

*Annual Review of Medicine*Peripheral Artery Disease:  
New Concepts, Treatments,  
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**Keywords**

peripheral artery disease, amputation, chronic limb-threatening ischemia, claudication, screening, disparities

**Abstract**

Peripheral artery disease (PAD) is a prevalent and underdiagnosed atherosclerotic condition affecting more than 10 million adults in the United States. PAD is a marker of systemic vascular disease and a strong predictor of myocardial infarction, stroke, and mortality. Despite its clinical importance, PAD remains underrecognized due to variable presentation, limitations in screening, and disparities in diagnosis and treatment. This review examines contemporary PAD epidemiology, diagnostic strategies (including the ankle-brachial index), and evidence-based management approaches, from supervised exercise to surgical revascularization. It also highlights the evolving debate on PAD screening guidelines and presents emerging evidence favoring targeted screening in high-risk populations. Importantly, the review explores structural inequities, racial and ethnic disparities, and geographic variation in PAD-related outcomes, particularly amputation. These disparities persist even after adjustment for comorbidities and socioeconomic factors. Addressing PAD effectively requires comprehensive strategies that include early diagnosis, equitable access to care, and policy initiatives.

## INTRODUCTION

Lower extremity peripheral artery disease (PAD) is an atherosclerotic, obstructive disease process that affects the arteries from the aortoiliac segment to the pedal arteries. It is a common form of cardiovascular disease that is estimated to affect 10–12 million individuals in the United States who are >40 years old and as many as 236 million people worldwide (1). The actual prevalence of PAD is unknown, as awareness of PAD is limited among both patients and healthcare professionals (2, 3), and screening guidelines are often conflicting (4–6). This lack of awareness and disease recognition is particularly concerning, not only because PAD is a major cause of disability but also because it is a marker for concurrent cardiovascular disease and a strong predictor of future myocardial infarction (MI) and stroke (7). In this article, we review PAD epidemiology and risk factors, disparities related to PAD, clinical guidelines for assessment and diagnosis, and treatment options.

## PERIPHERAL ARTERY DISEASE EPIDEMIOLOGY AND RISK FACTORS

PAD is the third leading cause of atherosclerotic morbidity, following coronary artery disease and stroke, and has a growing global impact. Between 2000 and 2010, the number of people living with PAD increased by 13.1% in high-income countries and 28.7% in low- and middle-income countries (8). Advanced age, diabetes mellitus (DM), smoking, chronic kidney disease, hypertension, and hyperlipidemia are the major risk factors for PAD. Of these risk factors, DM and smoking have a particularly strong association with the development of PAD.

### Peripheral Artery Disease and Diabetes Mellitus

Once considered a purely ischemic process, the influence of DM on the prevalence of PAD has substantially changed the risk profile of the disease. Patients with DM have an estimated 2–4 times increased risk of developing PAD during their lifetimes, and risk increases with worsening glycemic index control (9). With each 1% increase in hemoglobin A1C from baseline, there is an associated 14.2% increased relative risk of major adverse cardiovascular events (MACE) (10) and a 21–28% increased risk of PAD (11). Up to 34% of patients with DM will develop a foot ulcer over their lifetimes, 50% of which will become infected and require hospitalization or an emergency room visit (12, 13). Although many DM foot ulcers are neuropathic in origin, the prevalence of PAD in patients with a DM-related foot ulcer is 50%, and patients with both DM and PAD have 4 times greater risk of amputation than the national average (14).

### Peripheral Artery Disease and Smoking

Smoking is a major modifiable risk factor of PAD and is associated with a three- to fourfold increase in the risk of developing PAD (15). Unfortunately, registry data indicate that 22% of patients with symptomatic PAD continue to use tobacco (16). Cigarette smoking induces endothelial dysfunction, oxidative stress, and production of inflammatory and proatherogenic cytokines, causing a prothrombotic state with platelet aggregation and vasoconstriction (15). A dose–response relationship between smoking and the incidence of PAD has been demonstrated, and it has a significantly closer association than the relationship between smoking and coronary artery disease or stroke; even more disconcerting is that the elevated risk of PAD for smokers persists even after 30 years of smoking cessation (although it is still reduced compared to that of an active smoker) (17).

### Peripheral Artery Disease Risk Based on Sex, Race, and Ethnicity

Contrary to traditional belief, PAD does not affect men more than women (18). Rather, men are more likely to present with classic PAD symptoms, while women are more likely to have atypical

or asymptomatic disease (19). Recent population-based studies estimate that the prevalence of PAD in women may even be slightly higher than men (20). Overall, women are less likely to be prescribed optimal medical therapy for PAD, more likely to present with more severe disease, and less likely to have interventions for PAD than men (21, 22).

There are also significant race- and ethnicity-related risk factors for PAD that persist despite controlling for confounding variables. In a 2007 study evaluating data from seven community-based studies in the United States, Black men were found to have the highest prevalence of PAD compared to other racial and ethnic groups, as were Black women (23). A more recent study estimated lifetime risk of developing PAD to be 30% for Black men and 27% for Black women compared to 22% for Hispanic/Latino men and women and 19% for White men and women. In addition, this study found that despite adjusting for conventional risk factors, Black race independently increased the odds for developing PAD [adjusted odds ratio, 1.65; 95% confidence interval (CI), 1.48–1.84] (24).

## **PERIPHERAL ARTERY DISEASE–RELATED HEALTH DISPARITIES**

Significant variation in PAD-related amputation risk has been documented across socioeconomic, racial, ethnic, and geographic lines (25–31). While elevated prevalence of DM, cardiovascular disease, and tobacco use contributes to this risk, communities facing economic hardship and chronic external stressors experience disproportionately higher amputation rates (32), suggesting that health inequities and issues related to the social drivers of health may be at the root of these disparities.

A substantial body of literature details racial and ethnic disparities in PAD-related amputations (25, 33–45). Although these disparities are often attributed to confounding factors such as socioeconomic status and comorbidities, multiple studies have demonstrated that Black and Latino/Hispanic patients face higher risks of major amputation (above the ankle) than White patients, even after adjusting for disease severity, access to care, and other risk factors (25, 31, 33, 36, 39–41, 44). Similar findings have been reported in Native American/American Indian populations (46, 47). Geographic disparities also persist. Rural communities show consistently higher PAD-related amputation rates compared to urban areas, with rurality itself identified as a risk factor (13, 29, 30, 48). Intersectionality further compounds these inequities (49, 50). Examples include findings that rural Black patients have a higher risk for amputation than their urban Black counterparts (51), as well as higher-than-expected amputation rates for diabetic foot ulcers, beyond what would be anticipated if rural and racial risk factors were simply additive (52).

Of particular concern, race and ethnicity independently predict primary amputation (i.e., amputation without attempt at revascularization) (33, 36, 38, 39, 41, 44, 51, 53). This suggests the presence of additional, unmeasured contributors, including structural inequities (54, 55), implicit bias (56, 57), and potentially biological differences (55, 58), although researchers caution against interpreting race as a biological variable (59, 60).

## **PERIPHERAL ARTERY DISEASE SCREENING**

The role of screening for PAD in asymptomatic individuals has been debated for decades. Since 1996, the US Preventive Services Task Force (USPSTF) has advised against routine screening, citing insufficient evidence to assess benefits and harms, an opinion reaffirmed in 2005, 2013, and 2018 recommendations (4). In contrast, beginning as early as 2011 and formally by 2015, every major medical and surgical society involved in PAD management has recommended screening

high-risk asymptomatic individuals (5, 61). These include patients aged  $\geq 65$  years, individuals  $> 50$  years with atherosclerosis risk factors, and patients  $< 50$  years with DM and at least one other risk factor.

The ankle-brachial index (ABI), a noninvasive and inexpensive test, is the standard tool for PAD screening. Opponents argue that abnormal ABI results may prompt unnecessary advanced imaging, such as computed tomography angiography (CTA), magnetic resonance angiography (MRA), or invasive catheter-based angiography and overtreatment. A 2023 article from *The New York Times*, “They Lost Their Legs. Doctors and Health Care Giants Profited,” underscored the potential for harm when abnormal findings in asymptomatic individuals are exploited by aggressive practitioners (62). The USPSTF has also raised concerns about risks associated with initiating antiplatelet therapy or statins based solely on a PAD diagnosis.

Professional societies, including the American College of Cardiology, the American Heart Association, the Society for Vascular Surgery, and the Society for Interventional Radiology, strongly support targeted screening to reduce cardiovascular events and limb-related complications. In a 2018 joint response to the USPSTF, these groups highlighted four key concerns: (a) the USPSTF assessed screening in the general population rather than high-risk groups; (b) several important studies, including a Danish trial showing reduced mortality with screening, were excluded from consideration (6); (c) references opposing antiplatelet or statin use were of limited relevance; and (d) the recommendation may worsen disparities, particularly among non-White patients, who are more likely to present with atypical or asymptomatic PAD and are at greater risk for amputation (63).

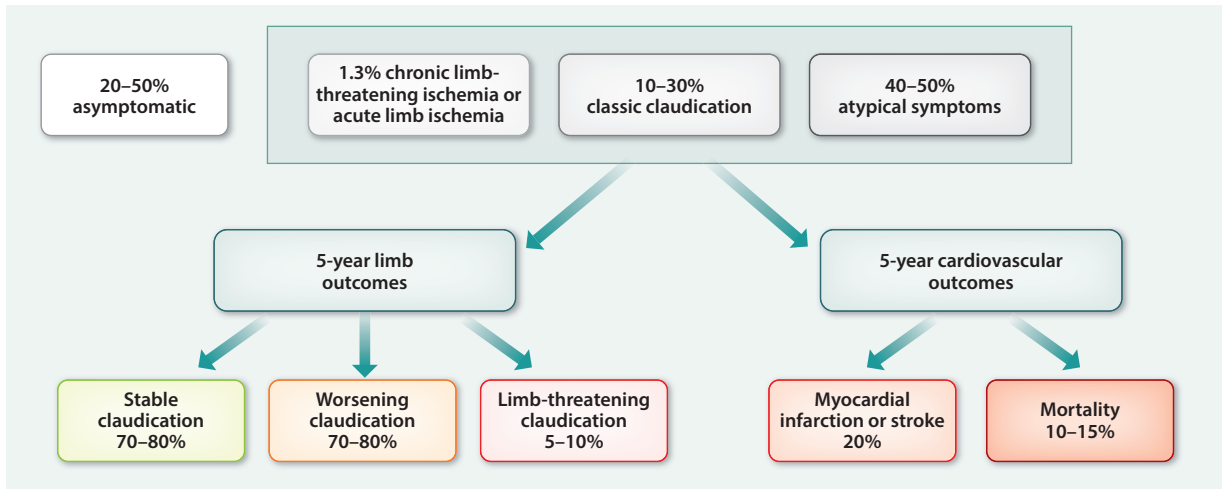
To address these gaps and improve access, several societies have supported the Amputation Reduction and Compassion Act, most recently reintroduced on January 9, 2025. The bill proposes Medicare and Medicaid coverage of PAD screening for high-risk individuals without cost sharing and includes provisions for education, alternative payment models, and quality measures aimed at reducing PAD-related amputations [H.R. Res. 307, 119th Cong. (2025)].

## PERIPHERAL ARTERY DISEASE CLINICAL PRESENTATION AND NATURAL HISTORY

The majority of patients with PAD either are asymptomatic (20–50%) or present with atypical symptoms (40–50%), while only 10–30% experience classic claudication, defined as exertional leg pain relieved within 10 minutes of rest. Just 1.3% initially present with limb-threatening ischemia (7) (**Figure 1**). Notably, many asymptomatic patients demonstrate functional impairment, having unconsciously modified their activity to avoid leg pain (64). Studies indicate that these individuals may be as limited as those with claudication, with many developing symptoms during objective walking tests (64, 65). Furthermore, asymptomatic PAD patients face a significantly increased 5-year risk of cardiovascular morbidity and mortality compared to those without PAD (66).

Patients with atypical leg symptoms may report pain at rest, discomfort that does not impede walking, or pain that inconsistently resolves with rest (67). These presentations often overlap with other conditions such as neuropathy, arthritis, or spinal stenosis, complicating diagnosis. As a result, patients may consult multiple specialists without receiving appropriate management for PAD, thus missing critical cardiovascular risk reduction strategies. Accordingly, patients with exertional leg symptoms and risk factors for atherosclerosis should be evaluated for PAD.

Among symptomatic PAD patients, the 5-year cardiovascular event or mortality risk may reach 20% (5). However, from a limb-related perspective, most patients will have stable or progressively worsening claudication, with only 5–10% progressing to limb-threatening ischemia (**Figure 1**).



**Figure 1**

Clinical presentation and 5-year limb and cardiovascular outcomes of people with symptomatic peripheral artery disease.

Limb-threatening ischemia includes chronic limb-threatening ischemia (CLTI) and acute limb ischemia (ALI). CLTI, defined by ischemic rest pain, nonhealing wounds, or gangrene lasting over 2 weeks, is the predominant form encountered in vascular surgery and accounts for most PAD-related amputations (68). ALI, by contrast, is a sudden reduction in limb perfusion that can result from embolism (e.g., atrial fibrillation, aneurysm) or in situ thrombosis of a native vessel or prior revascularization. In ALI, depending on the level of preexisting ischemia, limb viability can be compromised within 6 hours, requiring prompt revascularization.

## PERIPHERAL ARTERY DISEASE DIAGNOSIS

### History and Physical Exam

The presenting signs of PAD can be highly variable, and assessment begins with identifying patients at risk. This includes any patient  $\geq 65$  years, any patient  $> 50$  years with risk factors for atherosclerosis, and patients  $< 50$  years with DM and one atherosclerotic risk factor. Any patient with known atherosclerotic disease in another vascular bed should also be considered at increased risk. These patients require a comprehensive medical history to assess exertional leg symptoms, lower extremity rest pain, lower extremity wounds, and other ischemic skin changes. Location, frequency, exacerbating factors, and alleviating factors are all important for assessing leg pain as well. On physical exam, careful assessment for abnormal pulses should be performed, including the femoral, popliteal, dorsalis pedis, and posterior tibial arteries, taking care not to mistake the provider's own pulse for that of the patient. Additional physical exam findings include wounds, asymmetric hair growth, muscle atrophy, and dependent rubor (i.e., rubor that pales upon leg elevation).

In addition to a careful and thorough history, it is important to be aware of non-PAD etiologies of leg pain that may mimic PAD. These include musculoskeletal abnormalities, spinal disease, and neuropathy. The sidebar titled History and Physical Exam Findings with Peripheral Artery Disease and **Table 1** provide a thorough review of the history and physical exam findings pertinent to PAD as well as the differential diagnoses (1).

## HISTORY AND PHYSICAL EXAM FINDINGS WITH PERIPHERAL ARTERY DISEASE

### History

- Claudication
  - Aching, cramping, muscle fatigue, or discomfort causing a limp
  - Occurs in the muscle group(s) distal to the arterial occlusion (includes erectile dysfunction in aortoiliac occlusion)
  - Exacerbating factors are longer-than-typical distance, rushed pace or exercise, or uphill or uneven terrain
  - Alleviating factors include resolution within 10 min of no activity
  - Rule out joint pain, leg weakness without walking pain, pain that improves with movement, and pain that does not resolve within minutes
- Ischemic rest pain
  - Rule out isolated neuropathy without cardiovascular risk factors
- Nonhealing wound
  - Rule out venous leg ulcer (medial malleolus)

### Physical exam

- Sparse hair growth
- Dystrophic nails
- Dry or shiny skin
- Dependent rubor (and pallor with elevation)
- Weak pulse palpation (femoral, popliteal, dorsalis pedis, posterior tibial arteries)
- Gangrene
- Pedal ulcer or wound, especially if non- or slow-healing
- Anterior tibial wound, especially if non- or slow-healing

### Imaging

Diagnostic modalities for PAD range from noninvasive studies, such as the ABI and arterial duplex, to more invasive studies, including CTA, MRA, and angiography. It is important for the primary care practitioner to understand the role of each modality in the diagnosis and treatment of PAD, as well as the potential pitfalls.

**Table 1 Differential diagnoses for nonarterial leg pain**

Condition	Location(s)	Characteristics
Hip arthritis	Lateral hip, groin	Aching, not quickly relieved
Foot or ankle arthritis	Ankle, foot, arch	Aching, not quickly relieved
Nerve root compression	Radiates down leg	Sharp pain, improved with change in position and standing
Spinal stenosis (e.g., degenerative disc disease)	Bilateral buttocks, posterior legs	Relief with lumbar spine flexion, worse with standing
Popliteal (Baker's) cyst	Behind knee, upper calf	Calf tenderness, not intermittent
Venous claudication	Entire leg	Tight, bursting pain with walking; relieved with leg elevation
Chronic compartment syndrome	Anterior or posterior calf muscles	Tight, bursting pain in highly developed muscles or athletes

**Ankle-brachial index.** The ABI is a simple, noninvasive test that compares the blood pressure of the brachial artery to those of the pedal arteries. Blood pressure is checked using a cuff on each arm, and then on each leg. The ABI is the ratio of the higher systolic pressure in the ipsilateral dorsalis pedis and posterior tibial arteries divided by the higher of the left and right brachial artery systolic pressures (69). In symptomatic patients, a resting ABI has a sensitivity of 69% and a specificity of 83–99% (70). The normal range for the ABI is 0.9–1.2, and anything less than 0.9 is considered a positive study. In patients with symptoms consistent with claudication, but normal, or a borderline ABI, an exercise ABI can be performed. In this study, the patient ideally walks on a treadmill at an incline for 5 minutes or until they develop pain, and the ABI is measured immediately afterward (and at several time points until the numbers normalize). A positive test is defined as a decrease in ankle pressure of  $\geq 20$  mmHg, a  $\geq 20\%$  decrease from baseline, a decrease of the ABI of  $\geq 0.2$ , or failure of the ABI to return to baseline within 3 minutes. This test should not be performed if someone has an abnormal ABI at baseline. Some limitations to this test are reproducibility, as many vascular labs do not have access to treadmills, and patient limitations, as many high-risk patients are limited by other cardiovascular, pulmonary, and musculoskeletal issues.

**Toe-brachial index.** A major issue with the ABI is that its sensitivity drops dramatically in patients with DM and chronic kidney disease due to the medial calcinosis that affects their vessels (therefore making them difficult to compress and artificially elevating the readings). The digital arteries are less impacted by this process and therefore toe pressures, or toe-brachial indices (TBIs) can be used as an alternative study in patients with DM and chronic kidney disease. Of note, TBIs can still be inaccurate, and the addition of Doppler waveforms can help enhance sensitivity in this patient population (70).

Due to the increased interest in screening patients for PAD, a number of companies have arisen that offer ABI and TBI testing units that are not dependent on a vascular technologist and are more automated. These products represent a promising technology for individuals in low-resourced environments, who may not have easy access to a vascular lab. A review of these products is outside the scope of this article; however, these systems have varying degrees of accuracy and should be held against the known sensitivity and specificity of the ABI.

**Computed tomography angiography and magnetic resonance angiography.** Although valuable, CTA and MRA are not appropriate for confirmation of ABI findings or for making a diagnosis of PAD. The risks of the studies do not outweigh the benefits and should be reserved for use by specialists who may require them for surgical planning.

**Catheter angiography.** Catheter angiography is a fluoroscopic technique used to visualize the arterial anatomy using intra-arterial injection of contrast dye and X-rays. Angiography is an invasive procedure that carries risk of complications and is not indicated as a screening tool. There is no role for an angiogram in an asymptomatic patient to confirm a PAD diagnosis, and primary care practitioners should be wary of specialists who do disproportionately large numbers of diagnostic angiograms.

## PERIPHERAL ARTERY DISEASE TREATMENT

### Noninvasive Treatment

The nonsurgical management of PAD is critically important. Aggressive treatment of atherosclerosis prevents progressively worsening disease in the limb and also reduces the risk of MACE. In patients who do eventually require revascularization, patients who are already medically optimized have better surgical outcomes (71–73).

**Exercise.** Supervised exercise therapy is the most effective noninterventional approach to reduce symptoms of intermittent claudication. Regular walking increases calf blood flow, improves endothelial function, improves metabolic function, decreases inflammation, and improves pain-free walking distances (74). A Cochrane review of 32 randomized controlled trials concluded that exercise programs improved pain-free and maximum walking distances compared to usual care (75). A meta-analysis of 25 randomized controlled trials found that supervised treadmill exercise improved walking distance by 180 m compared to usual care (76). As of 2017, the Centers for Medicare and Medicaid Services provides insurance coverage for up to 36 sessions of supervised treadmill exercise over a 12-week period for patients diagnosed with claudication, but unfortunately, demand is greater than the available services. Further studies evaluating the effectiveness of structured community-based exercise programs, mobile applications, and distance coaching are underway, and funding mechanisms to improve access and availability of supervised exercise therapy are needed.

**Antithrombotic therapy.** In 2022, the USPSTF recommended against the use of daily aspirin for primary prevention of MACE in the general adult population (77). Patients with PAD, even asymptomatic PAD, have a higher cardiac risk profile than the general adult population, and expert consensus among vascular specialists is that patients with PAD and no contraindication should be prescribed an antithrombotic medication. The most commonly used drug is aspirin, but P2Y<sub>12</sub> receptor antagonists and low-dose direct oral anticoagulants are also used in patients with more complex disease and/or after revascularization. Although it should not be considered appropriate as a single-agent antiplatelet medication, cilostazol, a phosphodiesterase IIIa inhibitor, inhibits platelet aggregation, acts as a vasodilator, and improves pain-free walking distance when combined with an exercise program. A summary of clinical trials regarding selection of antithrombotic medications is available in **Supplemental Table 1**.

**Lipid-lowering therapy.** High-dose statins reduce mortality, MACE, and major adverse limb events and improve symptomatic outcomes in patients with PAD (78). A low-density lipoprotein goal of <70 mg/dL is recommended in all patients with PAD, but even if that goal is achieved with other drugs, high-dose statins like atorvastatin 40–80 mg or rosuvastatin 40 mg are recommended due to their pleomorphic effects. Namely, in translational studies, statins have been shown to improve endothelial function, inhibit smooth muscle proliferation, and stabilize plaque (79). In various clinical studies, starting high-intensity statins at the time of PAD diagnosis improved limb loss and mortality rates (80, 81).

## Operative Treatment

While all patients with PAD should be on optimal medical therapy and can benefit from supervised exercise therapy, revascularization is often needed to preserve a functional limb. For patients with intermittent claudication, the decision to pursue revascularization can be difficult depending on a patient's severity of limb-based symptoms, their comorbidity profile, the anatomical distribution of arterial occlusive disease, and the expected durability of the revascularization performed. Opinions regarding the threshold for intervention in patients with claudication, as well as what constitutes an appropriate intervention, vary widely across different surgical and interventional specialists. For the sake of transparency, both authors of this article are vascular surgeons and abide by the Society for Vascular Surgery's appropriate use criteria for intermittent claudication; this document provides a myriad of clinical scenarios to assist in decision-making (82).

For patients with CLTI, the goal of revascularization is to restore blood flow to the extremity to reduce pain, heal wounds, and/or prevent major limb amputation. The Society for Vascular Surgery's Wound, Ischemia, and Foot Infection staging system estimates the risk of limb

Supplemental Material >

amputation and the likelihood that revascularization will be of benefit (83). The 2019 global vascular guidelines on the management of CLTI describes many of the challenges in treating these patients, notes the weakness of many of the clinical recommendations, and reinforces the need for more prospective data to make strong, evidence-based plans that include a combination of medical and surgical therapies (68).

Due to the high degree of heterogeneity in clinical presentations, limb-based symptoms, patterns of occlusive disease, treatment durability, and life expectancy, there is significant debate around preferred revascularization strategies. Historically, long-segment arterial occlusions were treated with open surgical bypass, but the evolution of endovascular devices has allowed increasingly complex and long lesions to be treated percutaneously. In CLTI caused by infrainguinal occlusive disease, there are three randomized controlled trials comparing open to endovascular treatment:

- Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL-1), 2005. Amputation-free survival was similar at 6 months, but for the 70% who survived for 2 years, amputation-free survival was better in the open surgical bypass group (84).
- Bypass versus Angioplasty for Severe Ischaemia of the Leg with infrapopliteal disease (BASIL-2), 2023. The risk of limb amputation and death was higher in the open bypass group compared to the endovascular group (1.35; 95% CI, 1.02–1.80;  $p = 0.037$ ), but outcomes were largely driven by fewer deaths in the best endovascular treatment group (85).
- Surgery or Endovascular Therapy for Chronic Limb-Threatening Ischemia (BEST-CLI), 2022. Major adverse limb event-free survival was significantly better in patients who had bypass surgery using a single-segment great saphenous vein compared to best endovascular therapy (0.68; 95% CI, 0.59–0.79;  $p < 0.001$ ) (86).

**Open surgical techniques.** The general principle for surgical revascularization is to either remove or bypass the diseased arterial segment. Focal lesions in superficial locations such as the common femoral artery are often treated with thromboendarterectomy, wherein the artery is opened, the plaque is removed, and the artery is closed with a patch angioplasty to avoid restenosis. The most common complication, occurring in 7–16% of groin incisions, is surgical site infection (87, 88).

For longer and/or deeper occlusive disease that is prohibitive of endarterectomy, a bypass can be performed. This requires adequate arterial inflow and outflow vessels, as well as consideration of the conduit material and position. Autologous vein is the most durable conduit (89, 90) but must be at least 3 mm in diameter to be used. If no suitable vein is available, a variety of prosthetic conduits are available for revascularization, but long-term patency suffers. Complications after infrainguinal bypass surgery include surgical site infection and graft occlusion.

**Endovascular techniques.** The general principles of endovascular intervention center on choice of arterial access point and associated sheaths, catheters, and wires to reach and ultimately cross the lesion to be treated. Once the occlusion is crossed, the goal is to restore patency and reperfuse the distal tissue. Balloon angioplasty (including drug-coated balloons) with or without a stent is the mainstay of endovascular therapy. Multiple treatment adjuncts, such as atherectomy or intravascular lithotripsy, may remove or reshape bulky atherosclerotic plaques to improve the luminal gain achieved by balloon angioplasty. Due to the rapid pace of innovation and lack of comparative effectiveness trials (91), there are no clear guidelines on best endovascular therapy. Endovascular revascularization is less likely to be a durable treatment in smaller and more distal lesions, longer lesions, total occlusions, multifocal and multilevel disease, poor distal runoff, and recurrent stenoses (92, 93).

The most common complications of endovascular therapy are related to the access site, including hematoma, bleeding, pseudoaneurysm, or access artery occlusion (94). There is also the potential for distal embolization of plaque and loss of future bypass target vessels when endovascular therapy is used, and this should be considered when treating. Regardless of therapy type selected (i.e., open or endovascular), reocclusion and disease progression are common issues, and surveillance with ultrasound and lifelong follow-up with reintervention are necessary to maintain long-term patency.

## CONCLUSIONS

PAD remains a major public health concern with significant implications for cardiovascular morbidity, limb loss, and health equity. Despite advances in diagnosis and treatment, underrecognition and disparities in care persist, particularly among racially and socioeconomically marginalized populations. Improving outcomes requires early identification of at-risk patients, appropriate use of noninvasive diagnostics, and timely initiation of guideline-directed therapies. Equally critical is addressing structural barriers to care and expanding access to screening and treatment through policy initiatives. A multifaceted approach is essential to reduce preventable amputations and close the persistent gaps in PAD-related health outcomes.

## DISCLOSURE STATEMENT

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## LITERATURE CITED

1. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VES guideline for the management of lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J. Am. Coll. Cardiol.* 83:2497–604
2. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. 2001. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 286:1317–24
3. Bridgwood BM, Nickinson AT, Houghton JS, et al. 2020. Knowledge of peripheral artery disease: What do the public, healthcare practitioners, and trainees know? *Vasc. Med.* 25:263–73
4. US Preventive Services Task Force. 2018. Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index: US Preventive Services Task Force recommendation statement. *JAMA* 320:177–83
5. Society for Vascular Surgery Lower Extremity Guidelines Writing Group, Conte MS, Pomposelli FB, et al. 2015. Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: management of asymptomatic disease and claudication. *J. Vasc. Surg.* 61:2S–41S.e1

6. Lindholt JS, Søgaard R. 2017. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet* 390:2256–65
7. Criqui MH, Matsushita K, Aboyans V, et al. 2021. Lower extremity peripheral artery disease: contemporary epidemiology, management gaps, and future directions: a scientific statement from the American Heart Association. *Circulation* 144:e171–91
8. Fowkes FG, Rudan D, Rudan I, et al. 2013. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 382:1329–40
9. Barnes JA, Eid MA, Creager MA, Goodney PP. 2020. Epidemiology and risk of amputation in patients with diabetes mellitus and peripheral artery disease. *Arterioscler. Thromb. Vasc. Biol.* 40:1808–17
10. Althouse AD, Abbott JD, Forker AD, et al. 2014. Risk factors for incident peripheral arterial disease in type 2 diabetes: results from the Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes (BARI 2D) Trial. *Diabetes Care* 37:1346–52
11. Adler AI, Stevens RJ, Neil A, et al. 2002. UKPDS 59: hyperglycemia and other potentially modifiable risk factors for peripheral vascular disease in type 2 diabetes. *Diabetes Care* 25:894–99
12. Armstrong DG, Boulton AJM, Bus SA. 2017. Diabetic foot ulcers and their recurrence. *N. Engl. J. Med.* 376:2367–75
13. Skrepnek GH, Mills JL Sr., Armstrong DG. 2015. A diabetic emergency one million feet long: disparities and burdens of illness among diabetic foot ulcer cases within emergency departments in the United States, 2006–2010. *PLOS ONE* 10:e0134914
14. Stoberock K, Kaschwich M, Nicolay SS, et al. 2021. The interrelationship between diabetes mellitus and peripheral arterial disease: a systematic review. *Vasa* 50:323–30
15. Behrooz L, Abumoawad A, Rizvi SHM, Hamburg NM. 2023. A modern day perspective on smoking in peripheral artery disease. *Front. Cardiovasc. Med.* 10:1154708
16. Cაცობ PP, Abola MT, Baumgartner I, et al. 2009. Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Continued Health (REACH) Registry. *Atherosclerosis* 204:e86–92
17. Ding N, Sang Y, Chen J, et al. 2019. Cigarette smoking, smoking cessation, and long-term risk of 3 major atherosclerotic diseases. *J. Am. Coll. Cardiol.* 74:498–507
18. Criqui MH, Fronek A, Barrett-Connor E, et al. 1985. The prevalence of peripheral arterial disease in a defined population. *Circulation* 71:510–15
19. Porras CP, Bots ML, Teraa M, et al. 2022. Differences in symptom presentation in women and men with confirmed lower limb peripheral artery disease: a systematic review and meta-analysis. *Eur. J. Vasc. Endovasc. Surg.* 63:602–12
20. Sigvant B, Wiberg-Hedman K, Bergqvist D, et al. 2007. A population-based study of peripheral arterial disease prevalence with special focus on critical limb ischemia and sex differences. *J. Vasc. Surg.* 45:1185–91
21. Kim S, Pendleton AA, McGinagle KL. 2022. Women’s vascular health: peripheral artery disease in female patients. *Semin. Vasc. Surg.* 35:155–61
22. McGinagle KL, Browder SE, Strassle PD, et al. 2021. Sex-related disparities in intervention rates and type of intervention in patients with aortic and peripheral arterial diseases in the National Inpatient Sample Database. *J. Vasc. Surg.* 73:2081–89.e7
23. Allison MA, Armstrong DG, Goodney PP, et al. 2023. Health disparities in peripheral artery disease: a scientific statement from the American Heart Association. *Circulation* 148:286–96
24. Matsushita K, Sang Y, Ning H, et al. 2019. Lifetime risk of lower-extremity peripheral artery disease defined by ankle-brachial index in the United States. *J. Am. Heart Assoc.* 8:e012177
25. Feinglass J, Abadin S, Thompson J, Pearce WH. 2008. A census-based analysis of racial disparities in lower extremity amputation rates in Northern Illinois, 1987–2004. *J. Vasc. Surg.* 47:1001–7
26. Tseng C-L, Helmer D, Rajan M, et al. 2007. Evaluation of regional variation in total, major, and minor amputation rates in a national health-care system. *Int. J. Qual. Health Care* 19:368–76
27. Stevens CD, Schriger DL, Raffetto B, et al. 2014. Geographic clustering of diabetic lower-extremity amputations in low-income regions of California. *Health Aff.* 33:1383–90
28. Margolis DJ, Hoffstad O, Nafash J, et al. 2011. Location, location, location: geographic clustering of lower-extremity amputation among Medicare beneficiaries with diabetes. *Diabetes Care* 34:2363–67

29. Minc SD, Hendricks B, Misra R, et al. 2019. Geographic variation in amputation rates among patients with diabetes and/or peripheral arterial disease in the rural state of West Virginia identifies areas for improved care. *J. Vasc. Surg.* 71:1708–17.e5
30. McGinigle KL, Kalbaugh CA, Marston WA. 2014. Living in a medically underserved county is an independent risk factor for major limb amputation. *J. Vasc. Surg.* 59:737–41
31. Arya S, Binney Z, Khakharia A, et al. 2018. Race and socioeconomic status independently affect risk of major amputation in peripheral artery disease. *J. Am. Heart Assoc.* 7:e007425
32. Dircksen J, Prachand N, Adams D, et al. 2016. *Healthy Chicago 2.0: partnering to improve health equity, 2016–2020*. Rep., Chicago Department of Public Health. [https://www.chicago.gov/content/dam/city/depts/cdph/CDPH/HC2.0Plan\\_3252016.pdf](https://www.chicago.gov/content/dam/city/depts/cdph/CDPH/HC2.0Plan_3252016.pdf)
33. Tunis SR, Bass EB, Klag MJ, Steinberg EP. 1993. Variation in utilization of procedures for treatment of peripheral arterial disease: a look at patient characteristics. *Arch. Intern. Med.* 153:991–98
34. Lavery LA, Ashry HR, van Houtum W, et al. 1996. Variation in the incidence and proportion of diabetes-related amputations in minorities. *Diabetes Care* 19:48–52
35. Lavery LA, van Houtum WH, Ashry HR, et al. 1999. Diabetes-related lower-extremity amputations disproportionately affect Blacks and Mexican Americans. *South. Med. J.* 92:593–99
36. Collins TC, Johnson M, Henderson W, et al. 2002. Lower extremity nontraumatic amputation among veterans with peripheral arterial disease: Is race an independent factor? *Med. Care* 40:1106–16
37. Rucker-Whitaker C, Feinglass J, Pearce W. 2003. Explaining racial variation in lower extremity amputation: a 5-year retrospective claims data and medical record review at an urban teaching hospital. *Arch. Surg.* 138:1347–51
38. Eslami MH, Zayaruzny M, Fitzgerald GA. 2007. The adverse effects of race, insurance status, and low income on the rate of amputation in patients presenting with lower extremity ischemia. *J. Vasc. Surg.* 45:55–59
39. Abou-Zamzam AM Jr., Gomez NR, Molkara A, et al. 2007. A prospective analysis of critical limb ischemia: factors leading to major primary amputation versus revascularization. *Ann. Vasc. Surg.* 21:458–63
40. Henry AJ, Hevelone ND, Belkin M, Nguyen LL. 2011. Socioeconomic and hospital-related predictors of amputation for critical limb ischemia. *J. Vasc. Surg.* 53:330–39.e1
41. Durazzo TS, Frencher S, Gusberg R. 2013. Influence of race on the management of lower extremity ischemia: revascularization versus amputation. *JAMA Surg.* 148:617–23
42. Regenbogen SE, Gawande AA, Lipsitz SR, et al. 2009. Do differences in hospital and surgeon quality explain racial disparities in lower-extremity vascular amputations? *Ann. Surg.* 250:424–31
43. Barshes NR, Sharath S, Zamani N, et al. 2018. Racial and geographic variation in leg amputations among Texans. *Tex. Public Health J.* 70:22–27
44. Feinglass J, Rucker-Whitaker C, Lindquist L, et al. 2005. Racial differences in primary and repeat lower extremity amputation: results from a multihospital study. *J. Vasc. Surg.* 41:823–29
45. Limb Loss Task Force/Amputee Coalition. 2012. *Roadmap for preventing limb loss in America: recommendations from the 2012 Limb Loss Task Force*. Rep., Amputee Coalition. [https://static1.squarespace.com/static/54f8bdc9e4b05ef254a56822/t/570eb76f1d07c0c60ec2bbb8/1460582291787/lsp\\_Roadmap-for-Limb-Loss-Prevention-and-Amputee-Care-Improvement\\_291214-042841+%281%29.pdf](https://static1.squarespace.com/static/54f8bdc9e4b05ef254a56822/t/570eb76f1d07c0c60ec2bbb8/1460582291787/lsp_Roadmap-for-Limb-Loss-Prevention-and-Amputee-Care-Improvement_291214-042841+%281%29.pdf)
46. Rizzo JA, Chen J, Laurich C, et al. 2018. Racial disparities in PAD-related amputation rates among Native Americans and non-Hispanic whites: an HCUP analysis. *J. Health Care Poor Underserved* 29:782–800
47. Tan TW, Shih C-D, Concha-Moore KC, et al. 2019. Disparities in outcomes of patients admitted with diabetic foot infections. *PLOS ONE* 14:e0211481
48. Peacock JM, Keo HH, Duval S, et al. 2011. The incidence and health economic burden of ischemic amputation in Minnesota, 2005–2008. *Prev. Chronic Dis.* 8:A141
49. Carbado DW, Crenshaw KW, Mays VM, Tomlinson B. 2013. INTERSECTIONALITY: mapping the movements of a theory. *Du Bois Rev. Soc. Sci. Res. Race* 10:303–12
50. Heard E, Fitzgerald L, Wigginton B, Mutch A. 2020. Applying intersectionality theory in health promotion research and practice. *Health Promot. Int.* 35:866–76
51. Minc SD, Goodney PP, Misra R, et al. 2020. The effect of rurality on the risk of primary amputation is amplified by race. *J. Vasc. Surg.* 72:1011–17

52. Brennan MB, Powell WR, Kaikow F, et al. 2022. Association of race, ethnicity, and rurality with major leg amputation or death among Medicare beneficiaries hospitalized with diabetic foot ulcers. *JAMA Netw. Open* 5:e228399
53. Minc SD, Fogg LF, McCarthy WJ, Shah RC. 2017. Racial disparities in primary amputation vs revascularization for critical limb ischemia: a meta-analysis. *J. Am. Coll. Surg.* 225:e78
54. Geronimus AT, Bound J, Waidmann TA, et al. 2019. Weathering, drugs, and whack-a-mole: fundamental and proximate causes of widening educational inequity in U.S. life expectancy by sex and race, 1990–2015. *J. Health Soc. Behav.* 60:222–39
55. Sidawy AN, Schweitzer EJ, Neville RF, et al. 1990. Race as a risk factor in the severity of infragenicular occlusive disease: study of an urban hospital patient population. *J. Vasc. Surg.* 11:536–43
56. Santry HP, Wren SM. 2012. The role of unconscious bias in surgical safety and outcomes. *Surg. Clin. N. Am.* 92:137–51
57. Kalbaugh CA, Beidelman ET, Howard KA, et al. 2025. Implicit racial bias and unintentional harm in vascular care. *JAMA Surg.* 160:536–43
58. Gardner AW, Montgomery PS, Blevins SM, Parker DE. 2010. Gender and ethnic differences in arterial compliance in patients with intermittent claudication. *J. Vasc. Surg.* 51:610–15
59. Witzig R. 1996. The medicalization of race: scientific legitimization of a flawed social construct. *Ann. Intern. Med.* 125:675–79
60. Smedley A, Smedley BD. 2005. Race as biology is fiction, racism as a social problem is real: anthropological and historical perspectives on the social construction of race. *Am. Psychol.* 60:16–26
61. Rooke TW, Hirsch AT, Misra S, et al. 2011. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J. Am. Coll. Cardiol.* 58:2020–45
62. Thomas K, Silver-Greenberg J, Gebeloff R. 2023. They lost their legs. Doctors and health care giants profited. *The New York Times*, July 15. <https://www.nytimes.com/2023/07/15/health/atherectomy-peripheral-artery-disease.html>
63. American College of Cardiology, American College of Radiology, American Heart Association, Society for Vascular Medicine, Society of Interventional Radiology. 2018. *Joint comments to USPSTF on PAD ABI screening*. Rep., American College of Cardiology, American College of Radiology, American Heart Association, Society for Vascular Medicine, Society of Interventional Radiology. [https://www.heart.org/-/media/Files/Get-Involved/Advocacy/Joint-Comments-to-USPSTF-on-PAD-ABI-Screening-021218.pdf?sc\\_lang=en](https://www.heart.org/-/media/Files/Get-Involved/Advocacy/Joint-Comments-to-USPSTF-on-PAD-ABI-Screening-021218.pdf?sc_lang=en)
64. McDermott MM, Guralnik JM, Ferrucci L, et al. 2008. Asymptomatic peripheral arterial disease is associated with more adverse lower extremity characteristics than intermittent claudication. *Circulation* 117:2484–91
65. McDermott MM, Applegate WB, Bonds DE, et al. 2013. Ankle brachial index values, leg symptoms, and functional performance among community-dwelling older men and women in the lifestyle interventions and independence for elders study. *J. Am. Heart Assoc.* 2:e000257
66. Diehm C, Allenberg JR, Pittrow D, et al. 2009. Mortality and vascular morbidity in older adults with asymptomatic versus symptomatic peripheral artery disease. *Circulation* 120:2053–61
67. McDermott MM, Mehta S, Greenland P. 1999. Exertional leg symptoms other than intermittent claudication are common in peripheral arterial disease. *Arch. Intern. Med.* 159:387–92
68. Conte MS, Bradbury AW, Kolh P, et al. 2019. Global vascular guidelines on the management of chronic limb-threatening ischemia. *J. Vasc. Surg.* 69:3S–125S.e40
69. Aboyans V, Criqui MH, Abraham P, et al. 2012. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation* 126:2890–909
70. Tehan PE, Bray A, Chuter VH. 2016. Non-invasive vascular assessment in the foot with diabetes: sensitivity and specificity of the ankle brachial index, toe brachial index and continuous wave Doppler for detecting peripheral arterial disease. *J. Diabetes Compl.* 30:155–60
71. McGinagle KL, Kindell DG, Strassle PD, et al. 2020. Poor glycemic control is associated with significant increase in major limb amputation and adverse events in the 30-day postoperative period after infrainguinal bypass. *J. Vasc. Surg.* 72:987–94

72. Menard MT, Jaff MR, Farber A, et al. 2023. Baseline modern medical management in the BEST-CLI trial. *J. Vasc. Surg.* 78:711–18.e5
73. Poldermans D, Bax JJ, Kertai MD, et al. 2003. Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. *Circulation* 107:1848–51
74. Hamburg NM, Creager MA. 2017. Pathophysiology of intermittent claudication in peripheral artery disease. *Circ. J.* 81:281–89
75. Lane R, Harwood A, Watson L, Leng GC. 2017. Exercise for intermittent claudication. *Cochrane Database Syst. Rev.* 12:CD000990
76. Fakhry F, van de Luijngaarden KM, Bax L, et al. 2012. Supervised walking therapy in patients with intermittent claudication. *J. Vasc. Surg.* 56:1132–42
77. US Preventive Services Task Force. 2022. Aspirin use to prevent cardiovascular disease: US Preventive Services Task Force Recommendation Statement. *JAMA* 327:1577–84
78. Skeik N, Nowariak ME, Smith JE, et al. 2021. Lipid-lowering therapies in peripheral artery disease: a review. *Vasc. Med.* 26:71–80
79. Liao JK, Laufs U. 2005. Pleiotropic effects of statins. *Annu. Rev. Pharmacol. Toxicol.* 45:89–118
80. Arya S, Khakharia A, Binney ZO, et al. 2018. Association of statin dose with amputation and survival in patients with peripheral artery disease. *Circulation* 137:1435–46
81. Schanzer A, Hevelone N, Owens CD, et al. 2008. Statins are independently associated with reduced mortality in patients undergoing infrainguinal bypass graft surgery for critical limb ischemia. *J. Vasc. Surg.* 47:774–81.e1
82. Woo K, Siracuse JJ, Klingbeil K, et al. 2022. Society for Vascular Surgery appropriate use criteria for management of intermittent claudication. *J. Vasc. Surg.* 76:3–22.e1
83. Mills JL Sr., Conte MS, Armstrong DG, et al. 2014. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIFI). *J. Vasc. Surg.* 59:220–34.e2
84. Adam DJ, Beard JD, Cleveland T, et al. 2005. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL): multicentre, randomised controlled trial. *Lancet* 366:1925–34
85. Bradbury AW, Moakes CA, Popplewell M, et al. 2023. A vein bypass first versus a best endovascular treatment first revascularisation strategy for patients with chronic limb threatening ischaemia who required an infra-popliteal, with or without an additional more proximal infra-inguinal revascularisation procedure to restore limb perfusion (BASIL-2): an open-label, randomised, multicentre, phase 3 trial. *Lancet* 401:1798–809
86. Farber A, Menard MT, Conte MS, et al. 2022. Surgery or endovascular therapy for chronic limb-threatening ischemia. *N. Engl. J. Med.* 387:2305–16
87. Langenberg JCM, te Slaa A, de Groot HGW, et al. 2018. Infection risk following common femoral artery endarterectomy versus a hybrid procedure. *Ann. Vasc. Surg.* 53:148–53
88. Walker H, Chana MS, Mandalia K, et al. 2024. Observational study on the risk of surgical site infection in patients undergoing common femoral endarterectomy in conjunction with an endovascular procedure compared with common femoral endarterectomy alone. *EJVES Vasc. Forum* 61:116–20
89. Klinkert P, Schepers A, Burger DH, et al. 2003. Vein versus polytetrafluoroethylene in above-knee femoropopliteal bypass grafting: five-year results of a randomized controlled trial. *J. Vasc. Surg.* 37:149–55
90. Pomposelli FB, Kansal N, Hamdan AD, et al. 2003. A decade of experience with dorsalis pedis artery bypass: analysis of outcome in more than 1000 cases. *J. Vasc. Surg.* 37:307–15
91. Subherwal S, Patel MR, Chiswell K, et al. 2014. Clinical trials in peripheral vascular disease: pipeline and trial designs: an evaluation of the ClinicalTrials.gov database. *Circulation* 130:1812–19
92. Robinson WP III, Nguyen LL, Bafford R, Belkin M. 2011. Results of second-time angioplasty and stenting for femoropopliteal occlusive disease and factors affecting outcomes. *J. Vasc. Surg.* 53:651–57
93. Park UJ, Kim HT, Roh Y-N. 2018. Impact of tibial runoff on outcomes of endovascular treatment for femoropopliteal atherosclerotic lesions. *Vasc. Endovasc. Surg.* 52:498–504
94. Hackl G, Gary T, Belaj K, et al. 2015. Risk factors for puncture site complications after endovascular procedures in patients with peripheral arterial disease. *Vasc. Endovasc. Surg.* 49:160–65