Vascular Assessment of the Lower Extremity with a Chronic Wound

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KEYWORDS

- Ankle-brachial index • Skin perfusion pressure
- Transcutaneous oxygen pressure measurement • Near-infrared imaging

KEY POINTS

- A thorough history and physical examination of patients with chronic lower extremity wounds should be performed, including assessment of peripheral arterial disease risk in the patient's medical and surgical history, inquiry on the presence of intermittent claudication symptoms, visual assessment, and pulse palpation and auscultation. Auscultation of a femoral bruit, absence of pedal pulses, and monophasic signal on handheld Doppler examination are all concerning findings that should prompt further evaluation for PAD.
- Ankle and toe pressures and ankle and toe-brachial indices can be falsely elevated due to arterial calcification and provide vascular assessment at the level of the tourniquet only. Dividing the lower of the posterior tibial or dorsalispedis systolic pressures by the higher brachial artery to calculate the ankle-brachial index may help better identify patients with peripheral arterial disease. Variations in cut-off values for the toe-brachial index, less than 0.54 to 0.75, make it difficult to determine a proper diagnosis of peripheral vascular disease. Additional vascular studies are recommended if results are inconclusive.
- Transcutaneous oxygen pressure measurement (TCOM) and skin perfusion pressure (SPP) measurements have been reported to be better able to predict wound healing and the necessity for amputation than ankle and toe pressure measurements. Variation in cut-off values signifying adequate perfusion, 25 mmHg to 50 mmHg for TCOM and 30 mmHg to 40 mmHg and up to 70 mmHg in patients with end-stage renal disease on hemodialysis for SPP, along with need to extrapolate perfusion within the wound bed may limit their utility in accurate vascular assessment for healing.
- Hyperspectral and near-infrared image provide a means of vascular assessment not restricted by limitations of traditional vascular studies and provide the ability to assess perfusion directly within the wound bed. These modalities assess tissue oxygenation levels or local perfusion by means of a fluorescent dye. Decreased tissue oxygenation or decreased fluorescent dye in the wound bed and mottled signal appearance has been associated with peripheral arterial disease and delayed wound healing. These modalities may also assist in determining the presence of inflammation and infection in and about the wound.

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- The need for quantitative and accurate information of adequate blood supply is critical for timely intervention, if necessary, in patients with a chronic wound of the lower extremity. Proper vascular assessment should include a thorough history and physical examination and combination of routine and novel vascular studies.

INTRODUCTION

Peripheral arterial disease (PAD) exists on a spectrum ranging from asymptomatic to critical limb ischemia (CLI), affecting approximately 8.5 million people older than 40 years in the United States and 202 million people worldwide.[1–4] Its presence is associated with significant morbidity and mortality related to cerebral vascular accidents and cardiovascular events.[5] Patients with diabetes with or without amputation have a 5-year mortality rate of 46% to 48%, respectively, higher than mortality rates of prostate and breast cancer combined.[6] The true incidence of PAD may be underestimated due to the number of asymptomatic patients who go undiagnosed.[5] The initial diagnostic test for PAD screening is the ankle-brachial index (ABI).[2,7] However, controversy exists in the risk versus benefit of obtaining this test in asymptomatic patients.[5,8] Yet, more than 50% of patients with PAD are asymptomatic; further complicating this are those patients in whom routine noninvasive vascular studies have limitations.[3–5,9–12] Lower extremity PAD is often not recognized until a complication presents, such as severe pain, tissue loss with delayed healing, or gangrene.[13] For these reasons, the American Heart Association/American College of Cardiology (AHA/ACC) recommend patients with known PAD and those at increased risk for PAD with history and physical examination findings that suggest PAD should undergo diagnostic testing. Patients at increased risk for PAD per the AHA/ACC are listed in **Box 1**.[4] The guidelines for management of the diabetic foot from the Society for Vascular Surgery, the American Podiatric Medical Association, and the Society for Vascular Medicine recommend an ABI be obtained in all patients with diabetes older than 50 years.[14]

Delay in revascularization in patients with lower extremity tissue loss and PAD can further propagate complications of delayed healing, infection, amputation, and death.[5] Knowledge of signs and symptoms of PAD to look for in a patient's history and

Box 1
Patients at increased risk for peripheral arterial disease per the American College of Cardiology/American Heart Association practice guidelines

Age ≥65 years

Age 50 to 64 years, with risk factors for atherosclerosis (eg, diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of peripheral arterial disease

Age less than 50 years, with diabetes mellitus and 1 additional risk factor for atherosclerosis

Individuals with known atherosclerotic disease in another vascular bed (eg, coronary, carotid, subclavian, renal, mesenteric artery stenosis, or abdominal aortic aneurysm)

From Writing Committee Members, Gerhard-Herman MD, Gornik HL, et al. 2016 AHA/ACC Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease: Executive Summary. Vasc Med. 2017;22(3):NP1–NP43; with permission.

physical examination, limitations of current noninvasive vascular studies, and novel technologies for vascular assessment can better assist the treating provider in identifying PAD in patients with a lower extremity wound and developing the optimal treatment plan for resolution. The objective of this article is to present current and novel vascular assessment technologies to assist the provider in selection of which studies would be optimal in determining vascular status and the potential need for intervention when treating a patient with a wound of the lower extremity.

LOWER EXTREMITY VASCULAR ASSESSMENT

History

Lower extremity vascular assessment begins by obtaining a thorough history and physical examination. Questions to the patient regarding the presence of risk factors for PAD, in addition to being of older age, can heighten suspicion of its potential diagnosis. African American patients are at greater risk for PAD.[13] Patients should also be asked about personal history of coronary artery disease, cerebrovascular disease, including transient ischemic attacks and strokes, hypertension, hypercholesterolemia, obesity, chronic kidney disease, and diabetes, and a family history of PAD, cardiovascular disease, and renal insufficiency.[1,5,9,13,15,16] Presence of comorbidities can also be assessed through medication list reconciliation.[1] Surgical history of previous vascular-related procedures and surgeries such as carotid, coronary, and peripheral vascular procedures should also be obtained. Social history should also be obtained in regard to normal activity levels and previous and current tobacco use, both of which are known risk factors for PAD.[1,5,9,15,16] Cigarette smoking increased the risk of PAD from 2- to 6-fold.[17] There is an increased risk for PAD in younger patients in whom the presence of the abovementioned comorbidities and social history risk factors are present.[5]

As intermittent claudication is the most common symptom associated with PAD, its presence should be questioned. Intermittent claudication is defined as reproducible discomfort in a specific muscle group of the lower extremity that occurs after a predictable level of activity, is relieved by rest, and recurs in this same fashion.[1,17,18] Questioning should discern what muscle group in the lower extremity is affected, to determine possible level of arterial lesion and quantification of the duration of activity that produces the symptom; this provides a baseline for future reference and can speak to the potential severity of the arterial lesion. Knowing if this interferes and has limited the patient's mobility also helps determine potential PAD severity.[1,18,19] Other questions geared more to rest pain and severe PAD involve asking the patient if they experience in the foot, often localized to the ball of the foot, which wakes them up at night and is relieved by dangling the foot over the side of the bed. Some patients sleep sitting up to avoid this pain.[1]

The difficulty in diagnosis of PAD based on the presence of intermittent claudication is that up to 78% of patients with PAD are asymptomatic even though they have the same risk factor profile as symptomatic patients.[3–5,9–13] The absence of symptoms is of particular concern in patients with diabetes who can remain asymptomatic until advanced stages of PAD when ischemic ulceration and/or gangrene become apparent because of peripheral neuropathy.[11,13,19–21] Development of adequate collateral circulation can also prevent symptoms of intermittent claudication from occurring.[9] Patients with diabetes should be questioned about medications taken for glycemic control, what their glycemic control is like and how often it is checked, and the duration of diagnosis.[1] Patients with diabetes have a 4- to 10-fold increase in risk for lower extremity PAD with earlier onset and faster progression.[20] PAD in

patients with diabetes also typically affects the macro- and microvasculature of both lower extremities. Patients with diabetes diagnosis of greater than 10 years duration are at increased risk for lower extremity complications such as peripheral neuropathy, diabetic foot infection, and Charcot neuropathy.[21,22] Presence and history of all of these conditions should be inquired in a patient with diabetes.

Physical Examination

Physical examination of the lower extremity begins with visual assessment and pulse palpation. Findings on visual assessment that can heighten suspicion of a diagnosis of PAD include tar staining of the fingernails from smoking; surgical scars consistent with previous vascular procedures/surgeries on the neck, chest, abdomen, and lower extremities; and scars from previous healed wounds and amputated limbs or digits. The presence of active wounds should also be noted, particularly in areas of bony prominence and in between and on the distal aspects of the toes. Another test to perform is the Buerger's test. This is done by elevating the extremity approximately 45 to 60° from a supine position for 2 minutes and then in a dependent position for 2 minutes. Pallor on elevation and reactive hyperemia, also known as dependent rubor, is a positive Buerger sign, indicating distal or multisegmental arterial disease.[1,4,19,23] Although commonly performed, assessing lower extremity temperature and capillary refill time are not reliable indicators for PAD.[1] The presence of peripheral neuropathy should also be assessed, particularly in patients with diabetes, as its presence can mask symptoms of intermittent claudication and rest pain.[11,21]

Palpation and auscultation of the femoral, popliteal, posterior tibial, and dorsalispedis arteries should then be performed and is recommended in the guidelines by the International Working Group on the Diabetic Foot and the American Diabetes Association.[1,4,18,19] The popliteal pulse is relatively difficult to palpate. If it is easily felt this may indicate a popliteal aneurysm, which should be confirmed with an ultrasound study.[1] Lower extremity pulse palpation can be graded as follows: 0, absent; 1, diminished; 2, normal; or 4, bounding or simply as present or absent.[4] Although pulse palpation is not a sensitive tool for detection of PAD, absence of a palpable pulse has an excellent specificity for detection of PAD.[11] A significant difference in the amount of palpable pulses was found between patients with a normal ABI (mean 3.4), those with an ABI greater than or equal to 1.4 (mean 2.24) and those with an ABI less than or equal to 0.9 (mean 1.74). One or more missing or weak pedal pulses was found to have a significantly more sensitive and better negative predictive value than ABI less than 0.9 in predicting the presence of PAD.[19] Auscultation of a femoral bruit and absence of pedal pulses were both found to predict the presence of PAD.[9,15,18,19,24] Presence of a femoral bruit was found to be a risk factor for PAD independent of the presence of other cardiovascular risk factors.[15] Presence of all 4 pedal pulses was determined to be negative for PAD (sensitivity 72%, specificity 72%, positive predictive value 26%, negative predictive value 95%).[5] Combined with lack of a femoral bruit, the specificity increases to 98% for the absence of PAD.[9]

Pulse palpation is not without its faults though. For patients with more than or equal to 3 palpable pedal pulses, only 26% had PAD. Patients with diabetes and hypertension and active tobacco users were more likely to have a true positive or false negative for the presence of PAD.[5] Pulses can also be palpable in patients with PAD and affected by room temperature and the skill level of the provider performing the examination in addition to being nonpalpable due to congenital absence of the artery.[5,13,19,25–27] Complaints of intermittent claudication and pulse examination and auscultation taken individually have a low sensitivity and high specificity for detecting PAD (**Table 1**). Combination of these history and physical examination findings

Table 1
Detection of ankle-brachial index less than or equal to 0.9 based on intermittent claudication and pulse examination

Presence of History and Pulse Examination Finding	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Claudication	79	68	35	92	69
Palpable DP only	64	81	43	91	78
Palpable PT only	70	83	49	92	81
Palpable DP and PT	73	92	66	94	88
Femoral bruit only	36	92	51	86	82
Palpable DP and PT and no femoral bruit	58	98	81	95	94

Abbreviations: DP, dorsalis pedis; NPV, negative predictive value; PPV, positive predictive value; PT, posterior tibial.

Adapted from Armstrong DW, Tobin C, Matangi MF. The accuracy of the physical examination for the detection of lower extremity peripheral arterial disease. Can J Cardiol. 2010;26(10):e346–e350; with permission.

improve the accuracy of PAD detection, warranting the necessity of a thorough history and physical examination if the presence of PAD is a concern.[9]

Concerning findings on lower extremity pulse palpation examination warrants further evaluation through the use of a handheld Doppler. An 8-MHz handheld Doppler can be used to assess the posterior tibial and dorsalis pedis arteries as well as their connection at the pedal arch within the first intermetatarsal space of the foot. The probe should be held at an approximately 60° angle to the skin pointing in the direction of blood flow. It can then be manipulated to hear the clearest sound. The probe should be held so it is just in contact with the skin; holding the probe with excessive pressure to the skin can obliterate the arterial signal.[1] The arterial signal heard with a handheld Doppler is classified as triphasic, biphasic, or monophasic.[1] A triphasic signal is the audible signal heard from the 3 components of a normal waveform: high forward flow during systole due to left ventricular contraction, transient reversal of flow in early diastole due to reflection from a high-resistance outflow bed, and forward flow resulting from reflection from a closed aortic valve during late diastole. Biphasic waveforms result from loss of the audible signal of transient reversal of flow. A monophasic signal refers to forward flow only.[28] Audible handheld Doppler has a reported sensitivity of 42.8%, specificity of 97.5%, negative predictive value of 94.10%, and positive predictive value of 65.2% in predicting the presence of significant PAD.[29]

Lack of, or inadequate, training, inexperience, and time constraints account for the primary limitation of handheld Doppler use and correct interpretation of the audible signal heard.[12,30] Although studies conflict on the ability of clinicians of various years of experience to correctly interpret the audible signal heard, monophasic signal was the one most often correctly identified and the signal most concerning for PAD.[28,30] Other limitations of handheld Doppler use in assessing arterial signals are patient factors such as the presence of excessive edema, adipose tissue, fibrosis, and anatomic variations in artery location.[12] This can also cause difficulties in obtaining an ABI as discussed later.

Routine Noninvasive Vascular Studies

Ankle pressure and the ankle brachial index

Any abnormal findings on history and physical examination should be evaluated further with diagnostic testing to confirm the diagnosis of PAD. Obtaining an ABI is typically the initial test recommended in clinical guidelines.[4,5,8,14,18] The ABI is a measure of the systolic blood pressure of the posterior tibial or dorsalis pedis artery divided by the systolic blood pressure of the brachial artery. A resting ABI is typically first performed in which the patient is in a supine position and upper and lower extremity systolic blood pressure measurements are taken after a period of rest.[13] The systolic blood pressure of the upper and lower extremities should be equivalent with an ABI of 1.0 when PAD is not present.[20] An ABI less than or equal to 0.9 has a 90% sensitivity and 98% specificity for detection of stenosis of greater than or equal to 50% in the proximal lower limb, consistent with a diagnosis of PAD.[7,9] Variations in the number obtained aid in diagnosis and determination of severity of PAD (**Table 2**). The test is quick and easy to perform and involves minimal direct risk to the patient.[17] Controversy exists in using the ABI to screen asymptomatic patients due to the lack of evidence in the literature that support the benefit of reduced morbidity and mortality.[31] Although the direct risk of an ABI is minimal, indirect risks can include complications associated with administration of medications to treat hypertension and hyperlipidemia, exposure to contrast reagents if more invasive vascular studies ordered, and the potential anxiety created for the patient due to a false-positive reading.[17]

The main limitation of the ABI test is that it only provides information at the level of the artery being assessed and can be inaccurate due to systemic conditions affecting sensation, collateralization, and rigidity and presence of the vessel as well as recent tobacco use and caffeine intake.[1–3,13,16,20,31–34] A meta-analysis of 20 studies (2376 patients) found ABI to have a low prognostic accuracy in predicting lower extremity wounds that would heal (sensitivity 48%, specificity 52%). The ability to predict whether lower extremity amputation would occur was only slightly better (sensitivity 52%, specificity 73%).[31] ABI sensitivity in diagnosing PAD also varies in patients with diabetes and peripheral vascular disease versus those with diabetes and no peripheral vascular disease (100% vs 35% to 73%). ABI sensitivity and specificity are lower due to calcium build up within the lower extremity arteries, which makes the vessel noncompressible resulting in a falsely elevated ankle pressures.[2,3,20,31,33] This can occur in patients of older age, men, those with end-stage renal disease and rheumatoid arthritis, and tobacco users, although this is most often the concern in patients with diabetes.[2,9,19,32,35] Hardening of the arteries can result in an ABI result greater than or equal to 0.9 and palpable pedal pulses in the face of PAD. This is

Table 2
Diagnosis of peripheral arterial disease and severity based on ankle-brachial index results

Presence of PAD and Severity	ABI Result
Normal	1.0–1.3
PAD diagnosis	*≤0.9*
Falsely elevated	>1.3
Mild to moderate PAD	0.4–0.9
Severe PAD	<0.4

Data from Khan TH, Farooqui FA, Niazi K. Critical review of the ankle brachial index. Curr Cardiol Rev. 2008;4(2):101–106.

particularly problematic in patients with active lower extremity ulcerations in which undiagnosed and untreated PAD can lead to delayed healing and increased risk of amputation.[19] More than 50% of patients with diabetes and peripheral neuropathy with an ABI between 0.9 and 1.3 have PAD. The prevalence of PAD increases to 85% when the ABI is greater than or equal to 1.4.[20] Additional vascular studies are recommended in these circumstances.[19]

In patients with heel ulcerations, more than 50% of the ABI results obtained were based on the dorsalis pedis artery, which is not the primary vascular supply of the angiosome of the heel.[36] In addition, the methods in which the ABI is obtained and calculated can produce different results.[1,3,5,11,15,16,37] An oscillometric ABI has been reported to have a higher sensitivity and specificity compared with a manual Doppler ABI (97% and 98%, respectively, vs 95% and 56%).[3] The traditional method of calculating an ABI involves dividing the higher brachial systolic pressure by the higher of the posterior tibial or dorsalis pedis arteries.[1,7,11,15,16] However, various methods do exist.[5,7,32,37,38] Dividing the lower of the posterior tibial or dorsalis pedis systolic pressures by the higher brachial artery may identify more patients at risk for all-cause and cardiovascular mortality.[7,32,37,38] Performing an ABI after exercises may also assist in PAD diagnosis if there are concerns regarding the accuracy of the resting ABI result. The ABI result following exercise will decrease in respect to the patient's resting ABI if PAD is present. Patients can do a formal treadmill test for exercise or mimic a treadmill test by performing 20 heel-toe raises.[1]

Toe pressure and the toe brachial index

When the ABI is considered to be falsely elevated, toe pressures and calculation of the toe brachial index are often used, as the digital arteries are less likely to be affected by medial calcinosis.[2,13,20,39,40] Systolic toe pressure has been reported to have 100% sensitivity in detecting PAD whereas systolic ankle pressure is just greater than 50%.[20] Using a cut-off of 30 mmHg, systolic toe pressure measurements have a sensitivity and specificity of 15% and 97%, respectively,predicting adequate perfusion available for healing (positive predictive value 67% and negative predictive value 77%).[31] A toe brachial index (TBI) can also be obtained in which the systolic pressure of the toe is divided by the systolic pressure of the brachial artery. A review of 22 studies reported that a TBI between 0.54 and 0.75 indicates PAD with a sensitivity of 90% to 100% and specificity between 65% and 100%.[3] A TBI less than 0.7 has been reported in association with intermittent claudication and less than 0.2 in association with rest pain.[3]

Limitations of toe pressure and TBI are similar to those of the ABI; results only provide information of pressure measurement at the level of the digit and can be inaccurate due to size of the cuff used for testing, rigidity of the vessel, room and skin temperature, and patient factors such as female gender, tobacco and caffeine use, lack of designation of a consistent cut-off denoting the presence of PAD and lack of high-quality and contradictory literature to support its use as a screening or diagnostic test for PAD.[19,39,41] Use of a narrower cuff has been reported to result in higher toe pressure readings, whereas female gender is associated with lower toe pressure readings.[41] A systematic review and meta-analysis of 8 studies (909 patients) in the utility of toe pressure to predict healing of diabetic foot ulcerations reported a pooled sensitivity and specificity of 86% and 56%, respectively, using a cut-off value of 30 mm Hg.[40] A systematic review of 7 studies (566 lower limbs) reported the pooled sensitivity and specificity of TBI to detect PAD to range from 45% to 100% and 16% to 100%, respectively.[40] Heterogeneity existed between the studies, including variation in the cut-off TBI value used to signify PAD. TBI values consistent with PAD currently range

from less than 0.54 to 0.75.[41] Approximately 25% of patients with a toe pressure less than 30 mmHg have been reported to heal lower extremity ulcerations, whereas the same percentage with a toe pressure greater than 91 mmHg has delayed healing.[41] In addition, although obtaining a TBI is recommended when ABI results are falsely elevated due to the theory that the digital arteries are less often affected, this was not confirmed in a study comparing ABI and TBI results obtained in patients with diabetes and those without diabetes. Digital artery calcification was evident on 24% to 40% of plain film radiographs of the feet of patients with diabetes despite plain film radiographs having a reported limited sensitivity in detecting arterial calcification.[2] Obtaining a toe pressure and TBI is also not possible when digital ulceration is present or the patient lacks digits due to previous amputation.[31,33,34,42]

Transcutaneous oxygen pressure measurement

Transcutaneous oxygen pressure measurement (TCOM) is one of the most common skin perfusion measurements performed. TCOM measures capillary oxygen tension via probes placed on the skin that are heated to approximately 43°C. This causes local vasodilation and oxygen diffusion to the skin surface for measurement. A meta-analysis of the ability of 8 vascular studies to predict adequate perfusion for healing of a diabetic foot ulceration found that TCOM results were better able to predict wounds that would heal and the necessity for amputation compared with results of an ABI.[31]

Limitations of TCOM use are the variation in cut-off points used to determine adequate perfusion for healing, patient factors that can affect results, time and skilled personnel required to perform the examination, and that vascular assessment is provided at the point of probe placement only with no clearly defined cut-off value that indicates adequate perfusion for healing.[33,42,43] TCOM cut-off values to signify adequate perfusion range from 25 mmHg to 50 mmHg.[24,44] A TCOM greater than 25 mmHg has a reported 92% specificity for predicting wound healing. A TCOM of greater than 30 mmHg has been reported to be highly accurate in predicting symptom management and wound healing after implementation of conservative or surgical measures. A TCOM of greater than 40 mmHg is recommended as a cut-off value to signify adequate perfusion for healing if severe gangrene or calcaneal tissue loss is present.[24] One study found that a dorsal TCOM greater than 30 mmHg in a patient with a heal ulcer had CLI when a corresponding rearfoot TCOM was performed. Mean rearfoot TCOM results in these patients with heel ulceration and dorsal TCOM greater than or equal to 30 mmHg had a rearfoot TCOM result of 21 mmHg.[44] The TransAtlantic Inter-Society Consensus designated a TCOM less than 50 mmHg as objective criteria for CLI.[44] Patient factors that can adversely affect TCOM results include edema, dry flaky skin, maceration, callused or plantar skin, cellulitis, and probe placement over bones and tendons.[24,44]

Skin perfusion pressure

Skin perfusion pressure (SPP) measurements are most often obtained by use of a laser Doppler sensor placed on the foot or toe, whereas a blood pressure sensor is placed at the ankle or toe, respectively. The pressure at which skin perfusion returns following vascular occlusion and controlled release is the SPP. Multiple sites can be tested, one at a time, taking about 10 to 15 minutes per site. The skin can also be warmed to 42°C if necessary.[45–47] SPP has been reported to not be effected by artery calcification.[47] The ability to perform an SPP was found to be universal in 211 patients (403 limbs), whereas only 351 (87%) limbs, 367 (91%) limbs, and 380 (94%) limbs could have ankle pressue, toe pressure, and TCOM performed, respectively.[34]

Limitations of the SPP include the ability to provide vascular assessment at the site of blood pressure cuff placement, skin and body temperature, sympathetic tone, limb position, time and skilled personnel required to perform the examination, and lack of a clearly defined cut-off value that indicates adequate perfusion for healing.[46,48–50] Having the patient seated with their lower extremities extended along the table without a bend in the knee has been reported to be the optimal position for obtaining SPP measurements. Performing an SPP with the patient seated and the legs in a dependent position has been shown to result in elevated SPP results.[49,50] Although an SPP greater than 30 mmHg has a reported 100% sensitivity and 97% specificity of determining healing potential following a major lower extremity amputation, this decreases when looking at the potential to heal lower extremity wounds and partial foot amputations (61%–85% sensitivity, 67%–80%, respectively).[45,46] Increasing the cut-off SPP value will decrease sensitivity and increase specificity. A meta-analysis comparing a cut-off SPP value of 30 mmHg and 40 mmHg reported a decrease in sensitivity (79.9%–67.1%) and increase in specificity (78.2%–84.2%) with a larger SPP cut-off value.[47] Thus, an SPP of 30 to 40 mmHg has been deemed to predict the presence of adequate perfusion for healing.[42,45–47,51–54] Further designation is listed in **Table 3**. A cut-off value of greater than 70 mmHg has also been recommended as the minimum, indicating adequate perfusion and minimization for the potential for amputation as well as reduction in mortality rates for patients with end-stage renal disease on hemodialysis.[54,55]

Novel Vascular Studies

Hyperspectral and near-infrared imaging

Hyperspectral imaging measures tissue oxygenation levels. Tissue oxygenation saturation has been used for decades to determine cerebral perfusion, skin perfusion in sepsis and septic shock, irritant-induced inflammation, ischemia-reperfusion injury, the effect of ultraviolet irradiation, optical detection of cancer, and diagnosis of PAD.[56,57] The signal received is based on the oxygen-carrying status of blood within the microcirculation.[31,58] A systematic review of these imaging modalities found them to be a valuable measure of PAD through objective assessment of tissue mismatch in oxygen demand and supply in the area imaged.[59] The amount of deoxygenated hemoglobin present, postocclusive resaturation rates, and recovery times have been found to be representative of microvascular function and best correlate with ABI results.[56,60] Angiosome mapping based on imaging results from these studies, as opposed to angiography-based angiosome assessment, was found to have a sensitivity and specificity of 88% and 69%, respectively, in predicting arterial ulceration location.[48,58] This is hypothesized to be due to collateralization and other factors altering microcirculatory flow in patients with PAD, resulting in alteration of the major arterial supply to an angiosome.[58]

Table 3
Diagnosis of peripheral arterial disease and severity and average time to wound healing based on skin pressure perfusion results

Presence of PAD and Severity	SPP Result (mmHg)	Average Time to Wound Healing (d)
Normal	>50	235
Mild to moderate PAD	31–50	98
Severe PAD	≤30	52

Use of hyperspectral imaging during initial evaluation and through serial assessment of wounds in patients with type I and type II diabetes has also been shown to better predict wound resolution compared with the gold standard of wound measurements and 50% reduction in wound size at 4 weeks. These findings suggest that hyperspectral imaging is better able to predict wound resolution earlier, enabling physicians to begin earlier aggressive treatment of expedited wound resolution if deemed necessary.[56,61,62] A healing index, a proprietary device-calculation measurement in one type of hyperspectral imaging system, is obtained based on readings obtained from the wound base and a 0.5 to 2.5 cm margin of the periwound skin. A healing index greater than 0 had a sensitivity and specificity of 93% and 86%, respectively, and a 90% to 93% positive predictive value and 86% negative predictive value for wound resolution.

Although hyperspectral imaging is obtained in a noncontact, noninvasive fashion, other near-infrared imaging modalities require intravenous access for injection of dyes that fluoresces under near-infrared light. Parameters for assessment of tissue perfusion are most often based on time and intensity of the fluoresce signal produced; techniques in which these parameters are obtained varied on the device utilized. Devices that function with a larger dose of fluorescent dye use a more binary measurement system based on time and intensity of fluorescence onset and regress, as these devices do not perform any analysis on the images obtained. Other systems use smaller doses of fluorescent dye and provide analytical parameters that allow for subtle assessment of fluorescence signal onset, filling pattern, and regression[26,57] (**Table 4**).

A systematic review of 23 articles on near-infrared imaging, the majority using indocyanine green for the fluorescent dye, found it to be a valuable tool in diagnosing PAD or CLI, visualizing regional perfusion changes following revascularization procedures, providing early prediction on wounds not likely to heal, and assessing accurate level of amputation most likely to heal.[57] The parameters of $T_{1/2}$, PDE_{10}, and Td 90% were reported to be the most beneficial in vascular assessment. Near-infrared imaging parameters have a reported sensitivity and specificity range of 67% to 100% and 72% to 100%, respectively, for diagnosing PAD or CLI. ABI results have been shown to have significant correlations with $T_{1/2,}$ Td 90%, T_{max}, Td 75%, and intensity reading at 60 seconds, with Td 90% determined to be the most significant variable. A Td 90% of 25 seconds diagnostically predict PAD with a sensitivity and specificity of 82.6% and 73.3%, respectively.[63,64] $T_{1/2}$ has been able to distinguish between Fontaine II and IV[65] (**Table 5**). A PDE_{10} of 28 was found to be the optimal cut-off for detecting CLI defined as a TCOM less than or equal to 30 mmHg with a sensitivity and specificity of 100% and 86.6%, respectively.[66] All vascular assessment parameters have been noted to increase following successful vascular intervention, whereas no change occurred in patients in whom revascularization was not successful.[57] Lack of fluorescence in the wound bed and mottled appearance of signal has also been associated with delayed healing of wounds.[33] Review of the raw imaging sequence itself, particularly in systems using smaller doses of fluorescent dye, have also been reported to be of utility in diagnosing local ischemia and PAD. Patients with delayed time to onset of fluorescence and a mottled pattern of fluorescence filling have been noted to be characteristic of PAD.[26,67]

Benefits of this type of imaging is that it is easy; rapid to perform; provides real-time, site-specific vascular assessment; has reproducible results; is not affected by factors that limit results of routine noninvasive vascular studies; and allows for repeated study/image analysis without the need for repeated studies in addition to some modalities offering noncontact and noninvasive image capture.[26,33,42,48,56–58,67–71]

Table 4
Near-infrared imaging vascular assessment parameters

Parameter	Definition	Self-Determined Parameter	Device-Determined Parameter
Ingress	Magnitude of increase in fluorescence from baseline to max intensity		X
Ingress rate	Rate of fluorescence intensity increase from baseline to max intensity		X
Egress	Magnitude of decrease in fluorescence from max intensity to end of fluorescence		X
Egress rate	Rate of fluorescence intensity decrease from max intensity to end of fluorescence		X
T_{max}	Time from onset to maximum fluorescence intensity	X	
PDE_{10}	Intensity of fluorescence 10 s after onset of fluorescence	X	
$T_{1/2}$	Time to half maximum intensity	X	
Td90%	Time elapsed from maximum fluorescence intensity to 90% intensity	X	
Td75%	Time elapsed from maximum fluorescence intensity to 75% intensity	X	

Adapted from van den Hoven P, Ooms S, van Manen L, et al. A systematic review of the use of near-infrared fluorescence imaging in patients with peripheral artery disease. J Vasc Surg. 2019 Jul;70(1):286-297.e1; with permission.

Limitations primarily exist in regard to factors that can lead to altered fluorescence signal reading such as positioning during image capture, room lighting, presence of infection, inflammation, thickened skin, increased melanin content, angiogenesis, tissue within the wound base, such as eschar, slough, coagulum, and advanced tissue products, and variations in depth of penetration of the imaging device.[26,48,57,61,66,67] The positive predictive value of these imaging modalities was found to decrease by 6% in the presence of underlying osteomyelitis.[61] Algorithms are continuing to be

Table 5
Fontaine classification system[65]

Stage	Symptoms
I	Asymptomatic, incomplete blood vessel obstruction
II	Mild claudication pain in limb
IIA	Claudication at a distance >200 m
IIB	Claudication at a distance <200 m
III	Rest pain, mostly in the feet
IV	Necrosis and/or gangrene of the limb

created to offset difference in readings due to melanin content in the skin. These factors, in addition to limited comparison studies, may be the reason for lack of correlation of hyperspectral and near-infrared imaging study results with routine noninvasive vascular studies.[71] Other limitations involve those devices that require intravenous access for imaging, expense of the device, and time and staff training required for proper imaging capture and analysis.

SUMMARY

Current guidelines vary on whether or not asymptomatic patients should be screened for PAD.[4,8,14,18,39] In treating patients with a lower extremity wound, the primary concern shifts from the risk of PAD progression and mortality related to cardiovascular events to wound healing to prevent limb loss, an independent risk factor for increased morbidity and mortality. Vascular assessment of these patients typically relies on standard history and physical examination findings, which could delay appropriate intervention. Studies have shown that history and physical examination findings are insufficient to diagnosis PAD and recommend further vascular testing to aid in the diagnosis.[3–5,9–13,17,19,20,39,40] However, which tests to obtain remains controversial, given the limitations of routine noninvasive vascular studies.[27] The need for quantitative and accurate information of adequate blood supply is critical for timely intervention if necessary.[69]

Although limited studies have looked at the sensitivity and specificity of combining history and physical examination findings with vascular study results in accurately diagnosing PAD, recommendation has been made to combine various vascular study results to improve accuracy. Some studies recommend use of toe pressure/TBI and SPP over ABI and TCOM when possible.[27,42,70] An SPP greater than or equal to 40 mmHg in conjunction with a toe pressure greater than or equal to 30 mmHg was found to accurately predict the ability to heal lower extremity wounds in patients with PAD.[34,42,47] Other studies recommend combination of physical examination findings, with TCOM less than 40 mmHg or with SPP and TCOM results.[43,47] Novel vascular assessment modalities seem to supplement clinical assessment and routine noninvasive vascular studies, given that results are site specific and not limited by factors that can make results of noninvasive vascular studies unreliable.[69] The result of this review suggests that a thorough history focused on specific risk factors, pulse palpation, auscultation, and Doppler evaluation combined with hemodynamic measurements may help provide a more accurate diagnosis of PAD. Novel vascular assessment modalities may be an option to consider in patients in whom the accuracy of routine noninvasive vascular study results is questioned.

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DISCLOSURE

The author has nothing to disclose.

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