Peripheral Artery Disease
Overview of Diagnosis and Medical Therapy

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KEYWORDS

• Peripheral artery disease • Claudication • Ankle-brachial index • Limb ischemia

KEY POINTS

- Peripheral artery disease (PAD) is very common and affects approximately 230 and 5 million people worldwide and nationally, respectively.
- Race and socioeconomic status have profound impacts on PAD outcomes.
- PAD is an underrecognized and undertreated medical condition.

EPIDEMIOLOGY

The worldwide prevalence of peripheral artery disease (PAD) is estimated to be 5% with approximately 230 million people affected by this disease globally.[1] In the United States, at least 5 million people are impacted by this condition, as per the National Health and Nutrition Examination Survey conducted from 1999 to 2004. Within that cohort, PAD prevalence was significantly higher among those with low income and lower levels of education.[2] Specifically, those in the lowest income group had a greater than a twofold increased odds of PAD compared with the highest income group. Globally, low- and middle-income regions saw a near 30% increase in PAD from 2000 to 2010 compared with a 13% increase in high-income regions.[3]

Racial disparities also exist with a higher prevalence among black men when compared with non-Hispanic and Caucasian men.[4] Prevalence was similar between Hispanic, American Indian, and Caucasian men. Of note, Asian men had the lowest prevalence. Such trends were similar among women, other than Indian American women having similar prevalence to black women.[4] The overall lifetime estimate of PAD is 20% for Caucasians and 30% for black patients.[5]

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Key Points

- PAD is very common and affects approximately 230 and 5 million people worldwide and nationally, respectively.
- There is a higher prevalence of PAD in black patients, with an overall lifetime estimate of 30% for these individuals compared with 20% for Caucasians.

RISK FACTORS

Risk factors associated with the development of PAD are like its counterpart, coronary artery disease (CAD). Such risk factors include age, family history, socioeconomic status (SES), tobacco smoking, diabetes mellitus, and hypertension (systolic pressure).[2,4,6–9] Neither sex[10,11] nor low-density lipoprotein (LDL) levels[12,13] have consistently correlated to an increased risk of PAD. However, multiple studies have found a link between high-density lipoprotein (HDL) levels and total cholesterol:HDL levels and PAD.[13–15] Of note, tobacco smoking is the strongest risk factor, followed closely by diabetes.[3]

The Scottish Heart Health Extended Cohort examined over 15,000 individuals aged 30 to 75 years who had either PAD or CAD, but not both, and followed the participants for 15 to 25 years. Although many of the risk factors discussed above overlapped between the two conditions, in the PAD population, tobacco smoking and inflammatory markers dominated, whereas cholesterol levels and body mass index (BMI) were less consistent risk factors. Specifically, increasing age, C-reactive protein levels, tobacco smoking, systolic blood pressure, and SES delegated the highest hazard ratios for PAD.[16]

Key Points

- The risk factors for PAD overlap for CAD. However, inflammatory markers, increasing age, and SES are associated with greater hazard ratios for PAD compared with CAD.
- Tobacco smoking is the strongest risk factor for PAD.

SOCIOECONOMIC AND RACIAL DISPARITIES

Although low SES has been linked with worse outcomes for CAD, diabetes, hypertension, and smoking, previously there was little research on SES and PAD outcomes. However, over the past few years, several studies have highlighted the negative impact on outcomes in PAD associated with low SES and race. Specifically, low SES was associated with higher rates of amputation not only across every race, but also within each subgroup of race (ie, diabetics, CKD).[17] Several studies have highlighted the vast disparities of PAD outcomes within metropolitan areas. Zip codes with lower SES were associated with higher amputation rates, even with adjustments for clinical and demographic factors.[18] Furthermore, within these low SES zip codes, black patients overwhelmingly account for the vast majority of these cases. Not surprisingly, zip codes associated with high numbers of black residents were associated with some of the highest amputation rates.[18] Black patients, on average, were two- to threefold more likely to have an amputation when admitted to the hospital with critical limb ischemia compared with their white counterparts.[19] Among Medicare beneficiaries, black patients were less likely than their white counterparts to be offered limb-salvaging procedures, likely due to a combination of more severe disease and racial biases in health care.[20] Black patients were also more likely to have higher incidences of femoral-tibial or popliteal-tibial bypass when compared with whites.[21] This is likely due to blacks, on average, having more severe PAD at the time of the initial

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diagnosis when compared with whites[20,22,23] and in part due to blacks having lower rates of prescriptions for statin and antiplatelet agents.[17]

Key Points

- Race and SES have profound impacts on PAD outcomes.
- Zip codes with low SES have the highest amputation rates.
- Black patients are more likely than Caucasians to undergo an amputation when admitted to the hospital and are less likely to be offered limb-salvaging procedures.

CLINICAL PRESENTATION AND DIAGNOSIS

The initial diagnosis of PAD remains a challenge for providers as nearly 50% of patients with PAD are unaware of their disease along with 30% of providers being unaware of their patients having PAD.[24] The clinical diagnosis is made even more challenging as only 10% of patients will present with classic intermittent claudication symptoms, whereas 50% will have atypical symptoms such as exertional lower extremity pain that does not resolve with rest or discomfort that does not consistently limit exercise at increasing distances. The remaining 40% will be asymptomatic.[25] A greater likelihood of atypical symptoms is likely due in part to the common comorbidities that accompany patients with PAD, such as arthritis, neuropathy, spinal canal pathology, fibromyalgia, and chronic pain syndromes.[26–28]

For these reasons, clinicians should be more cognizant of the possibility of PAD, particularly for patients with risk factors for this condition, and incorporate a pulse and skin assessment as a routine part of the examination for patients over the age of 40 years or those with the aforementioned risk factors. Findings such as pale white skin with elevation, erythema with limb lowering, areas of hair loss, poor wound healing, and in severe cases, distal ulceration can be seen. Palpation of peripheral pulses of the extremities usually reveals diminished or absent pulses distal to the site of stenosis. If one is unable to feel a pulse at a certain location, use of Doppler, if available, can be helpful to further assess the likelihood of PAD. A bruit may be heard at the interface between the stenotic lesion and upstream blood flow. Of note, the presence of either a diminished pulse or bruit significantly increases the likelihood of PAD.[29] **Fig. 1** provides an overview of the evaluation of a patient with suspected PAD.

A resting ankle-brachial index (ABI) should be performed on any patient, in which there is suspicion for PAD. In symptomatic individuals, a resting ABI of less than or equal to 0.90 is nearly 95% sensitive for detecting arteriogram-positive PAD and 100% specific in identifying healthy individuals.[30] Several studies have also correlated ABI cutoffs with symptom severity. These categories are as follows: ABI 0.9 to 0.4 is associated with intermittent claudication, ABI 0.4 to 0.2 is associated with rest pain, and ABI 0.4 to 0 is associated with gangrene/ulcers.[31–33] In addition, an ABI less than 0.90 correlated with a significant increased risk of 10-year cardiovascular mortality in both men and women with hazard ratios of 2.9 and 3.0, with adjustment for Framingham Risk Scoring.[34] Although the ABI has high diagnostic capability for detecting PAD, it is unable to reliably judge the severity or anatomical location of the vessel stenosis. Such patients should be referred to a vascular expert and additional imaging should be obtained such as duplex ultrasonography, computed tomography angiography (CTA), magnetic resonance angiography (MRA), or angiography. Of note, an ABI greater than 1.4 is also considered abnormal and usually indicates noncompressible vasculature, usually due to severe

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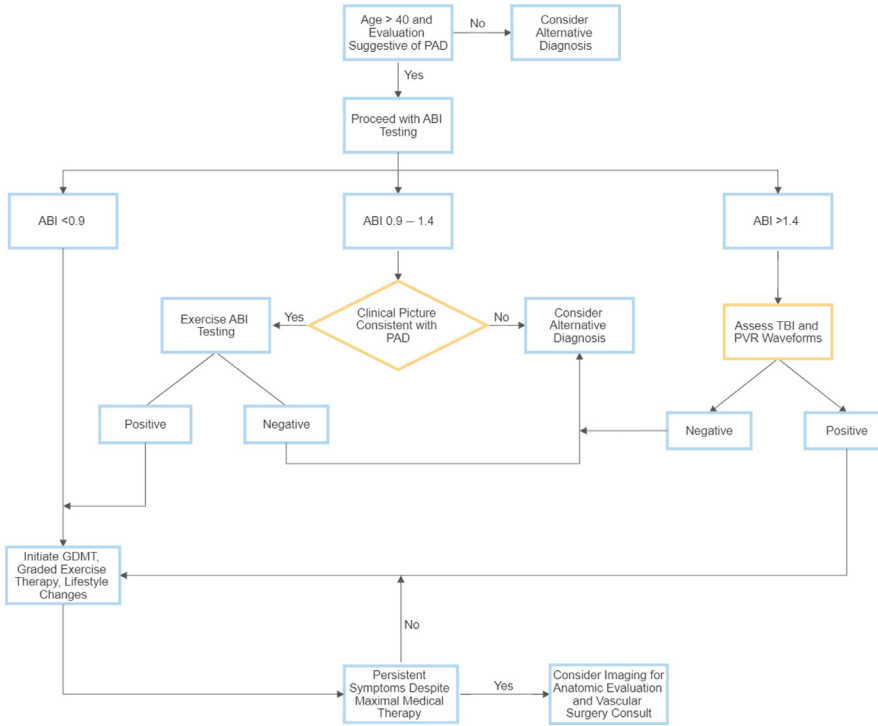

Fig. 1. An overview of the evaluation of a patient with suspected PAD. ABI, ankle brachial index; TBI, toe brachial index; PVR, pulse volume recording.

vessel calcification. Most common among those with diabetes, this finding should also be further investigated as ABIs greater than 1.4 correlate with major adverse cardiovascular events (MACEs).[35–37] A low toe-brachial index (TBI) is sometimes used in place of the ABI to diagnose PAD in patients with noncompressible vessels.[38,39]

For those patients who have symptoms suggestive of PAD, but a normal resting ABI, exercise testing is recommended. Although the American Heart Association (AHA) criteria for a postexercise ABI decrease of greater than 20% are widely used,[38] other methods including measuring transcutaneous PO_2 during exercise (with > 15 mm Hg delta of PO_2 being diagnostic of PAD) are also becoming widely accepted.[40–42] Using a combination of the above criteria including a postexercise ABI measurement (defined as a decrease of $\geq$ to 18.5%) and changes in the postexercise $TcPO_2$ demonstrated a significantly higher overall sensitivity.[43]

Key Points

- Fifty percent of patients with PAD are unaware of their disease, whereas 30% of providers do not know that their patients have PAD.
- Most of the patients with PAD either have atypical symptoms or are asymptomatic. Most patients with PAD *do not* present with classic, intermittent claudication.
- An ABI has excellent sensitivity and specificity for diagnosing PAD.
- An exercise ABI should be pursued in patients with a high suspicion for PAD who have a normal, resting ABI.

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DISEASE CLASSIFICATION SCHEMES

Several classification schemes exist to stratify patients based on their initial disease burden. These systems are not intended to guide treatment decisions, but rather attempt to quantify disease burden and prognosis.

Both the Rutherford classification and Fontaine system have been widely used for decades. These classification schematics grade the severity of walking impairment using treadmill testing and a specific walking distance, respectively.[44,45] They also account for pain at rest as well as any tissue damage/loss associated with ischemic ulceration/gangrene. These classification systems were originally created to grade the severity of ischemia in patients with PAD alone but are becoming less reliable given the rising prevalence of diabetes, neuropathy, and other chronic illnesses that decrease the diagnostic usefulness of these systems through common symptomatology. The Wound, Ischemia, foot, Infection (WIfI) schematic, which uses a 0 to 3 scale to grade any wounds, severity of ischemia, and severity of foot infection if present, has become widely popular among vascular surgery societies as it is useful not only for initial staging of disease burden but also for restaging after intervention. The use of this scale has been validated by several studies demonstrating correlation with wound healing rate and time after 1 year.[46–48] It has also been helpful in determining the 1-year risk for major amputation rates.[49] Anatomical classification schemes also exist, such as the Trans-Atlantic Inter-Society Consensus, which defines arterial lesions as Type A, B, C, or D using anatomic distribution, number of lesions, types of lesions (stenosis, occlusions) and the predicted success rate of treatment using endovascular or surgical intervention. Such systems guide surgeons in treatment decisions, as short segments of vascular disease may be appropriately managed with endovascular intervention, while longer, more heavily occluded segments may require more aggressive surgical management.[30]

Key Points

- Several classification schemes exist to categorize PAD.
- The WIfI scheme is now endorsed by multiple societies to classify patients with limb-threatening ischemia.

MEDICAL THERAPY

Asymptomatic Disease

Patients with asymptomatic PAD represent a unique population that is poorly understood. Two large randomized clinical trials, the Prevention of Progression of Arterial Disease and Diabetes trial and the Aspirin for Asymptomatic Atherosclerosis trial, investigated the effect of aspirin on cardiovascular outcomes in patients with asymptomatic PAD.[50,51] Both trials found no significant difference in cardiovascular or cerebrovascular events between the aspirin and placebo groups. The American Heart Association/American College of Cardiology Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease from 2016 concluded that it is reasonable (grade IIa recommendation) to start antiplatelet therapy in patients with asymptomatic PAD if they have an ABI $\leq$ 0.9 to reduce the risk of major MACEs.[38] Because of a lack of proven benefit, the 2017 European Society of Cardiology Guideline on PAD did not recommend the routine use of antiplatelet therapy in patients with asymptomatic, isolated PAD.[52] The benefit of statin therapy in patients with asymptomatic PAD who lack other evidence of cardiovascular disease is also unclear. The American College of Cardiology suggests that statin therapy should be considered in all individuals with an atherosclerotic cardiovascular disease

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(ASCVD) risk greater than 7.5%, which is commonly the case in all individuals with PAD.[53]

Key Points

- Randomized clinical trials did not show a cardiovascular benefit of antiplatelet therapy in asymptomatic PAD patients.
- The ACC guideline issued a grade IIa recommendation to start antiplatelet therapy in asymptomatic patients, given the lack of high-quality data supporting its use.
- It is reasonable to start statin therapy in patients with asymptomatic PAD, because most patients will likely have an ASVD risk score greater than 7.5%.

Symptomatic Disease

Antiplatelet/antithrombotic therapy

As platelet activation plays a fundamental role in atherosclerosis and arterial thrombosis, medical management of PAD includes antiplatelet and antithrombotic therapy.[38,54,55] The Antithrombotic Trialists' Collaboration conducted a meta-analysis of trials studying the efficacy of various antiplatelet agents in patients at high risk for occlusive vascular events, finding that antiplatelet therapy protects against vascular events in patients with stable angina, intermittent claudication, and atrial fibrillation.[56,57] Although the benefit of antiplatelet therapy for symptomatic PAD is undisputed, the choice of antiplatelet agent is debated. The Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial demonstrated that daily clopidogrel reduced the risk of stroke and myocardial infarction (MI) more effectively when compared with aspirin in patients with a recent ischemic stroke, MI, or symptomatic PAD.[58] In fact, the PAD subgroup in this study experienced the greatest risk reduction with clopidogrel.[55,58] However, the use of even more potent antiplatelet monotherapy has not been consistently shown to incur additional benefit. Superiority for ticagrelor monotherapy, compared with clopidogrel, was not established in the EUCLID (Examining Use of Ticagrelor in Peripheral Artery Disease) trial.[59] The efficacy of dual-antiplatelet therapy was studied in the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance trial, which showed that the combination of clopidogrel and aspirin, compared with aspirin alone, had an overall neutral effect on most vascular outcomes but was associated an increased risk of bleeding complications.[60] Given the above studies, most guidelines recommend either aspirin or clopidogrel monotherapy in patients with symptomatic PAD.[38,52]

The combination of a vitamin k antagonist and antiplatelet therapy, compared with antiplatelet monotherapy, was associated with an increased risk of life-threatening bleeding without additional vascular benefit in the Warfarin Antiplatelet Vascular Evaluation trial.[61] However, more recent studies have analyzed the efficacy of dual-pathway inhibition (DPI), using a low dose of an anticoagulant in combination with antiplatelet therapy. Specifically, the Cardiovascular Outcomes for People Using Anticoagulation Strategies trial compared rivaroxaban (2.5 mg twice daily) plus aspirin to aspirin alone and rivaroxaban alone (5 mg twice daily) in patients with stable coronary and/or peripheral arterial disease. The rivaroxaban plus aspirin group had lower rates of cardiovascular death, stroke, or MI (MACEs) as well as major adverse limb events (MALEs) compared with the aspirin alone group, although with higher rates of bleeding.[62] DPI has also been studied in PAD patients who have undergone surgical management. Specifically, the VOYAGER (Vascular Outcomes Study of ASA

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[acetylsalicylic acid] Along with Rivaroxaban in Endovascular or Surgical Limb Revascularization) trial found that in patients with PAD who had undergone lower extremity revascularization, rivaroxaban added to daily aspirin reduced the risk of acute limb ischemia, MI, stroke, or cardiovascular death compared with aspirin alone.[63] The use of DPI therapy in daily clinical practice is evolving, and guideline recommendations regarding its use are forthcoming.

Key Points

- Aspirin or clopidogrel is recommended to lower the risk of MACEs in symptomatic PAD patients.
- Higher potency antiplatelet monotherapy (such as with ticagrelor) has not been consistently shown to provide additional cardiovascular benefit compared with lower potency antiplatelet monotherapy.
- Both high-dose anticoagulation and dual-antiplatelet therapy are associated with unfavorable risk/benefit profiles compared with antiplatelet monotherapy.
- DPI with low-dose rivaroxaban and aspirin lowers the risk of adverse cardiac and limb events, as compared with antiplatelet monotherapy, but is associated with a higher risk of bleeding. The risk/benefit profile for DPI likely becomes more favorable with higher baseline risks for cardiovascular events (such as those with polyvascular disease) or limb complications (such as those with prior episodes of limb-threatening ischemia or multiple revascularization procedures).

Lipid management

LDL-C plays a critical role in the development of atherosclerosis in peripheral arterial disease. The penetration of LDL into the arterial intima precipitates an inflammatory response involving reactive oxygen species, pro-inflammatory cytokines, and the recruitment of foamy macrophages and smooth muscle cells that ultimately leads to the formation of a plaque.[64] Reducing LDL lowers the risk of lower limb complications and the development of serious vascular events while halting the exacerbation of claudication symptoms.[52,64–67]

More recent data investigating the effects of inhibitors of proprotein convertase subtilisin–kexin type 9 (PCSK9) have shed additional light on the effects of LDL-C reductions in patients with atherosclerotic disease, including PAD patients. The Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk trial found that evolocumab, combined with statin therapy, lowered the risk of MACEs in patients with stable cardiovascular disease.[68] In this trial, 13.2% of all patients had established PAD. PAD patients treated with evolocumab had a significantly lower rate of MACE compared with patients only on statin therapy and the level of MACE reduction correlated with the degree of LDL lowering. In addition, all patients treated with evolocumab had a lower incidence of MALEs (acute limb ischemia, major amputation, or urgent revascularization).[69] Moreover, The Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab trial demonstrated that the PCSK9 inhibitor, alirocumab, reduced the incidence of coronary death, MI, stroke, and unstable angina in patients with recent acute coronary syndrome and dyslipidemia compared with statin monotherapy.[70]

Given the above data, the European Atherosclerosis Society and European Society of Vascular Medicine guidelines recommend a goal LDL of less than 55 mg/dL in symptomatic PAD patients.[71] This LDL goal has also been most recently endorsed for patients with a very high risk of MACE (which includes most patients with symptomatic PAD) in the 2022 ACC Expert Consensus Decision Pathway for Integrating

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Atherosclerotic Cardiovascular Disease and Multimorbidity Treatment statement. Typically, patients are started on statin therapy and the anti-lipid regimen is adjusted for the aforementioned LDL goal.[72] The role of lipoprotein(a) [Lp(a)] lowering in patients with cardiovascular disease is evolving. Studies have shown that elevated Lp(a) levels are an independent risk factor for PAD.[16,73] There are fewer studies analyzing the role of Lp(a) levels in secondary prevention of PAD complications after revascularization. Tomoi and colleagues found that in patients with PAD treated with revascularization, elevated Lp(a) levels were independently associated with MACE and MALE postsurgery, irrespective of LDL levels or statin use.[74] Although an elevated Lp(a) level is considered a risk-enhancing factor, guidelines have not established targeted Lp(a) levels, given a lack of high-quality evidence.

Key Points

- All patients with symptomatic PAD should be prescribed statin therapy, regardless of baseline LDL levels.
- The anti-lipid regimen should be adjusted to achieve a goal LDL of less than 55 mg/dL in most patients with symptomatic PAD.
- Although Lp(a) levels correlate with the risk of PAD and its complications, guidelines have not recommended interventions specifically targeting Lp(a).

Smoking cessation

Smoking cessation is critical in the treatment of PAD patients. The 2016 AHA/American College of Cardiology (ACC) Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease declared that patients with PAD who smoke tobacco should be advised at every visit to quit smoking. Physicians should assist patients in developing a plan for quitting that may involve referral to a smoking cessation program and/or pharmacotherapy such as varenicline, bupropion, and/or nicotine replacement therapy.[38]

Glycemic control

As stated earlier, diabetes is a known risk factor for PAD. The prevalence of PAD in patients with diabetes mellitus is estimated to be around 29%.[75] Furthermore, the atherosclerosis in diabetic patients with PAD is more aggressive, and amputation rates in diabetic patients with atherosclerosis of the lower extremity are much higher than non-diabetics.[76,77] The Society for Vascular Surgery suggests optimizing diabetes control (hemoglobin A1c goal of <7.0%) in patients with intermittent claudication.[76]

Blood pressure control

Hypertension is a known risk factor for PAD. The EUCLID trial found that in patients with symptomatic PAD, 78% had hypertension and that every 10 mm Hg increase in systolic blood pressure above 125 mm Hg was associated with an increased risk of MACE and an increased risk of MALE/lower extremity revascularization.[78] Similarly, multiple other trials have shown that blood pressure control is associated with improved cardiovascular outcomes in PAD patients.[79,80]

Sodium–glucose cotransporter-2 inhibitors and glucagon-like peptide-1 agonists

Both sodium–glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) agonists are relatively new and promising antidiabetic drugs. The Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients trial assessed cardiovascular outcomes in diabetic patients treated with empagliflozin and standard of care compared with placebo and standard of care. Empagliflozin

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significantly decreased the risk of cardiovascular disease (CVD) death, nonfatal MI, or nonfatal stroke compared with placebo.[81,82] Among patients with PAD, empagliflozin reduced all-cause and cardiovascular mortality, hospitalization for heart failure, and progression of renal disease.[81,83] The combined Canagliflozin Cardiovascular Assessment Study (CANVAS) and CANVAS-Renal trial studied patients with Type 2 diabetes mellitus (T2DM) on canagliflozin compared with placebo. Although canagliflozin reduced cardiovascular death, MI, and stroke rate, patients treated with canagliflozin were found to have a significantly higher rate of lower extremity amputation.[83,84] Interestingly, this increased amputation risk was not discovered in any other canagliflozin trial or trials with other SGLT-2 inhibitors. Yuan and colleagues conducted a retrospective review of patients with T2DM exposed to canagliflozin or non-SGLT2 antidiabetic agents and found that there was no increased risk of below-knee amputation in patients treated with canagliflozin.[83,85]

Data on the association and impact of GLP-1 agonists on PAD outcomes are more limited. Multiple retrospective reviews have found that in patients with T2DM, GLP-1 agonists were associated with a significant reduction in hospitalization for PAD and lower limb complications in comparison with other antidiabetic agents.[86–88] In addition, Marso and colleagues found that patients with T2DM treated with semaglutide had lower rates of peripheral revascularization than patients treated with placebo.[87,89]

Key Points

- Smoking cessation should be actively pursued in all patients with PAD.
- PAD patients with hypertension should be prescribed antihypertensive medications to achieve a goal blood pressure of less than 140/90. Both the American and European guidelines have issued grade IIa recommendations for angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs) as initial therapy for hypertension in PAD patients.
- Data regarding the beneficial cardiovascular effects of SGLT-2 inhibitors and GLP-1 agonists specifically for PAD patients are emerging but promising.
- Early concerns regarding the amputation risk associated with certain SGLT-2 inhibitors have been allayed following analyses of recent data. The Food and Drug administration (FDA) has removed the black box warning of amputation for this class of drugs but advises prescribers to cautiously use this class of medications in patient at high risk of amputations, including PAD patients.

UNDERTREATMENT OF PERIPHERAL ARTERY DISEASE

When compared with CAD, there are substantially less clinical trials assessing the impact of medical management in regard to PAD.[90] However, it is still well-documented that statins and antiplatelet medications significantly reduce serious events associated with PAD.[38,91] Hess and colleagues conducted a review that showed that among roughly 250,000 PAD patients, 40% were not on any lipid-lowering therapy.[92] Furthermore, medical management was less likely to be used in black patient populations, with black women having the lowest rate of lipid-lowering therapy utilization.[93,94] Berger and Ladapo's study using the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey databases ($n = 1982$) aimed at identifying outpatient physician trends in PAD management and found that only 38% of patients were on antiplatelet agents, 35% were on statins, and 31% used ACEi agents. In addition, exercise and diet were discussed only 20% of the time, and smoking cessation was addressed during 36% of encounters.[90] Even with the increased use of antiplatelet and statin therapy from 2006 to 2013, when

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demographics and comorbidities are controlled for, this increase is not significant.[90] Although the low rate of secondary prevention in the outpatient setting is not entirely understood, studies have demonstrated higher prescription rates in the hospital setting on discharge when compared with outpatient physician offices, a rather worrisome trend.[95–97] When compared with cardiologists, internists and family practitioners were significantly less likely to prescribe lipid lowering and antiplatelet agents, even though they see a substantially higher volume of PAD patients annually.[98]

One possible explanation may be the confounding findings of several antiplatelet trials. In the CAPRIE trial, clopidogrel was superior to aspirin in PAD patients compared with those with a history of stroke or CAD.[58] A subsequent meta-analysis found that aspirin is not as effective in preventing adverse cardiovascular outcomes in PAD as it is in CAD.[99] Given these findings, along with the recent EUCLID trial showing similar outcomes in PAD with Clopidogrel versus Ticagrelor,[59] there could be confusion regarding the appropriate medical management for patients with PAD who also have coexisting CAD.[100]

Key Points

- Historical and current data continue to highlight gaps of care for patients with PAD, compared with their CAD counterparts. The foundation of medical therapy for these patients, such as antiplatelet and statin therapy, is not used in the majority of cases.
- The undertreatment of PAD is even more profound in minority patients.

DISCLOSURE

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