. CKD, chronic kidney disease; PAD, peripheral artery disease.

comorbid patients reflects the frail CKD–PAD population seen in routine practice; (3) and the joint involvement of nephrology and vascular teams provides an integrated care pathway.

However, some limitations should be acknowledged. Firstly, EXACT CKD–PAD evaluates only one exercise modality (home-based interval walking), which may not be appropriate for all patients. Secondly, eligibility criteria and the specific health-care setting may limit generalizability to patients with different CKD stages, PAD presentations, or organizational contexts. Thirdly, the true effectiveness of the intervention will depend not only on its physiological effects but also on adherence and feasibility in this frail population, which remain to be determined. Finally, even if the results are positive, additional studies will be required to confirm and extend these findings to broader CKD–PAD populations.

Conclusions

The coexistence of CKD and PAD represents a clinical scenario with a particularly high morbidity, disability, and health-care burden. Despite advances in pharmacological therapies, the residual risk remains substantial, underscoring the need for complementary lifestyle strategies.

Physical activity and exercise-based interventions, which are already supported by evidence in both CKD and PAD separately, offer a unique opportunity to bridge this therapeutic gap. The routine integration of PAD screening into nephrology care, and vice versa, as well as CKD screening into vascular medicine, facilitates the early identification of at-risk patients who may benefit most from physical activity and exercise training. The ongoing EXACT CKD–PAD trial is expected to clarify the efficacy and safety of home-based exercise programs in patients with concurrent CKD and PAD.

Author Contributions

Conceptualization, Y.B.; investigation, F.C., F.B., and C.B.; writing and editing—original draft, F.C.; writing—review and editing, Y.B.; supervision, C.K., M.A., and A.S.; visualization, N.L., T.C., and B.M.; validation, F.M., R.M., K.R.W., and M.V.

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