

## JAMA Clinical Guidelines Synopsis

## Management of Peripheral Artery Disease

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**GUIDELINE TITLE:** 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease

**DEVELOPERS AND FUNDERS:** American College of Cardiology and American Heart Association

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**PRIOR VERSIONS:** 2016

**TARGET POPULATION:** Patients with peripheral artery disease (PAD)

#### SELECTED RECOMMENDATIONS

- Patients with symptoms and signs of PAD should have a resting ankle-brachial index (ABI) measured, and exercise treadmill ABI should be performed for those with normal or borderline resting ABI and noncompressible arteries (class of recommendation [COR]: 1; level of evidence [LOE]: B).
- For patients with chronic symptomatic PAD (vascular claudication, recent revascularization, previous amputation)

or chronic limb-threatening ischemia (CLTI), low-dose rivaroxaban (2.5 mg twice daily) combined with aspirin (81 mg/d) is recommended to reduce risk of major adverse cardiovascular events (MACE) and major adverse limb events (MALE) (COR: 1; LOE: A). Patients with PAD and type 2 diabetes should also receive glucagon-like peptide 1 agonists and sodium-glucose cotransporter 2 inhibitors to lower cardiovascular risk of major cardiovascular events (COR: 1; LOE: A).

- Structured exercise at a pace inducing ischemic leg symptoms, in supervised or community-based programs using behavioral change techniques such as health coaching and activity tracking, is recommended for people with PAD to improve walking performance, functional status, and quality of life (QOL) (COR: 1; LOE: A).
- Endovascular revascularization improves pain-free ambulation, walking distance, and QOL in patients with hemodynamically significant aortoiliac or femoropopliteal disease and functionally limiting claudication despite medical therapy and structured exercise (COR: 1; LOE: A).

#### Summary of the Clinical Problem

PAD, defined as a partial or complete obstruction of at least 1 peripheral artery due to atherosclerosis, affects more than 200 million people worldwide.<sup>1</sup> PAD has 4 clinical subsets: asymptomatic, chronic symptomatic, CLTI, and acute limb ischemia. Established effective medical therapies for PAD include exercise, smoking cessation, diabetes management, antiplatelet agents (aspirin or P2Y12 antagonists), lipid-lowering medications, antihypertensives, and cilostazol. Patients with refractory symptoms or those at risk of limb loss often undergo revascularization for QOL and decreased risk of amputation. Herein we review updated recommendations for lifestyle modifications, diagnostic testing, pharmacotherapy, and revascularization for patients with PAD.<sup>2</sup>

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#### Characteristics of the Guideline Source

The guideline committee consisted of experts in general and interventional cardiology, radiology, surgery, nursing, wound care, exercise physiology, podiatry, and vascular clinical research (eTable in the Supplement).<sup>2</sup> COR was graded as 1 (strong and recommended; n = 64), 2 (moderate and reasonable; n = 47), 3 (no benefit; n = 6), or 4 (harm; n = 6). LOE was assigned A (high), B (moderate), or C based on quality and number of randomized clinical trials (RCTs) or nonrandomized trials.

#### Evidence Base

For patients with claudication or non-joint-related exertional leg symptoms and signs suggestive of PAD (eg, pulse deficits, leg wounds),

resting ABI should be measured (abnormal:  $\leq 0.9$ ; borderline: 0.91-0.99; normal: 1.00-1.40; noncompressible arteries:  $>1.40$ ). The ABI has a sensitivity of 69% to 79% and a specificity of 83% to 99% for detection of PAD vs angiography. The ABI has a lower sensitivity (35%-73%) in people with diabetes or chronic kidney disease, which are associated with noncompressible tibial arteries that may elevate ABI ( $>1.4$ ).<sup>1</sup>

For patients with symptomatic PAD, low-dose rivaroxaban (2.5 mg twice daily) combined with low-dose aspirin (81-100 mg/d) is recommended to reduce risk of MACE and MALE. In an RCT (n = 6391), patients treated with rivaroxaban and aspirin vs aspirin alone had a significantly decreased rate of MALE (2.6% vs 1.5%;  $P = .01$ ) at a median of 21 months.<sup>2</sup> Rivaroxaban and aspirin are also recommended for patients with prior lower extremity revascularization. In an RCT (n = 6564), low-dose rivaroxaban with aspirin (vs aspirin alone) lowered incidence of MACE and MALE from 19.9% to 17.3% ( $P = .009$ ; median follow-up, 28 months).<sup>3</sup>

For patients with functionally limiting PAD who have an inadequate response to medication and exercise, endovascular revascularization is recommended to improve walking performance and QOL. An RCT of 1830 patients with CLTI and infra-inguinal disease compared surgical bypass with endovascular revascularization. Patients who had an adequate great saphenous vein conduit for surgical revascularization had a lower incidence of MALE (median follow-up, 2.7 years) vs those assigned endovascular revascularization (42.6% vs 57.4%, respectively;  $P < .001$ ).<sup>4</sup> However, in an RCT of 345 patients with CLTI and infrapopliteal disease, death or amputation (median follow-up, 40 months) occurred more often in those

assigned surgical than endovascular revascularization (63% vs 53%, respectively;  $P = .04$ ).<sup>5</sup> Thus, for patients with CLTI, retrospective studies suggest that a multidisciplinary team with expertise in vascular care, revascularization, wound healing, podiatry, and foot surgery should guide treatment (COR: 1; moderate LOE).<sup>6</sup>

For patients with chronic symptomatic PAD, structured exercise therapy with exercise conducted at a pace that induces ischemic leg symptoms is recommended. Exercise programs can be home based and/or supervised or community-based structured programs. Exercise sessions should be 30 to 45 minutes at least 3 times a week for at least 12 weeks. The LITE trial demonstrated that low-intensity home-based exercise conducted at a pace without ischemic leg symptoms was significantly less effective for improving 6-minute walk test vs high-intensity home-based exercise.<sup>7</sup> Another RCT (190 patients with PAD and intermittent claudication) showed that a home-based walking exercise intervention improved 6-minute walking distance at 3 months for the intervention group vs usual care (adjusted mean between-group difference, 16.7 m; 95% CI, 4.2-29.2 m;  $P = .009$ ; minimum clinically important difference, 8-20 m).<sup>8</sup> No compelling evidence supports unstructured exercise for treatment of PAD.

### Potential Harms

To limit procedural risks such as acute kidney injury associated with intravenous contrast dye, allergic reactions, and discomfort, patients with confirmed PAD should not undergo imaging studies solely for anatomical assessment when surgery is not being considered. In addition, combination low-dose rivaroxaban (2.5 mg twice daily) and low-dose aspirin (81-100 mg/d) may increase bleeding risk. In the COMPASS trial, major bleeding was 3.2% in those treated with rivaroxaban and aspirin vs 2.0% with aspirin alone ( $P = .01$ ).<sup>2</sup> However, major bleeding in the VOYAGER trial was not statistically different in those treated with rivaroxaban and aspirin vs aspirin alone (2.7% vs 1.9%;  $P = .07$ ).<sup>3</sup>

### Discussion

PAD impairs walking and is linked to complications such as amputation, myocardial infarction, stroke, and decreased QOL. Diagnosis involves patient history, physical examination, and ABI.<sup>2</sup>

Addressing health disparities across geography, socioeconomic status, sex, and race and ethnicity are important to improve outcomes. Black patients with PAD have a 2- to 4-fold higher risk of amputation vs White patients with PAD, and this disparity increases in patients aged 65 years or older.<sup>9</sup> Potential contributors to these disparate outcomes may include lower use of pharmacological therapies and less access to structured exercise programs among Black individuals.

Smoking cessation is a key component of PAD care. Ongoing smoking is associated with a significant increase in PAD-related hospitalizations, revascularization procedures, and health care costs. Five-year mortality among patients with chronic symptomatic PAD and active smoking is 40% to 50%.<sup>10</sup> Up to 90% of patients presenting for revascularization due to severe limb symptoms (eg, severe claudication, ischemic rest pain, gangrene) are current smokers.<sup>10</sup> For these patients, smoking cessation should be encouraged at every health care visit.

### Areas in Need of Future Study or Ongoing Research

Studies are needed to determine the benefit of screening for PAD in asymptomatic at-risk individuals. Novel ways to implement telehealth technology effectively may improve patient access to structured exercise therapy, including in diverse patient populations. Research should better define optimal antiplatelet and antithrombotic regimens, including drug, dose, and duration, for patients with PAD who have undergone revascularization. Studies comparing various revascularization strategies, including specific devices for CLTI, should address adequacy of wound healing and limb salvage, as well as consideration of the costs and functional outcomes of multidisciplinary care.

### ARTICLE INFORMATION

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