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Review

# Exercise-Based Cardiac Rehabilitation for Peripheral Artery Disease

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## Abstract

Peripheral artery disease (PAD) is a pervasive atherosclerotic condition affecting well over 100 million adults worldwide and associated with major functional limitations, reduced quality of life, and elevated risks of myocardial infarction, stroke, limb events, and mortality. Exercise therapy—preferably supervised or delivered through structured, monitored home-based programs—is a first-line, guideline-endorsed therapy that improves walking performance and patient-reported outcomes and contributes to comprehensive secondary prevention. This review synthesizes mechanistic underpinnings (endothelial, angiogenic, metabolic, autonomic) and appraises the comparative effectiveness, safety, and implementation models of supervised exercise therapy (SET), structured home-based and hybrid programs, and alternative modalities in PAD. Finally, we summarize policy aspects and persistent gaps to guide clinical practice and future research.

**Keywords:** cardiac rehabilitation; exercise training; peripheral artery disease

## 1. Introduction

Lower-extremity peripheral artery disease (PAD) is a chronic, occlusive manifestation of atherosclerosis. Diagnostic confirmation relies on a resting ankle-brachial index (ABI)  $\leq 0.90$ , with toe pressures and transcutaneous oxygen measurements helpful in suspected chronic limb-threatening ischemia. PAD confers high risks for major adverse cardiovascular events (MACE) or major adverse limb events (MALE) and impaired function even among patients without classic claudication. Contemporary multisociety guidelines (ACC/AHA 2024; ESC/ESVS 2024) re-affirm structured exercise as a core component of care, along with high-intensity statin therapy, smoking cessation, antithrombotic strategies, and individualized consideration of revascularization where indicated [1].

The global epidemiology of PAD points to an aging population burden with sex, socioeconomic, and geographic disparities. The Lancet Global Health 2019 GBD assessment estimated  $\approx 113$  million people  $\geq 40$  years living with PAD in 2019; newer analyses confirm high contributions from modifiable risk factors and rising total numbers despite heterogeneous age-standardized trends. These data underscore the need for scalable exercise solutions integrated with preventive therapies [2,3].

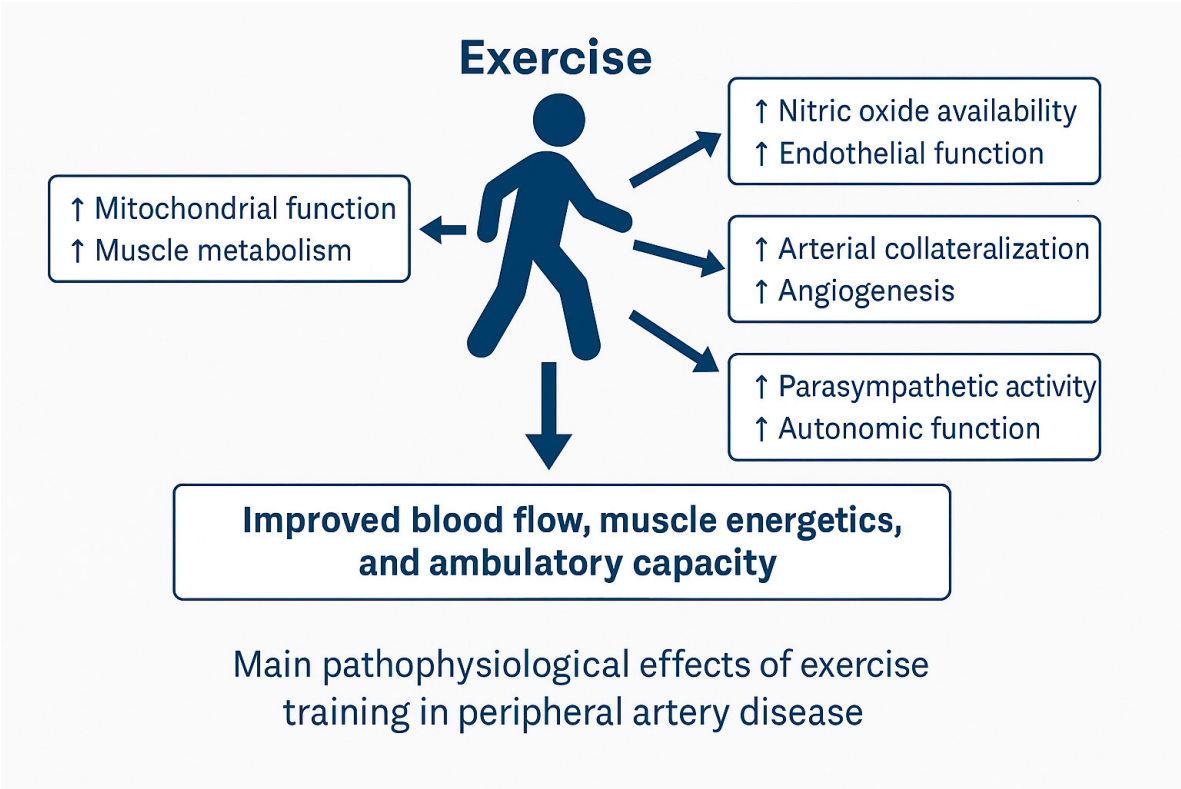
## 2. Beneficial Effects of Exercise Training in PAD: Mechanistic Overview

### 2.1. Endothelial Function and Nitric Oxide (NO)

Intermittent ambulatory exercise increases pulsatile and mean shear stress across conduit and resistance vessels, activating endothelial NO synthase (eNOS) and improving vasodilator reserve. This shear stress-dependent mechanism is a central pathway through which exercise exerts favorable effects on endothelial function and vascular adaptation [4]. Exercise also modulates oxidative stress and enhances antioxidant enzyme expression, further preserving NO bioactivity and reducing endothelial dysfunction [5].

Mechanistically, the hemodynamic stimulus of repeated exercise bouts increases endothelial shear stress, upregulates eNOS expression and phosphorylation, and enhances NO release, while exercise-induced upregulation of antioxidant defenses mitigates NO degradation by reactive oxygen species, collectively improving vasodilator capacity [6].

Brachial artery flow-mediated dilatation (FMD) is widely used as a surrogate for endothelial function and is predictive of cardiovascular risk [7], and each 1 % decrement in FMD is associated with an approximately 8–13 % increase in future cardiovascular events [8]. Meta-analytic evidence in PAD specifically shows that structured exercise improves brachial artery FMD, while broader cardiovascular populations corroborate exercise-induced FMD gains [9,10] (Figure 1).



**Figure 1. Main Pathophysiological effects of exercise training in peripheral artery disease.** Repeated ischemia-reperfusion during structured walking and adjunct modalities (e.g., cycling, resistance training) increases endothelial shear stress (↑eNOS/NO; improved brachial FMD), stimulates collateral vessel growth and capillarization (↑VEGF signaling), improves mitochondrial function and oxidative metabolism in ischemic skeletal muscle (↑PGC 1α-driven biogenesis; delayed lactate accumulation), and rebalances autonomic control (↑parasympathetic tone; improved HRV). These adaptations translate into higher pain free and maximum walking distances, better 6 minute walk performance, modest ABI gains, and improved quality of life; importantly, they complement risk factor modification and comprehensive cardiac rehabilitation.

## 2.2. Angiogenesis and Collateralization

Repeated ischemic stimuli during exercise trigger a cascade of pro-angiogenic mediators, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and hypoxia-inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ), which promote capillary rarefaction reversal, and stimulate the formation of collateral vessels [11].

Experimental work in skeletal muscle, including single-cell transcriptomic analysis in animal models, indicates that specific subsets of endothelial cells are metabolically primed for angiogenesis. Endothelial cells expressing high levels of transcription factors such as ATF3/4, enriched in oxidative muscle regions, exhibit greater angiogenic potential and proliferative responses to exercise stimuli, possibly through metabolic regulation of amino acid uptake and vascular expansion pathways [12]. While quantifying human collaterals non-invasively is challenging, improved treadmill and 6-minute walk performance after SET is consistent with physiologic flow redistribution and microvascular remodeling [13] (Figure 1).

## 2.3. Skeletal Muscle Metabolism and Mitochondria

PAD muscle exhibits mitochondrial dysfunction, fiber type shifts, and impaired oxidative phosphorylation. Exercise training (particularly walking to moderate–severe claudication) enhances mitochondrial biogenesis ( $\uparrow$ PGC-1 $\alpha$ ), oxygen extraction, and lactate kinetics—delaying pain onset and increasing endurance. Functional gains (PFWD, MWD, 6MWD) observed across trials reflect these peripheral adaptations even when ABI changes are modest [13,14] (Figure 1).

## 2.4. Autonomic Balance and Baroreflex

PAD is often accompanied by sympathetic predominance and blunted heart-rate variability. Exercise training favorably modulates autonomic control and baroreflex function, which correlates with improved ambulatory capacity and may contribute to systemic risk reduction [15] (Figure 1).

## 2.5. Inflammation and Oxidative Stress

Exercise exerts anti-inflammatory and antioxidant effects.

Chronic inflammation is a key driver of atherosclerosis [16]. Pro-inflammatory cytokines such as interleukins (ILs) and tumor necrosis factor (TNF)- $\alpha$  contribute to vascular dysfunction by triggering endothelial activation via NF- $\kappa$ B signaling [17], promoting eNOS uncoupling [18], and increasing the expression of adhesion molecules that facilitate monocyte attachment and differentiation into macrophages [17,19]. These processes further enhance platelet aggregation and coagulation, ultimately accelerating atherosclerotic progression, with C-reactive protein (CRP) implicated in PAD development and severity [20].

In patients with PAD, exercise showed reductions in CRP or IL-6 [21,22].

A meta-analysis in PAD found significant FMD improvement without parallel reductions in CRP/IL-6/TNF- $\alpha$ , suggesting that endothelial benefits can occur independently or precede measurable systemic inflammatory change, possibly reflecting early or localized vascular adaptations [9] (Figure 1).

# 3. Supervised Exercise Therapy (SET): The Gold Standard

## 3.1. Protocol and Implementation

Guidelines advise structured, intermittent walking aiming for moderate–severe claudication (3–4/5 pain scale) before resting, 30–45 (up to 60) minutes per session, at least three days/week, over 12 weeks or longer. Programs should individualize treadmill grade/speed, monitor hemodynamics and symptoms, and embed education and risk-factor management. CMS covers up to 36 sessions (with potential extensions), catalyzing program creation though copays and access remain barriers [1]. Key Trials, Meta-analyses, and Real-World Studies on Exercise Therapy in PAD are reported in Table 1.

Table 1. Key Trials, Meta-analyses, and Real-World Studies on Exercise Therapy in PAD.

| Study (Year)                               | Population/S Arms/Intervention                         | Primary Outcome                                                                               | Key Results                          | Follow-up                                                                                                          | Notes                                                                  |
|--------------------------------------------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| CLEVER (2012; 18-mo analysis 2013)         | Aortoiliac PAD with claudication                       | OMC vs Stent vs SET                                                                           | Peak walking time (graded treadmill) | SET > Stent at 6 mo for treadmill performance; both SET and Stent > OMC at 18 mo; QoL favored Stent early          | 6 and 18 mo<br>Functional vs QoL trade-offs; importance of maintenance |
| ERASE (JAMA 2015; CEA 2021)                | Intermittent claudication (aortoiliac/femoropopliteal) | SET vs Endovascular + SET                                                                     | Max walking distance                 | +282 m (99% CI 60–505) for ER+SET vs SET; cost-effective from societal perspective                                 | 12 mo<br>Supports synergy when anatomy warrants intervention           |
| LITE (JAMA 2021; AJC 2025 PROMs)           | PAD with diverse symptoms                              | High-intensity (symptom-eliciting) vs Low-intensity (pain-free) home-based walking vs Control | 6MWD                                 | High-intensity +34–45 m at 12 mo; low-intensity ≈ no benefit vs control; PROMs improved mainly with high-intensity | 12 mo<br>Coaching weekly; accelerometer-monitored                      |
| JAMA Netw Open IPD MA (2023)               | PAD RCTs (n≈719)                                       | Home-based walking vs Supervised treadmill (vs controls)                                      | 6MWD and treadmill outcomes          | Home-based > Supervised for 6MWD (+≈24 m); Supervised > Home for treadmill distance                                | 6 mo<br>Task specificity (community vs treadmill)                      |
| WalkingPad RCT (Front Cardiovasc Med 2023) | IC; single-center                                      | HBET + behavior change ± smartphone app                                                       | PFWD/MWD/6MWD; QoL                   | Both arms improved at 3 mo; MWD advantage with app at 6 mo in sensitivity analyses                                 | 3–6 mo<br>Digital augmentation potentially helpful                     |
| HY-PAD feasibility (CJC Open 2025)         | PAD; pre-post                                          | 4 wk supervised then 8 wk home with calls                                                     | 6MWD; WIQ                            | +56 m 6MWD; high adherence; few adverse events                                                                     | 12 wk<br>Feasibility; needs controlled trials                          |
| Safety of HBEP (Waddell 2021)              | IC; 27 studies; 147,810 patient-hours                  | Home-based programs (varied)                                                                  | Complication rate                    | ≈1 related event/36,953 patient-hours; most without cardiac screening                                              | Varied<br>Supports safe HBEP with prudent screening                    |
| BMJ Open 2025 MA (HBET efficacy)           | IC; 7 RCTs                                             | Home-based exercise vs control                                                                | PFWD/MWD                             | Significant PFWD benefit; MWD NS overall; heterogeneity high                                                       | 6–52 wk<br>Intensity/adherence likely moderators                       |
| Endothelial Function MA (PAD/CAD) 2024     | PAD/CAD cohorts                                        | Structured aerobic training                                                                   | Flow-mediated dilation               | Increased brachial FMD following training                                                                          | Varied<br>Mechanistic support for vascular benefit                     |

### 3.2. Effectiveness

Randomized trials and meta-analyses consistently show SET improves maximal and pain-free walking distances and 6-minute walk distance versus usual care. Notably, in the CLEVER study (aortoiliac disease), six months of SET improved peak walking time more than primary stenting; at 18 months, both SET and stenting remained superior to medical therapy alone, with functional outcomes broadly comparable [23]. Systematic umbrellas confirm robust effects on walking and quality of life [14,23,24].

### 3.3. Endovascular Therapy Plus SET vs SET Alone

The ERASE trial randomized patients with claudication to selective endovascular revascularization plus SET versus SET alone. At 12 months, the combination achieved greater improvements in MWD and PFWD, with favorable cost-effectiveness from societal perspectives—supporting the “exercise-first, revascularize-when-appropriate” paradigm and highlighting synergy when anatomy and symptoms warrant [25,26].

### 3.4. HIIT and Alternative Intensities Within SET

Although high-intensity interval paradigms can improve endothelial function in cardiometabolic populations, PAD trials emphasize ischemia-inducing walking as the stimulus most consistently linked to functional gains. The LITE trial found that home-based low-intensity walking (avoiding symptoms) did not improve 12-month 6MWD compared with high-intensity walking that provoked leg symptoms. Supervised protocols should therefore target symptom-limited intensities with careful monitoring [27].

## 4. Home-Based and Hybrid Exercise Models

### 4.1. Why We Need Them

Despite reimbursement, SET uptake remains low. Early Medicare data (2017–2018) showed only ~1.3% of beneficiaries diagnosed with claudication participated in SET; most did not complete all sessions. Barriers include limited program availability, copayments, travel/time, and low provider referral rates. Surveys in urban PAD cohorts confirm physician non-referral and copays as common obstacles [28,29].

### 4.2. Safety of Home-Based Programs

A systematic review of 27 studies (147,810 patient-hours) reported only four related adverse events (~1 per 36,953 hours), three cardiac, mostly occurring when walking to high pain levels; safety appears greater with pre-exercise cardiac screening. Importantly, structured, monitored home programs differ from unstructured “go home and walk” advice [30].

### 4.3. What Works at Home

McDermott’s GM-CBT trial demonstrated that a structured home-based walking program using group-mediated cognitive behavioral strategies improved 6MWD by ~53 m at six months vs attention control, with gains in patient-perceived walking ability and physical activity.

Recent large randomized data confirm that structured home-based walking exercise significantly improves 6-minute walk distance compared with control, with adherence unaffected by age, sex, or baseline functional status, although certain comorbidities may influence adverse events [31].

Conversely, a trial relying primarily on wearable monitoring plus telephone coaching (HONOR) showed no improvement, underscoring that behavioral structure and periodic in-person support drive efficacy [32,33]. A recent meta-analysis demonstrated that home-based exercise interventions

significantly improve both pain-free walking distance and maximal walking distance compared with control groups, with clinically meaningful effects on walking performance [34].

#### 4.4. Digital and Hybrid Designs

Contemporary randomized data (e.g., WalkingPad RCT) show that adding app-supported behavior-change to prescribed home-based walking can improve PFWD/MWD and quality of life versus prescription alone. Hybrid models that begin with brief supervised phases and transition to monitored home training (e.g., HY-PAD) have shown high adherence and clinically meaningful functional gains, offering scalable pathways where SET capacity or patient logistics are limiting [35].

Extending this behavioral paradigm, the GAMEPAD trial demonstrated that gamification combined with automated coaching significantly increased daily ambulatory activity compared with wearable monitoring alone, demonstrating that behavioral economic strategies can enhance ambulatory activity in PAD [36]. Whether these activity gains translate into durable improvements in functional performance and clinical outcomes warrants further study.

#### 4.5. Real-World Outcomes and Program Completion

Within a large health system's first five years of CMS coverage, just 773/5,320 PAD patients were referred and 415 enrolled; only ~50% completed SET, yet completers achieved significant functional and quality-of-life improvements. Such findings reinforce the need for system-level referral prompts, copay mitigation, and integrated vascular/cardiac rehabilitation teams [37].

### 5. Alternative and Adjunct Exercise Modalities

#### 5.1. Resistance Training

Lower-limb resistance training increases strength and may improve walking capacity; meta-analyses suggest meaningful effects on strength, with variable transfer to walking compared with treadmill-based SET. When orthopedic limitations or severe pain preclude walking, resistance sessions (2–3×/week, major muscle groups, 1–3 sets of 8–12 reps at moderate intensity) can be used as a bridge or adjunct [14].

#### 5.2. Arm Ergometry (Arm-Crank)

Upper-body endurance training can elicit cross-transfer benefits to leg function by improving systemic cardiovascular fitness and autonomic regulation when lower-limb ischemia limits adherence—useful particularly in early phases or for patients awaiting revascularization [38,39].

#### 5.3. Cycling

Stationary cycling is often better tolerated than treadmill walking and improves cardiorespiratory fitness, though walking-specific improvements are generally smaller than with SET because the ischemic stimulus to calf musculature is less targeted. Cycling can complement walking to accumulate aerobic minutes within symptom tolerances [13].

#### 5.4. Hydrotherapy

Small controlled studies report that combining a supervised program with lower-limb whirlpool massage can improve impedance plethysmography indices and 6MWD versus exercise alone—hypothesized via vasodilation and reduced peripheral resistance—though the evidence base remains early and requires replication [40,41].

## 6. Clinical Outcomes

### 6.1. Functional Performance

Across RCTs and meta-analyses, SET produces large improvements in MWD (~120–200 m or more), PFWD, and 6MWD, with clinically meaningful changes that exceed those achieved by usual care and often rival those after revascularization at medium-term follow-up. Patient-reported walking impairment domains (distance, speed, stairs) also improve substantially [14,23,42,43].

### 6.2. Endothelial Function

Exercise training increases brachial FMD in PAD; mechanistic work suggests benefits are optimized at moderate–vigorous intensities and accrue across diverse cardiometabolic states. Given the prognostic value of FMD, these vascular adaptations may represent an important pathway linking exercise to event risk reduction [9,10,44,45].

### 6.3. Quality of Life (QoL)

Both SET and revascularization improve disease-specific QoL; in CLEVER, certain QoL scales favored stenting early while treadmill performance favored SET, indicating complementary roles. Combination strategies (ER+SET) can provide larger short-term gains where anatomy and symptoms justify intervention [23,25].

### 6.4. ABI and Hemodynamics

ABI may rise modestly in some trials, yet functional improvement frequently exceeds hemodynamic change, reflecting dominant peripheral adaptations. Clinicians should therefore prioritize symptom-targeted training and function-based outcomes rather than ABI alone [13].

### 6.5. Mortality and Hospitalizations

Although PAD exercise trials are typically underpowered for mortality, participation in comprehensive cardiac rehabilitation programs is associated with improved survival and risk-factor control in PAD cohorts. Observational evidence suggests that SET may reduce the subsequent need for endovascular/surgical procedures compared with non-participants [28,46,47].

## 7. Prehabilitation and Post-Revascularization Rehabilitation

Prehabilitation—4–8 weeks of structured training before planned interventions—aims to improve functional reserve and perioperative resilience. Post-revascularization, combining SET with guideline-directed medical therapy improves walking distances more than either strategy alone and may reduce repeat interventions by addressing the systemic and peripheral drivers of exertional limitation [1,25,48–50].

## 8. Safety, Risk Stratification, and Contraindications

SET is safe when delivered under direct supervision with appropriate screening and monitoring; adverse events are rare. For home-based programs, systematic review evidence indicates very low event rates, with most complications occurring when patients push to severe pain intensities and in programs lacking cardiac screening—hence the importance of initial evaluation, progressive loading, and clear stop rules. Absolute contraindications mirror those in general cardiac rehabilitation (e.g., unstable angina, decompensated heart failure, critical limb ischemia with infection) [1,30,51].

## 9. Implementation and Policy

Despite coverage and strong guidelines, SET referral and completion are modest: in early national data only ~1.3% of eligible Medicare beneficiaries enrolled within 19 months of coverage; copays and travel/time logistics were key barriers, and most referring clinicians had not prescribed SET. Health-system registries confirm low referral rates but meaningful gains among completers. Addressing copays, embedding referral prompts in vascular/cardiology clinics, and co-locating PAD programs within cardiac rehabilitation are pragmatic steps forward [28,29,37]. The 2024 ESC/ESVS consensus and ESVS guideline for asymptomatic PAD/claudeication emphasize supervised or structured community/home-based programs as core therapy, while acknowledging unmet needs and disparities across Europe. This converges with 2024 ACC/AHA guidelines, which elevates structured exercise alongside pharmacotherapy and selective revascularization [13,52].

## 10. Practical Exercise Prescription in PAD (SET or Structured Home Programs)

Assessment and baseline: ABI with waveforms, symptom profile, risk amplifiers (diabetes, CKD, smoking), fall risk/orthopedic issues; consider baseline 6MWT and/or graded treadmill test to individualize speed/grade and monitor calf muscle StO<sub>2</sub> if available [1].

Aerobic component (walking-centered): 3–5 days/week; warm-up 5–10 min; walk at a speed/grade that brings on moderate–severe claudication within 3–5 min; continue walking until 3–4/5 pain, then rest until symptoms resolve; repeat cycles to total 30–45 min; cool-down 5–10 min. Progress by increasing grade/speed or reducing rest intervals as tolerated; seek ischemic stimulus but avoid maximal, intolerable pain [1].

Adjunct modalities: Cycle ergometry or arm-crank on non-walking days to accumulate 150–300 minutes/week moderate-to-vigorous aerobic activity if feasible; add 2–3 days/week of resistance training targeting lower limbs to augment strength, balance, and daily function [13,14].

Behavioral scaffolding for home or hybrid: Use pedometers/accelerometers, app-supported goal setting, and scheduled coaching; consider a brief supervised phase to establish intensity and technique, then transition to monitored home training with periodic in-person reassessments [35].

Safety tips: Educate on red flags (chest pain, syncope, new rest pain/wounds, infection); consider pre-exercise cardiac screening in higher-risk patients; titrate intensity to symptom targets; maintain foot care and appropriate footwear; ensure hydration and medication adherence [30].

## 11. Special Populations

Older adults and frailty: Prioritize safety, balance, and progressive loading; consider seated/recumbent modalities early. Even small functional gains can translate into meaningful independence improvements [13,53].

Diabetes and microvascular disease: Glycemic variability influences walking tolerance; careful glucose monitoring around sessions and foot surveillance are critical. Exercise also improves endothelial function in diabetes, supporting its inclusion as a vascular health intervention [54].

Women and socioeconomically disadvantaged groups: Epidemiology indicates disproportionate impacts and access barriers; flexible scheduling, transportation support, and copay assistance can help close gaps in participation [2,55,56].

## 12. Clinical Pathway for PAD management in CR

A clinical pathway for PAD management in CR is proposed:

- 1) Confirm diagnosis and phenotype (asymptomatic, claudication, CLTI) with ABI and targeted testing;
- 2) Initiate guideline-directed medical therapy (statin, antiplatelet, smoking cessation; consider rivaroxaban 2.5 mg bid + aspirin in appropriate patients for MACE/MALE risk reduction);

- 3) Enroll in SET (or structured hybrid/home if SET access limited), delivering a progressive, symptom-targeted walking program with risk-factor management;
- 4) Reassess at 12 weeks: If insufficient improvement and anatomy is amenable, consider selective endovascular/surgical revascularization, with post-procedure rehabilitation to consolidate gains;
- 5) Long-term maintenance through community programs, digital tools, and periodic supervised “boosters”.

## 12. Unresolved Questions and Research Priorities

Despite robust evidence supporting structured exercise therapy as first-line treatment for claudication, several critical gaps remain in our understanding of how exercise should be optimized, personalized and integrated into comprehensive PAD care.

Most randomized trials of supervised or home-based exercise in PAD have been powered for functional endpoints such as maximal walking distance or 6-minute walk distance, with limited data on major clinical events. Although increased physical activity is associated with lower cardiovascular mortality in PAD cohorts, definitive evidence that structured exercise independently reduces MACE or MALE is lacking [1]. Prospective, event-driven studies are needed to determine whether exercise confers incremental prognostic benefit beyond guideline-directed medical therapy and whether functional improvements translate into reduced hospitalizations, revascularization procedures, amputation, or mortality, particularly in high-risk subgroups (e.g., diabetes, polyvascular disease) where mechanistic benefits have been inferred but not directly linked to clinical endpoints.

Moreover, although walking to moderate–severe claudication pain has traditionally been considered the most effective stimulus for improving walking performance in PAD, emerging evidence suggests that the optimal training intensity may vary substantially across individuals and according to the outcomes prioritized. The LITE (Low-Intensity Exercise Intervention in PAD) trial suggests a potential paradox in community-based exercise therapy for PAD, as patients who walk through pain often achieve greater functional improvements but limited gains in quality of life, whereas those who avoid pain may report better quality of life despite smaller functional improvements [27]. Also, a network meta-analysis showed variable effects of exercise intensity (high-pain vs low-pain protocols) on functional outcomes [57].

These findings suggest that the efficacy of exercise therapy in PAD cannot be defined solely by objective functional metrics, but should also incorporate patient-reported outcomes, including perceived walking ability, symptom burden, and quality of life. In clinical practice, exercise prescriptions should therefore be considered dynamic and individualized, with training intensity titrated according to symptom tolerance, functional response, and patient priorities.

Systematic integration of patient-reported outcomes alongside objective measures may facilitate a more patient-centered evaluation of treatment effectiveness and guide the ongoing adjustment of exercise prescriptions.

Future studies should aim to define individualized intensity thresholds, integrate real-time symptom monitoring and patient-reported outcomes, and determine whether adaptive exercise strategies can improve both adherence and long-term clinical outcomes in PAD rehabilitation.

## 13. Conclusions

Exercise training is the therapeutic linchpin for claudication: it addresses the peripheral problem (ischemic muscle energetics), vascular dysfunction (endothelial/angiogenic), and systemic risk (autonomic balance and fitness), delivering durable improvements in walking ability and quality of life. SET remains the gold standard where available; structured, monitored home or hybrid programs are safe and effective solutions to reach more patients. Embedding exercise within comprehensive cardiac rehabilitation, reducing copays, and expanding referral pathways are essential to translate the science into routine care for the millions living with PAD.

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