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Use of a fluorescence angiography system in assessment of lower extremity ulcers in patients with peripheral arterial disease: A review and a look forward

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ARTICLE INFO

ABSTRACT

The prevalence of chronic wounds is sharply rising throughout the world due to an aging population and increases in the incidence of obesity, diabetes, and cardiovascular diseases. People with diabetes, hypertension, and hyperlipidemia are at increased risk for developing peripheral arterial disease (PAD). PAD affects 8 to 12 million people over the age of 40 years in the United States and it is a major contributing factor to the development of lower extremity ulcers. Although a number of noninvasive diagnostic tests are available to detect PAD in lower extremities, they have several clinical limitations. In this review, current understanding of the pathophysiology of commonly seen lower extremity ulcers is described and vascular assessments typically used in practice are evaluated. In addition, application of the LUNA Fluorescence Angiography System (Novadaq, Bonita Springs, FL) for the screening and treatment of complex nonhealing wounds in patients with PAD is discussed.

1. Introduction

An upward trend in the prevalence of obesity, diabetes, and cardiovascular disease parallels the increase in chronic wounds. In the United States, chronic wounds afflict an estimated 6.5 million people [1]. The prevalence of chronic wounds, pressure ulcers, venous, arterial, and diabetic wounds is expected to grow 7.6% by 2020 [2,3]. In addition, people with diabetes, hypertension, and hyperlipidemia are at increased risk for developing peripheral arterial disease (PAD) [4]. PAD affects 8 to 12 million people over the age of 40 years in the United States and it is a major contributing factor in the development of lower extremity ulcer (LEU) [5-7].

PAD develops as a result of atherosclerosis of the aorta, iliac, and lower extremity arteries. In patients with poorly controlled blood glucose, hyperlipidemia and hypertension; endothelial cell dysfunction; and smooth cell abnormalities can develop [8]. Structural changes in blood vessels can lead to inadequate blood supply to the tissues. Compromised peripheral blood supply leads to ischemia and hypoxia. Hyperglycemia is also associated with an increase in thromboxane A2, a vasoconstrictor and platelet aggregation

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http://dx.doi.org/10.1053/j.semvascsurg.2015.12.002
0895-7967/$ - see front matter © 2015 Elsevier Inc. All rights reserved.

agonist, which can increase the risk for blood clotting disorders [9]. Changes in extracellular matrix can also lead to stenosis of arterial lumen [9]. In addition, the presence of bacterial infection in LEUs is well documented [10,11], which, if left untreated, can lead to serious complications for the patient. LEUs pose a significant clinical and economic burden. It is not uncommon for wound care specialists to see patients who have suffered for years or faced amputation of the limb as their only option to alleviate the pain.

Early detection and ongoing monitoring of PAD is essential in effective management and prevention of complications such as ulcers, gangrene, and amputation. Although noninvasive vascular assessments offer clinicians a simple and cost-effective method to evaluate PAD, these tests have several clinical limitations and practical challenges. There continues to be a pressing need for a more efficient vascular screening tools that can aid treatment decisions in patient with LEU. The LUNA Fluorescence Angiography System (FAS) (Novadaq, Bonita Springs, FL) offers wound care specialists a novel technology to document baseline tissue perfusion and validate or revise treatment by assessing perfusion after therapies such as vascular intervention, hyperbaric oxygen therapy (HBOT), and negative pressure wound therapy.

In this review, the current understanding of the pathophysiology of commonly seen LEUs is described and vascular examinations typically used in practice are evaluated. Furthermore, clinical application of LUNA FAS in screening and treatment of complex nonhealing wounds in patients with PAD are discussed.

2. Pathophysiology of lower extremity ulcers

LEUs can have more than one etiology [12–14]. Most LEUs are caused by venous disease [12]. Reflux is the most common underlying cause of dysfunction in venous return from incompetent valves in the superficial, perforating or deep veins, outflow obstructions in the deep veins, or calf muscle pump failure because of disease influencing lower limb mobility.

The second most common cause for LEUs is arterial disease. PAD is a major contributor of arterial disease, which results in narrowing or blockage of the blood vessels in the legs. Atherosclerotic obstruction usually occurs in the iliac, femoropopliteal, and the distal branches, (ie, peroneal and tibial arteries). Patients with PAD have heightened endothelial and platelet activation secondary to a prothrombotic state. Some risk factors for PAD include diabetes mellitus, elevated low-density lipoprotein, hypertension, elevated fibrinogen, and advanced age [15,16].

3. Vascular assessments

Vascular assessment in patients with LEUs may include palpation of femoral, popliteal, posterior tibial, and dorsalis pedis pulses. The ankle-brachial index (ABI) is usually the most common test performed in the evaluation of patients with PAD. ABI is the ratio of blood pressure measured at the ankle to that measured at the arm. An ABI <0.75 indicates that there is a high probability that arterial insufficiency is present (positive predictive value 95% in a general practice population). It should be noted that incompressible, calcified arteries and presence of kidney disease or advanced age can cause a falsely elevated ABI [17–19]. Further, 10% of the general population have a congenital absence of the dorsalis pedis or posterior tibial artery [20]. In a cross-sectional study that compared pulse oximetry and ABI in patients with type 2 diabetes, Paameswaran et al. noted that ABI had a sensitivity of only 63% (95% confidence interval, 46%–77%) and a specificity of 97% (95% confidence interval, 91%–99%) [21].

In clinical cases where ABI cannot be interpreted, toe brachial index (TBI) may be used. TBI is the ratio between toe pressure and the higher of the two brachial pressures. TBI is taken more distally in the lower limb, thus there is a greater chance of arterial pressure changes caused by stenosis located below the knee in diabetes patients [22]. While TBI is more sensitive than ABI in diabetes patients, there is limited evidence on the validity of the assessment. Although several guidelines recommend a TBI <0.70 as a cutoff, it is not strictly evidence-based [17–19,23–26]. Clinical presentations, such as skin ulcers, gangrene, or prior digital amputation, can preclude measurement of toe pressures.

Transcutaneous oxygen monitoring (TCOM) is another commonly used noninvasive vascular testing method. TCOM gives an indication of the amount of oxygen that has diffused from capillaries through the epidermis. TCOM is used for wound-healing prediction, amputation-level determination, and qualification of HBOT. While TCOM is not affected by calcified leg arteries, it does have other physical limitations; the probe cannot be placed over the plantar foot because the thickness of skin does not allow for oxygen permeation and it cannot be used in patients with edema and inflammation [27].

Skin perfusion pressure (SPP) is the pressure required for restoring microcirculatory blood flow after the release of carefully controlled occlusion. It provides an indication of the status of the proximal arterial system. Measurement of SPP has been shown to be useful in the assessment of PAD and critical ischemia [28–31]. SPP is not affected by arterial wall calcification and can be measured in the limbs when patients present with skin lesions on toe or digital amputation precludes measurement of the toe pressure. One of the disadvantages of SPP is that the area measured must be able to fit a cuff and the blood flow occlusion can be painful.

4. Fluorescence angiography system

LUNA is an emerging FAS that enables clinicians to distinguish between perfused and nonperfused tissue. The system uses an injectable dye, indocyanine green (ICG), which produces a fluorescence image showing blood flow in vessels and perfusion. The system offers the clinician full control of the imaging head and produces images immediately on a computer monitor, allowing visualization of real-time tissue perfusion. Being able to predict perfusion and viability of the tissue allows for more effective treatment strategies and wound healing outcomes. The application and effectiveness of LUNA FAS in vascular surgery and wound therapy has been documented in a number of studies [32–39].