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REVIEW

Assessing chronic wound perfusion in the lower extremity: current and emerging approaches

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Kevin Y Woo[1]
Timothy M Brandys[2]
Joseph A Marin[1]

[1]School of Nursing, Faculty of Health Sciences, Queen's University, Kingston, [2]Department of Surgery, The Ottawa Hospital, Ottawa, ON, Canada

Abstract: Current evidence suggests that vascular and wound bed perfusion assessment should be integral to the care of people with chronic wounds in the lower extremities. Peripheral artery diseases can be insidious, with many affected individuals unaware of circulation issues and failing to seek medical help until they develop foot ulcers, gangrene, and other related complications. Measuring tissue perfusion is a useful diagnostic marker for chronic wounds and may help determine a wound's potential for healing. A complete patient history and physical examination is imperative to help determine the correct diagnosis of lower extremity ulcers. This article aims to discuss current and emerging wound perfusion assessment techniques, including ankle–brachial index, toe–brachial index, transcutaneous oxygen pressure, near-infrared spectroscopy, digital subtraction angiography, magnetic resonance angiography, computed tomographic angiography, and indocyanine green angiography.

Keywords: tissue perfusion, peripheral arterial disease, oxygen, wound healing

Introduction

Vascular and wound bed perfusion assessment should be integral to the care of people with associated atherosclerotic risk factors and chronic wounds in the lower extremities. Peripheral artery diseases (PADs) can be insidious, with many affected individuals unaware of circulation issues and failing to seek medical help until they develop foot ulcers, gangrene, and other related complications.[1] With an aging population and growing prevalence of complex comorbidities, these non-healing wounds are recognized as a burgeoning health problem placing significant burden on the affected individuals and the health care system.[2,3] There are a number of methods to assess for perfusion and wound-tissue oxygen balance that can be integrated into clinical practice. Accurate assessment will help determine healing potential and trigger early intervention to correct wound perfusion, such as hyperbaric oxygen therapy and revascularization. This article aims to discuss current and emerging wound perfusion assessment techniques that can be utilized for the advancement of patient care and wound-healing outcomes.

Correspondence: Kevin Y Woo
School of Nursing, Faculty of Health Sciences, Queen's University,
92 Barrie Street, Kingston, ON,
Canada K7L 3N6
Tel +1 613 533 6000 ext 74747
Fax +1 613 533 6770
Email kevin.woo@queensu.ca

Chronic wounds and perfusion

Cells and tissues are dependent on the vasculature for transport of oxygen and other essential nutrients. Disturbances in macro- or microvascular supply, such as ischemia (low perfusion pressure) and hypoxia (low oxygen content), can have profound effects on local tissue viability and repair. Adequate tissue perfusion and oxygenation is particularly relevant in healing tissue due to an increased energy demand for

reparative processes.[4] An expanding base of experimental and clinical investigation, as well as advancements in techniques to obtain accurate wound-tissue oxygen measurements, has begun to reveal that sufficient tissue oxygenation is critical for nearly all wound-healing processes. Emerging evidence for oxygen's central role in wound healing includes:[5–13]

- Antimicrobial action
  - Oxygen levels have a positive prevention effect on wound infection rates
  - Stimulation of selective leukocyte microbial killing in wound bed
  - Insufficient oxygen may lead to an increased bacterial load
- Cell metabolism
  - Essential in production of high-energy metabolites (ATP) required for reparative processes
- Collagen synthesis
  - Involved in the hydroxylation of proline and lysine in procollagen that is crucial for collagen maturation; insufficient oxygen may lead to poor collagen deposition
  - Supports cell motility and extracellular matrix formation
- Neovascularization
  - Induces angiogenesis, which restores tissue perfusion, reestablishes microcirculation, and increases oxygen tension to normal levels
  - Oxygen induces vascular endothelial growth factor mRNA levels in endothelial cells and macrophages in vivo
  - Supplemental oxygen administration has been shown to sustain and accelerate vessel growth
- Cell differentiation
  - May facilitate wound contraction by triggering the differentiation of fibroblasts to active contracting myofibroblasts
  - Increases keratinocyte differentiation, migration, and reepithelialization.

Chronic wounds are notably hypoxic, with transcutaneous oxygen tensions ($TcPO_2$) measured from 5 mmHg to 20 mmHg, compared to control tissue values of 30 mmHg to 50 mmHg.[14] Temporary hypoxia after injury is a necessary trigger for the initial phases of wound healing, stimulating processes such as the release of growth factors and angiogenesis.[13] However, chronic or prolonged periwound and wound bed hypoxia delays healing due to the imbalance between decreased oxygen delivery/availability and increased tissue demand during recovery from tissue injury. Chronic low $TcPO_2$ and perfusion pressure may be associated with accumulation of necrotic tissue and poor formation of granulation tissue,[15] and may contribute to the accumulation of harmful substances in the periwound microenvironment such as lactic acid (from hypoxia-induced anaerobic metabolism) that are further deleterious to wound healing.

Pathologies related to poor oxygen perfusion

Multiple pathologies are capable of impairing wound-tissue oxygen balance. PAD is one of the leading conditions that can alter perfusion and thereby increase susceptibility to localized tissue ischemia, contributing to delayed healing of lower extremity ulcers.[16] PAD is primarily caused by progressive atherosclerotic changes in the arteries reducing normal blood flow to the lower extremities. It is thought to affect approximately 4% of the population over the age of 40 years and 20% over 75 years or an estimated 25 million individuals in North America and Europe.[17] If severe arterial disease is left untreated, insufficient oxygen and nutrients to the tissue could result in complications such as ulceration, gangrene, and eventually amputation. Several studies demonstrate that enhancing wound bed perfusion and tissue oxygenation improves wound healing and reduces bacterial colonization.[10] Revascularization is now considered a standard therapeutic option for individuals with severe PAD and chronic leg ulcers to facilitate an increase in localized blood flow and oxygen delivery. Diabetes causes significant and extensive structural changes in the vascular system, increasing the risk of developing atherosclerosis (large- and medium-sized arteries) and inducing a specific lesion in microcirculation (small vessels). Hyperglycemia is responsible for the excess production of reactive oxygen species that damage and interfere with normal endothelial functions.[13]

Lifestyle or exogenous factors causing insufficient perfusion, vasoconstriction, or damage to the microvasculature can also result in poor wound healing.[18] Smoking is known to increase the risk of heart and vascular disease and has been shown to have a negative impact on wound healing via several mechanisms, notably the creation or worsening of wound hypoxia.[19] Components of cigarette smoke, such as the triad of nicotine, carbon monoxide, and hydrogen cyanide, can interfere with oxygen supply by inducing tissue ischemia via vasoconstrictive effects and impair cellular oxygen metabolism.[13] Obesity can produce wound-healing complications as a result of relative hypoperfusion and ischemia in the subcutaneous adipose tissue. Increased wound tension in obese individuals may lead to increased tissue pressure and a subsequent reduction in microperfusion and

availability of oxygen to the wound.[13] Sedentary habits or immobility can cause sustained external pressure, leading to local skin ischemia and pressure ulcer formation. Chronic physiologic stress and vasoconstricting medications have also shown relevance to tissue perfusion, oxygen delivery, and wound healing.

The identification and management of patients with poor perfusion often presents as a challenge for both the patient and the practitioner. Currently, chronic wounds consist of 98% of all lower extremity wounds.[1] More so, the common venous and diabetic etiologies associated with lower extremity wounds have been shown to also have an arterial component.[2,3] However, early diagnosis is difficult because many patients with arterial disease may remain asymptomatic for months or years until they develop leg ulcers.[4] Poor vascular supply to the wound results in poor cellular function and senescence.[5] Many clinics are dependent on simple assessment observations to identify arterial wounds, such as pain, recurrent slough, or punched-out borders. Others have noninvasive arterial study devices, which can more accurately define the patient's perfusion status. Selecting an ideal device to complete a perfusion assessment depends on the goals of the practitioner. While most technologies are designed to provide an estimation of the arterial flow to the extremity, a paucity of research is available to determine perfusion at or around the wound-tissue.

Clinical assessment

Treatment of chronic wounds requires a systematized approach under the tenets of wound bed preparation, which highlights the importance of optimizing perfusion and correcting underlying pathologies prior to local wound care. A complete patient history and physical examination is imperative to help determine the correct diagnosis of lower extremity ulcers. One of the most common and earliest manifestations of PAD is intermittent claudication, described as pain in a lower extremity muscle group (buttock, thigh, or calf), that is elicited by exertion and relieved within a few minutes of rest. However, only 10%–30% of individuals with PAD complain of claudication.[20] In other words, the majority of people (>50%) with this condition may remain asymptomatic without any clinically obvious signs or symptoms for a relatively long time. The Edinburgh claudication questionnaire (ECQ) is a validated tool that consists of six questions to measure symptoms of PAD.[21] The questions are:

1) Do you get pain or discomfort in your legs when you walk? 2) Does this pain ever begin when you are standing still or sitting? 3) Do you get it when you walk uphill or hurry? 4) Do you get it when you walk at an ordinary pace on the level? 5) What happens to it if you stand still? 6) Where do you get this pain or discomfort?

The ECQ has 91.3% sensitivity and 99.3% specificity in detecting claudication in the general population, compared with the diagnosis of PAD made by clinical examination. Positive predictive value (PPV) and negative predictive value (NPV) for the ECQ have been documented to be 100% and 81%, respectively.[21]

To obtain a comprehensive assessment of pain, multidimensional measurements are available to evaluate the many facets of pain and its impact on daily functioning, mood, social functioning, and other aspects of quality of life. The key questions to ask about pain can be remembered by PQRST:

- P – provoking and palliating factors: What makes your pain worse? What makes your pain better (eg, keeping feet warm; putting feet in dangling position and warm weather may alleviate pain, while walking and exposure to cold weather may exacerbate pain)?
- Q – quality of pain: What does your pain feel like? Descriptors, such as burning, electrical shocks, pricking, and tingling pins, are often used to describe neuropathic pain that is common in people with PAD and/or diabetes.
- R – regions and radiation: Where is the pain and does the pain move anywhere (eg, in and around the wound, the wound region, unrelated)? Patient with critical ischemic leg may complain of sudden onset with pain starting off distally, progressing proximally, and increasing in severity over time.
- S – severity or intensity: How much does it hurt on a scale of 0–10 with 0 representing no pain and 10 representing pain as bad as it could possibly be?
- T – Timing or history: When did the pain start? Is it present all the time? A pain diary may help to map out the temporal pattern of pain (eg, the pain worsens at night).

The peripheral artery questionnaire (PAQ) is a quality-of-life measure specifically designed for people with PAD.[22] The questionnaire consists of 20 items to evaluate patients' physical limitations, symptoms, social function, treatment satisfaction, and quality of life. The PAQ is reliable with Cronbach's alpha =0.80–0.94.[22] Patients who had undergone revascularization achieved a significant improvement in PAQ score substantiating the sensitivity of the PAQ to change.[22] Construct validity has been established by demonstrating correlations with other measures of patient health status.

With chronic hemodynamic and metabolic modifications, patients with arterial disease may exhibit trophic changes consistent with chronic ischemia. The skin may become pale, bluish, or dusky in color; dry; thin; hairless; shiny; and cool to touch, and there can be thickening of the nails and alterations in the foot structure.[23] Ischemic feet may appear erythematous, especially when the feet are arranged in dependent positions, also known as dependent rubor. This finding can sometimes be confused with cellulitis or gout. Abnormal capillary refill time (likelihood ratio [LR], 1.90; 95% confidence interval [CI], 1.20–3.20) is another clinical maneuver that can be incorporated into routine assessment of patients' feet.[24] Ulcers associated with arterial insufficiency tend to appear round or punched-out with scanty exudate. The wound bed may be covered with dry necrotic tissue involving structures such as muscle, tendon, and bone in the base. According to a systematic review of the evidence by Khan et al,[24] cool skin (LR, 5.9; 95% CI, 4.1–8.6) and pulse abnormalities (LR, 4.7; 95% CI, 2.2–9.9) were considered the most useful indicators for lower extremity PAD.

Ankle–brachial index

Ankle–brachial index (ABI) is widely accepted as a simple, noninvasive, inexpensive, yet reliable measurement for PAD and cardiovascular risk assessment. According to a systematic review of eight international guidelines on screening for perfusion deficits, ABI was unanimously recommended as the primary diagnostic tool for PAD in the case of clinical suspicion based on symptoms and clinical findings.[25] However, international studies indicate that screening is rarely performed in the primary care setting.[26,27] The PAD awareness, risk, and treatment: new resources for survival study identified several barriers to the adoption of screening using ABI in primary care settings, including time constraints, reimbursement, staff availability, and staff training.[27] The need to raise awareness and establish screening for PAD in the practice community is apparent.

ABI measurement can easily be obtained by any trained health care professional with a blood pressure cuff and a Doppler ultrasonic sensor in 10–15 minutes. To ensure accurate measurement, the following instructions are recommended:

1) Ask patients to recline and rest for 5–10 minutes in a supine position. 2) Measure systolic blood pressure in both arms and in both ankles from the dorsalis pedis and posterior tibial arteries. 3) Choose appropriate cuff size with cuff width approximately 20% larger than the limb diameter. 4) Place the blood pressure cuff approximately 2–3 cm above the medial malleolus. 5) Locate and listen to the pulse signal. Normal pulse generates three arterial components or triphasic signals. Stenosis is associated with monophasic sounds. 6) Inflate the cuff to at least 20 mmHg beyond the calibration where the pulse signal disappears. 7) Slowly deflate the cuff until the signal returns, concordant with the measurement of systolic pressure for that vessel.

ABI is defined as the ratio of the highest ankle systolic blood pressure divided by the highest brachial systolic blood pressure. In case of possible subclavian artery stenosis that renders falsely low blood pressure, the higher of the two brachial pressures is recommended as the denominator for the calculation. The American College of Cardiology Foundation/American Heart Association Task Force 2011 guidelines define normal values between 1.0 and 1.4.[1] An ABI of less than 0.9 is diagnostic for PAD; the lower values indicate more severe PAD. The values higher than 1.4 suggest that the arterial walls are calcified and cannot be compressed, as may be the case in some patients with diabetes or end-stage renal disease with medial calcinosis. A recent meta-analysis of eight studies comprising a total of 2,043 patients documented a high level of specificity (83.3%–99.0%) and accuracy (72.1%–89.2%) for an ABI $\leq$0.90 in detecting $\geq$50% stenosis as identified by other imaging methods, including angiography.[28] However, the levels of sensitivity were less optimal (15%–79%) due to falsely elevated ABI that occurs when blood vessels are noncompressible. Exercise promotes vasodilation, leading to a drop in ankle blood pressure. To augment accuracy, ABI could be measured immediately after exercise, especially among individuals in whom PAD is suspected according to clinical presentation despite a normal ABI at rest (Table 1).

Toe-brachial index

Recognizing the limitation of ABI to establish the diagnosis of lower extremity PAD due to incompressible vessels, toe-brachial index (TBI) has been proposed as a reliable alternative means since toe vessels are less susceptible to calcification. The TransAtlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) considered absolute toe pressure of $<$30–50 mmHg or a TBI $<$0.70 as an abnormal finding,[29] although the normal lower limits of TBI could range from 0.49 to 0.74 according to a recent review of the literature.[30] Previous studies demonstrate reliability of the measurement of toe pressures in patients with diabetes and varying severity of PAD with intraclass correlations ranging from 0.77 to 0.99 in intrarater

reliability and 0.85 to 0.93 in interrater reliability.[31–33] Using values of less than 0.6–0.75 as diagnostic criteria, the TBI has a sensitivity of 90%–100%, specificity of 65%–100%, PPV of 47%–100%, and NPV of 96%–100% for detecting peripheral artery disease (PAD) as identified by other imaging techniques (Table 1).[30]

Transcutaneous oxygen pressure ($TcPO_2$)

Transcutaneous oxygen pressures are measured by placing a heated probe (44°C) against the skin eliciting vasodilation and a local reactive hyperthermia. The probe measures oxygen that is released from red blood cells and diffuses through the epidermis. Byrne et al compared transcutaneous oxygen measurement with angiography.[34] $TcPO_2$ had a sensitivity of 77% and specificity of 100% in detecting the presence of arterial disease at rest; both sensitivity and specificity improved to 100% after exercise (Table 1). The normal $TcPO_2$values are greater than 55 mmHg, and wound healing could be significantly impaired if the value drops to <30 mmHg. $TcPO_2$ is a good predictor of wound healing with an accuracy rate of 83%.[35] Of note, $TcPO_2$ can be affected by oxygen uptake in the respiratory system and oxygen transport by the availability of hemoglobin and the function of the circulatory system.

Skin perfusion pressure

Skin perfusion pressure (SPP) is a noninvasive test using a laser Doppler to evaluate post-occlusive reactive hyperemia and determine the pressure that is required for restoring microcirculatory blood flow following a controlled release of occlusion (underneath the blood pressure cuff). Unlike ABI, SPP is not affected by conditions such as arterial wall calcification. SPP has been found to be significantly correlated with ABP, TBP, and TcPO2 (r=0.75, 0.85, and 0.62, respectively; all $P<0.0001$).[36] In a study of 113 patients with critical limb ischemia (123 limbs) who had undergone endovascular therapy, SPP of 30 mmHg was useful for predicting wound heal with a sensitivity of 81.4% and a specificity of 69.2%. Patients with SPP values of over 30 mmHg after endovascular therapy achieved a 90.8% healing rate compared with 50% in those having SPP values less than 30 mmHg.[37] In another study of 100 patients with chronic extremity wounds, SPP values ≥30 mmHg were highly sensitive (89.7%; 95% CI,

Table 1 Summary of common bedside perfusion assessment techniques

Test	Range	Evidence	Comments
Palpable pedal pulse (PPP)	80 mmHg	Absent or reduced pedal pulses increases the likelihood of PAD (LR, 4.70; 95% CI, 2.20–9.90; $P<0.001$ for heterogeneity).[24] PPP compared to color duplex imaging: patients with diabetes and PAD, sensitivity =81%, specificity =56%, and PPV =42%[25]	PPP can be affected by edema
ABI	>0.5 and <1.4	Using imaging techniques as reference tests, ABI is able to detect PAD with sensitivity =15%–79% and specificity =83.3%–99%.[54] ABI compared to color duplex imaging: patients with diabetes and PAD, sensitivity =53%, specificity =95%, and PPV =80%[25] Audible signals: sensitivity =42.8%, specificity =97.5%, NPV =94.10%, PPV =65.22%, positive likelihood ratio =17.52, and negative likelihood ratio =0.59[55]	False elevation in patients with calcified vessels[26] ABI–TBI index dropped if ABI was 1.4[27] Cuff inflation can be painful
$TcPO_2$	>30 mmHg	Below the knee, values of <30 mmHg predict the need for above the ankle amputation in diabetic patients; sensitivity =77% and specificity =83%[1] >30 mmHg predicts healing of DFU; sensitivity =15%, specificity =97%, PPV =79%, and NPV =94%[28]	Accuracy of the test can be affected by the presence of edema, dry flaky skin, maceration, callused or plantar skin, and cellulitis This method does not measure oxygen tension within the wound A time-consuming test
TBI	0.6–0.75	Sensitivity =90%–100%, specificity =65%–100%, PPV =47%–100%, and NPV =96%–100%	Large toe is of a small caliber without a fully developed adventitial layer to allow circumferential calcium deposits Cannot be calibrated with previous toe amputation

Abbreviations: PPP, palpable pedal pulse; PAD, peripheral artery disease; LR, likelihood ratio; CI, confidence interval; PPV, positive predictive value; ABI, ankle brachial index; ABI, ankle–brachial index; NPV, negative predictive value; TBI, toe-brachial index; $TcPO_2$, transcutaneous oxygen tension; DFU, diabetic foot ulcer.

81–95) but non-specific (38.5%; 95% CI, 14–68) for the prediction of wound healing.[38] The calculated PPV was 90.7% (95% CI, 82–96) and NPV was 35.7 (95% CI, 13–65). The accuracy of this test could be affected by movements, excess tremors, and incorrect placement of the sensor over bone or large vessels, or on nonblanching tissue.

Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) provides an estimation of changes in the concentrations of oxy- and deoxyhemoglobin in tissue.[39] Vardi and Nini[40] reviewed 21 studies using NIRS for the evaluation of PAD. Compared to people without PAD, individuals with claudication symptoms exhibited a lower resaturation rate of oxyhemoglobin (HbO_2) and longer recovery times, after both walking and arterial occlusion. There is evidence that half time of recovery to baseline values (T_{50}) for participants with PAD was significantly longer than people without PAD. Sensitivity and specificity ranged from 50% to 80%. NIRS is correlated with ABI.

Hyperspectral imaging

Hyperspectral imaging (HSI) involves using a spectral sensor to detect the wavelength of light reflected from red blood cells in the skin.[39] Since there is a difference in the wavelengths of light absorbed and emitted by red blood cells with oxyhemoglobin or deoxyhemoglobin, HSI can provide an accurate estimation for the levels of oxygenation and microvascular supply. It is desirable to have high levels of both oxyhemoglobin and deoxyhemoglobin that correlate with potential for wounds to heal.[41] HSI is recognized as a valuable diagnostic tool to predict wound healing with reported sensitivity 86%–93%, specificity 86%–88%, PPV 93%–96%, and NPV 86%.[41,42] Traditional contrast-based vascular imaging modalities are designed to confirm the diagnosis of PAD and to potentially plan for an intervention. These include conventional digital subtraction angiography (DSA), magnetic resonance angiography (MRA), and computed tomographic angiography (CTA). These investigations identify anatomic flow limiting stenoses/occlusions in large-, medium-, and small-sized arteries and allow surgeons and interventionalists to target revascularization with angioplasty/stent, endarterectomy, or bypass to improve wound perfusion. In general, the least diseased runoff artery is selected for revascularization based on the assumption that it could provide uninterrupted blood flow to the foot.[43] While the majority of the procedures are technically successful, wound perfusion remains inadequate to support healing.[44] More recently, the concept of angiosome-driven revascularization has challenged traditional thinking by suggesting that procedures should be directed to restore maximal blood flow to the tissue region where the wound is located.[45] In the future, anatomic-based imaging studies may therefore need to be supplemented by the tissue perfusion studies such as the ones outlined in this document to improve wound-healing rates.

Digital subtraction angiography

Contrast-based imaging techniques and modalities such as CTA are often selected as the first-line investigation for PAD due to ease of accessibility, and rapidity with which results are available; conventional angiography remains the true gold standard for challenging cases. DSA offers precise imaging of even the most distal vasculature of the limb. Direct arterial access also permits the unique opportunity for immediate therapeutic interventions such as angioplasty or stenting. The risk of contrast-induced nephropathy in patients with preexisting renal insufficiency can be overcome by substituting iodinated contrast with carbon dioxide (CO_2). CO_2 can be used as a contrast agent and still provides high-quality images for interpretation.

Magnetic resonance angiography

MRA is a noninvasive technique that applies magnetic fields and radio waves to produce images of the blood vessels and perfusion patterns without any ionizing radiation or nephrotoxic contrasts. Klein et al[46] compared MRA with DSA for the evaluation of crural arteries in 15 patients prior to free vascularized fibular flap transfer procedure. Results indicated a substantial agreement of stenosis severity scores between the two imaging techniques with Cohen's kappa of 0.64. The sensitivity of MRA to detect a stenosis compared with that of DSA was 79% (95% CI, 60–91) and the specificity was 98% (95% CI, 97–99). In a meta-analysis that involved 1,022 patients with known or suspected PAD of the lower extremities, the sensitivity of contrast-enhanced MRA was 94.7% (95% CI, 92.1%–96.4%) and the specificity was 95.6% (95% CI, 94.0%–96.8%) for diagnosing segmental steno-occlusions.[47] MRA was able to provide correct assessment in 95.3% of the studied arterial segments. Limitations to MRA include length of time required to complete studies, pro-arterial imaging may be obscured by venous artifact, and concerns over nephrogenic systemic fibrosis when gadolinium is used in patients with renal impairment. Conventional MRA studies may be enhanced in the future with techniques to provide information on

skeletal muscle perfusion, such as arterial spin labeling, blood oxygen level-dependent MRI, and first-pass dynamic contrast-enhanced MRI.[48]

CTA

CTA continues to be one of the most commonly used contrast-based imaging modalities in the investigation of lower extremity peripheral vascular disease. Within a few minutes, high-resolution images of the lower extremity arterial tree from the aorta to pedal vessels can be performed.[49] Drawbacks of CTA include the use of both ionizing radiation (potential cancer risk) and iodinated contrast with the potential for contrast-induced nephropathy.[50] Heavily calcified tibial vessels may pose problems for interpretation and lead to alternative studies being required to provide an accurate representation of the vasculature. New technologies such as single-photon emission computed tomography/computed tomography (CT) and positron emission tomography/CT seek to enhance the utility of CT scanning by adding a physiologic assessment of tissues. The addition of molecular imaging to traditional CT scans will allow for the high-resolution anatomic images of CT scan to be enhanced with direct visualization of active areas of inflammation or infection.[51] This information can play a key role in directing wound care.

Indocyanine green angiography

Indocyanine green (ICG) is a fluorescent dye that binds to plasma proteins and remains predominantly in the intravascular space until it is excreted by the hepatobiliary system. ICG is activated and illuminated by near-infrared light (between 700 nm and 1,000 nm) that penetrates at least 3 mm below the surface of the skin. Subdermal perfusion can then be measured and expressed quantitatively in terms of fluorescence intensity in pixels, the time to maximum intensity (perfusion index), and the time from fluorescence onset to half the maximum intensity ($T_{1/2}$). In a study that evaluated 22 limbs in 16 patients with PAD using indocyanine green angiography (ICGA), $T_{1/2}$ for more than 10 seconds was significantly correlated with an ABI value of <0.7 (sensitivity: 0.85, specificity: 1.0).[52] According to another study of 30 patients with symptomatic PAD, perfusion index measure by ICGA was significantly related to collateral circulation in the lower extremities ($P=0.003$). A receiver operating characteristic curve analysis for the perfusion index revealed a positive LR of 6.00 and a negative LR of 0.00 with an area under the curve of 0.949 to discriminate critical and non-critical PAD.[53]

Conclusion

The complexity of healing depends on many intrinsic and extrinsic factors, which regulate the complex biochemical and cellular events that culminate in closure of a wound with fibrotic scar tissue. Unlike acute wounds, chronic wounds, such as pressure ulcers, venous leg ulcers, and diabetic foot ulcers, do not always follow predictable temporal overlapping phases of healing due to inadequate tissue perfusion. Chronic or prolonged wound hypoxia is a key factor in the development and poor prognosis of chronic wounds. When oxygen availability to a wound is reduced by hypoperfusion from macrovascular arterial disease, microvascular failure, local edema, or infection, wound healing is invariably impaired. A systematic, multi-faceted, and personalized health care approach is required for optimal wound care management and healing outcomes. Careful attention should also be made to identify underlying diseases and lifestyle and exogenous factors that may be contributing to poor wound perfusion and healing outcomes in order to reverse and correct their deleterious effects. This proactive approach to institute early treatment based on quality clinical assessment may prevent or delay progression of the vascular disease, reduce the risk of further cardiovascular complications, ameliorate related symptoms, improve wound healing outcomes, minimize the risk of long-term disability, and improve overall quality of life.

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