The role of fluorescein angiography in the management of orphan heel syndrome

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Abstract:

Heel ulcers are common, and regardless of the etiology they may become ischemic because of the unique blood supply to the heel (Orphan Heel Syndrome). Measurement of tissue perfusion in the assessment of heel ulcers is critical, and common non-invasive vascular testing can often be misleading. The following case report demonstrates the use of Fluorescein angiography to assess and monitor perfusion to a heel ulcer and surrounding soft tissues during treatment.

We present an 81-year-old diabetic female with a right postero-lateral heel ulcer, non-palpable pulses, and an abnormal doppler exam. She also had monophasic dorsalis pedis and perforating peroneal arteries with no signal in the posterior tibial artery. Initial Fluorescein angiography revealed no fluorescence in the wound base and little inflammatory reaction surrounding the ulcer. She underwent placement of a popliteal stent, resulting in triphasic doppler signals in the dorsalis pedis and perforating peroneal arteries with no audible posterior tibial artery. The immediate post-operative Fluorescein study demonstrated improved perfusion to the ulcer and a peri-ulcerative area that was maintained at the 6-week follow-up period. With local wound care and off-loading, the patient healed in six weeks.

All patients presenting with a heel ulcer should be assessed for coexisting arterial insufficiency. Because of the distribution of arterial branches to the heel, and the possibility of regional ischemia, the clinician should be suspicious of Orphan Heel Syndrome whenever a heel ulcer is present. Fluorescein angiography is a tool that can identify a regional ischemia, thus leading to appropriate treatment and avoidance of a major amputation.

Key words: Flourescein Angiography, Heel Ulcer, Orphan Heel Syndrome

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INTRODUCTION

Heel ulcers are common, occurring secondary to 1) combined neuropathy and repetitive trauma, 2) immobilization with prolonged skin pressure, or 3) direct trauma.[1,2] Heel ulcers heal slower than forefoot ulcerations, and unfortunately more amputations occur in the presence of heel ulcers.[3,4]

The likely explanation for slower healing relates to a circulatory component to the disease process. The heel has a unique arterial supply including contributions from the posterior tibial artery and the perforating peroneal artery with an increased potential for tissue ischemia.[5] This associated ischemia may lead to non-healing ulcers and major complications such as infection, sepsis, amputation, and death. Therefore, all patients with heel ulcers should be assessed for associated ischemia.

Due to the specific arterial supply of the heel, understanding and using the concept of angiosomes in evaluating patients with heel ulcers is essential. No artery-to-artery connections between the posterior tibial arterial branches and the branches of the peroneal artery exist in the heel.[5] Due to the distinctive vascularity and potential for the multi-vessel distal disease, focal ischemia may be present. The presence of heel ulcers associated with focal ischemia is referred to as Orphan Heel Syndrome.

Revascularization plays an important role in treating Orphan Heel Syndrome. Ideally, when revascularizing ischemic heel ulcers the concept of angiosome-guided revascularization should be strongly considered. When possible, direct revascularization leads to increased rates of limb

salvage and complete wound healing. However, if direct revascularization is not possible, it remains beneficial to perform revascularization through an indirect method.[6,7]

Due to the under appreciated presence of regional heel ischemia, it is critical to measure tissue perfusion in patients with heel ulcers to properly identify those with associated ischemia. Current methods used to evaluate tissue perfusion at the heel include ankle-brachial index, toe pressures, skin perfusion pressure test (SPP), forefoot pulse volume recordings (PVR), and transcutaneous oximetry (tcpo2). These tests are often limited by medial calcinosis, scarring, previous amputations, or ulcer location that can lead to little clinically pertinent data and the inability to dictate appropriate intervention methods or monitor treatment efficacy.[8]

Fluorescein angiography offers an additional method to assess real-time tissue perfusion and assess the healing potential for ulcers.[8] This modality is considered minimally invasive, safe, easy to perform, easily accessible, and low cost.[9] Fluorescein angiography is useful in identifying heel ischemia and documenting improved perfusion following revascularization and therapy treatments. Likewise, Fluoroscein angiography allows for early recognition of arterial insufficiency, which leads to modified treatment and the potential to heal ulcers while preventing major amputations. If regional ischemia is not identified, revascularization is not likely to be performed, and the risk of limb loss increases.

This case study demonstrates the utility of Fluorescene angiography in identifying regional heel ischemia in a patient with a heel ulcer. In addition, this report documents increased perfusion to the wound and surrounding tissue using an indirect revascularization approach.

Case Report

An 81-year-old female with a medical history with poorly-controlled insulin-dependent Type 2 Diabetes Mellitus (DM) with neuropathy, nephropathy, hypertension, and hyperlipidemia presented to the limb preservation clinic. She had a painful right postero-lateral heel ulceration that had been present for three weeks *(Figure 1)*. Initial pulse examination revealed non-palpable pedal pulses and an abnormal bedside doppler examination. The posterior tibial artery was non-audible, while the dorsalis pedis and perforating peroneal arteries were monophasic. Non-invasive vascular testing revealed a right lower extremity ankle-brachial index (ABI) of 0.51 mmHg with waveforms suggestive of moderate to severe arterial disease. Outpatient Fluorescein angiography showed a lack of perfusion to the ulcer bed and minimal inflammatory response.

Figure 1. Clinical appearance of wound at initial visit.

Initial treatments included topical dressings (initially cadexomer iodine, later conversion to collagenase), heel offloading, instruction to remain non-weightbearing to the lower extremity, and CT angiography. An arteriogram demonstrated popliteal arterial occlusion and single vessel runoff through the perforating peroneal artery *(Figure 2)*. A popliteal stent was placed *(Figure 3)*. Following the stent placement, arterial flow to the foot improved with a triphasic dorsalis pedis doppler signal, but no posterior tibial signal was appreciated.

Twenty-four hours after revascularization, a repeat Fluorescene angiography study was performed to the right heel ulceration area. It showed improved perfusion to the ulcer and improved surrounding inflammatory reaction. Following revascularization, the patient had regular follow-up visits. Visits allowed for wound monitoring, regular sharp debridement provision, and assurance of continued use of non-weight

bearing heel off-loading. Additionally, she was treated on two different occasions with topical application of amniotic biologics.

Two weeks post popliteal artery stent placement, she also had a monophasic posterior tibial arterial signal. At six weeks, the Fluorescein

Figure 2. Appearance of artery prior to stenting.

Figure 3. Appearance of artery following popliteal arterial stenting.

angiography was repeated and showed significantly less peripheral inflammatory reaction with much improved vascular perfusion to the entire wound bed. This showed increased healing potential *(Figure 4)*. Two weeks following the last Fluorescein angiography study, her ulcer was completely epithelialized *(Figure 5)*. She was transitioned to extra-depth diabetic shoes with appropriate accommodative orthotics.
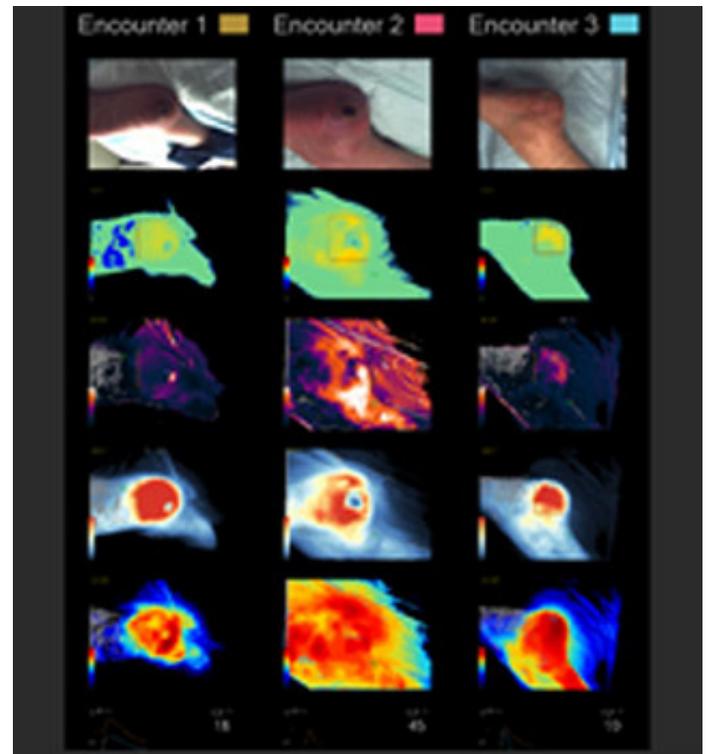

Figure 4. Images obtained during Fluorescein angiography on three separate encounters: Encounter 1 is baseline; Encounter 2 is immediately post stenting; and Encounter 3 is six weeks status post stenting.

Figure 5. Clinical appearance of healed wound.

DISCUSSION

The etiology of heel ulcers occurs from biomechanical or mechanically induced forces with shearing/friction or increased pressures leading to increased tissue hypoxia and chronic inflammation. Pressure to the heel is a cause of ischemia and is harmful either with longer periods of time or increased force.[2] The onset and continuation of these forces can go unnoticed due to neuropathy and ischemia. However, for patients with peripheral arterial disease, much less time or pressure is required to create an ulcer. Internationally, pressure ulcers of the heel account for approximately 23% of all pressure ulcers.[2] Limb salvage rates for patients with heel ulcers have been estimated to be between 65-89%. This is much lower than limb salvage rates for digits, forefoot, or midfoot ulcers.[10] One explanation for a decreased salvage rate would be the lack of vascular testing. A study observing hospitalized patients demonstrated that up to 70% of the patients with heel ulcers did not receive thorough vascular testing. Consequently, the one-year mortality rate for the 65 and older patients in the study was around 70%.[11]

Peripheral vascular disease affects between 8 to 12 million patients over the age of 40 in the United States. Risk factors for the development of peripheral arterial disease (PAD) are DM, hypertension, hypercholesterolemia, and smoking. Diabetes mellitus is a risk factor for PAD with prevalence rates cited between 10-40% of all diabetic patients. Diabetic patients are at a four-fold risk to develop PAD.[12] Diabetic patients have more distal arterial manifestations; their disease state progresses more rapidly; and they have a significantly higher mortality rate.[12,13,14] Due to their poor arterial flow these patients have an increased risk of ulceration, which can lead to infection and, ultimately, amputation. Understanding the frequent presentation and risk factors of diabetic patients is required when conducting a thorough vascular examination. In patients with diabetic foot ulcers, up to 50% had various degrees of PAD.[13]

Besides arterial issues in the macroscopic level of the artery, there are matching events microscopically. Even at the molecular level, when a diabetic artery is directly compared to a non-diabetic artery, it has been found to have a decreased wall to lumen ratio, stiffer vessels, and issues with angiogenesis. Due to many factors associated with DM, the artery displays derangement in the extracellular matrix and displays dysfunctionality of the smooth muscle and endothelium.[14]

Patients with heel ulcers incur more amputations and heal more slowly than those with forefoot ulcers.[3] The arterial anatomy of the heel is variable. The heel has a unique arterial supply with a potential for ischemia, and it requires an enhanced method to assess local heel tissue perfusion.

The foot and ankle consist of six different angiosomes. These derive from the posterior tibial artery, the anterior tibial artery, or the peroneal artery. However, the foot has several arterial-to-arterial connections that allow for immediate continued blood flow to an area if the direct route is damaged or occluded. Understanding this can assist in the patient's physical exam and determining the predominate artery with a particular angiosome. Testing can be performed with a doppler, and occlusion of the artery with pressure distal and proximal to the placement of the probe. The choke vessel can provide indirect vascular flow to an area that is outside its normal angiosome distribution. A simple doppler exam can determine if the flow is indirect from a choke vessel or from direct pressure. If it is a manual occlusion, the artery proximal to the doppler elicits a distal audible signal and there can be reasonable certainty that the flow is supplied by a different artery.[5]

The heel is a unique angiosome because it receives blood supply from two sources, the posterior tibial artery and the peroneal artery. No direct artery-to-artery connections exist in this area.[5] Due to the distinctive vascularity, when considering angiosomes of the heel and multi-vessel diseases of diabetic patients, Orphan Heel Syndrome must be considered in patients that

present with ischemic ulcers of the heel. This situation is indicative of only one vessel partially distributing blood flow to the region, with little to no artery-to-artery reconstitution occurring to the area.[15]

Both the angiosome distribution of an ulcer and a thorough patient evaluation to determine any possible artery-to-artery connections supplying that area cannot be underestimated. This is especially true for planning revascularization. Due to multiple levels of distal arterial occlusions, and the tendency for it to occur in multiple vessels, the reality of revascularization is more challenging. Several studies have evaluated limb salvage outcomes and ulcer healing rates of direct angiosome revascularization. They have shown similar or improved results when compared to indirect revascularization.[6,13] A recent systemic review has found that reported rates of limb salvage at one year and three years were better for open revascularization. At one year, diabetic patients displayed increased limb salvage rates (between 78-85%) when having a revascularization procedure performed than if treated without revascularization (54%). At five years, the estimated average limb salvage rate was 77.5%.[13]

By relying on and understanding dorsalis pedis artery bypass, favorable results (86.5%) have been shown in the healing of heel ulcerations.[16] This connection is not a guarantee, which is an argument for direct revascularization procedures. Studies have shown results that were statistically significant for complete wound healing in direct revascularization procedures (90.0% vs. 61.9%) than when not engaged with direct revascularization procedures. Direct revascularization also showed an amputation rate four times less than in those having an indirect procedure.[6] While many studies find direct revascularization to be preferable for ulcer healing, indirect revascularization should be considered in cases that do not allow for a direct procedure.[7,17] This concept is extremely important in understanding and predicting the healing potential of a heel ulcer.[18]

Measurement of tissue perfusion is critical in assessing patients with heel ulceration. Current methods used to evaluate tissue perfusion to the foot include ABIs, toe pressures, SPP, forefoot PVR, and tcpo2. Following the physical exam, the ABI and Toe-Brachial Index (TBI) are frequently used as initial non-invasive vascular tests to determine disease status, location, and severity.

However, the ABI has shown to be ineffective in measuring disease in diabetic patients. Often the results are falsely elevated due to non-compressible arteries affected by medial artery calcification. The ABI also has issues with detecting any smaller vessel disease distal to the ankle. A recent study found the ABIs specificity to be high (92.68%), but the sensitivities were low (45.16%). The TBI can be useful when more distal detection of arterial disease occurs and is less affected by arterial calcifications common in DM. The exact accuracy has been debated, and more studies will be required. Recent sensitivities were found to be 63% with specificities around 82% in patients with DM.[12]

Toe pressures are difficult to obtain in patients with skin ulcers, gangrene, pain, or previous amputations.[8] Both ABI and TBI have decreased sensitivities as compared to non-DM patients.[12] Additionally, the ABI has been calculated to be based off the anterior tibial artery in 53.06% of feet and thus would not be directly applicable to the anticipated healing potential of all foot ulcers.[19] A study by Taylor included a patient population with heel ulcers in which 38% had normal ABI measurements but notably severe perfusion decrease when angiography was performed.[15] Transcutaneous oxygen monitoring is another tool that can be useful to evaluate wound healing. Testing is limited in the plantar foot due to the skin's thickness.[20]

CT angiography can only be used to visualize the vessel's lumen and cannot be used to determine the end amount of tissue perfusion. The major complication rate of peripheral arteriogram is approximately 2.9%.[21] The arteriogram is far too invasive, with concern for causing damage to the vessel, to be used as an

initial modality to determine location and severity of arterial disease status.

Fluorescein angiography can assess tissue perfusion and identify the healing potential for heel ulcers. This modality is considered minimally invasive, safe, easy to perform, and inexpensive.[9] It consists of using indocyanine green (ICG) as an intravenous injectable and monitoring its dissemination into the tissues. Fluorescein angiography/imaging has been found to provide reliable qualitative and quantitative imaging to determine local tissue perfusion in mild to moderate degrees of PAD.[9] This has also shown to be useful in obtaining baselines and assessing efficacy during treatment.

Though many clinicians use the modality to see real time tissue perfusion qualitatively, a study evaluated the quantitative data that can be obtained during the use of ICG imaging.[22] This data can be reliably derived from the images. The most reliable parameter is the time it takes the ICG to reach maximum intensity. The case report demonstrates the utility of Fluorescein angiography in identifying ischemia in a patient with a heel ulcer. The recognition of arterial insufficiency in patients with heel ulcers leads to altered treatment, lower potential heal ulceration, and prevention of major amputation.

CONCLUSION

All patients presenting with a heel ulcer should be assessed for coexisting arterial insufficiency. Because of the distribution of arterial branches to the heel, regional ischemia may occur. This condition has been labeled Orphan Heel Syndrome. This condition may occur with normal ABIs and a palpable DP pulse. Understanding the concept of angiosomes and the unique blood supply to the heel leads to a high index of suspicion and further assessment of perfusion to the heel. Many of the initial non-invasive modalities are limited by medial calcinosis, scarring, wounds, prior toe amputations, and infection. Current methods can also be technically challenging, costly, and time consuming, and they do not measure global perfusion of the foot or regional perfusion of the heel. New and advanced modalities such as Fluorescein angiography can be used to evaluate the healing potential of ulcers prior to and following surgical intervention. It has also been shown to provide both qualitative and quantitative information in healing potentials, and can assess the level of amputation and efficacy of treatments. Heel ischemia identification and treatment may lead to improved heel ulcer healing and a decreased amputation rate.

References

1. Clark M, Black J, Alves P, et al. Systematic review of the use of prophylactic dressings in the prevention of pressure ulcers. *Int Wound J.* 2014;11:460-471.

2. Salcido R, Augustine L, Chulhyun A. Heel pressure ulcers: purple heel and deep tissue injury. *Adv Skin Wound Care.* 2011;24.8:374-380.

3. Yosuf MK, Mahadi SI, Mahmoud SM, et al. Diabetic neuropathic forefoot and heel ulcers: management, clinical presentation and outcomes. *J Wound Care.* 2015;24(9):420-425.

4. Pickwell KM, Siersma VD, Kars M, et al. Diabetic foot disease: impact of ulcer location on ulcer healing. *Diabetes Metab Res Rev.* 2013;29(5):377-383.

5. Clemens MW, Attinger CE. Angiosomes and wound care in the diabetic foot. *Foot Ankle Clin.* 2010;15(3):439-464.

6. Neville RF, Attinger CE, Bulan EJ, et al. Revascularization of a specific angiosome for limb salvage: does the target artery matter? *Ann Vasc Surg.* 2009;23(3):367-373.

7. Kabra A, Suresh KR, Vivekanand V, et al. Outcomes of angiosome and non-angiosome targeted revascularization in critical lower limb ischemia. *J Vasc Surg.* 2013;57(1):44-49.

8. Samies JH, et al. Use of a fluorescence angiography system in assessment of lower extremity ulcers in patients with peripheral arterial disease: A review and a look forward. *Semin Vasc Surg.* 2015;28 (3-4):190-194.

References (continued)

9. Kang Y, Lee J, Kwon K, Choi C. Dynamic fluorescence imaging of indocyanine green for reliable and sensitive diagnosis of peripheral vascular insufficiency. *Microvasc Res*. 2010;80(3):552-555.

10. Shojaiefard A, Khorgami Z, Mohajeri-Tehrani MR, Larijani B. Large and deep diabetic heel ulcers need not lead to amputation. *Foot Ankle Int*. 2013;34(2):215-221.

11. Malik R, Pinto P, Bogaisky M, et al. Older adults with heel ulcers in the acute care setting: frequency of noninvasive vascular assessment, surgical intervention, and 1-year mortality. *J Am Med Dir Assoc*. 2013;14(12):916-919.

12. Tehan PE, Bray A, Chuter VH. Non-invasive vascular assessment in the foot with diabetes: sensitivity and specificity of the ankle brachial index, toe brachial index and continuous wave Doppler for detecting peripheral arterial disease. *J Diabetes Complications*. 2016;30(1):155-160.

13. Hinchliffe RJ, Brownrigg JRW, Apelqvist J, et al. Effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. *Diabetes/Metabolism Research and Reviews*. 2016;32(S1):136-144.

14. Ruiter MS, Van Golde J, Schaper NC, et al. Diabetes impairs arteriogenesis in the peripheral circulation: review of molecular mechanisms. *Clinical Science*. 2010;119(6):225-238.

15. Taylor Z. The diagnostic triad of orphan heel syndrome: posterior tibial and peroneal artery occlusive disease, poorly controlled diabetes, and renal failure. *J Vasc Surg*. 2013;2(58):565.

16. Berceli, SA, Chan AK, Pomposelli FB Jr, et al. Efficacy of dorsal pedal artery bypass in limb salvage for ischemic heel ulcers. *J of Vasc Surg*. 1999;30(3):499-508

17. Aerden D, Denecker N, Gallala S, et al. Wound morphology and topography in the diabetic foot: hurdles in implementing angiosome-guided revascularization. *Int J Vasc Med*. 2014;2014:672897.

18. Faglia E, Clerici G, Caminiti M, et al. Heel ulcer and blood flow: the importance of the angiosome concept. *Int J Low Extrem Wounds*. 2013;12(3):226-230.

19. Wiest A, Meyer AJ. Accuracy of the ankle-brachial index in the assessment of arterial perfusion of heel decubitus ulcerations. Poster presentation. Presented at the American College of Foot and Ankle Surgeons, Annual Scientific Conference. Feb. 2016.

20. Yamada T, Ohta T, Ishibashi H, et al. Clinical reliability and utility of skin perfusion pressure measurement in ischemic limbs—comparison with other noninvasive diagnostic methods. *J Vasc Surg*. 2008;47(2):318-323.

21. Egglin TK, O'Moore PV, Feinstein AR, Waltman AC. Complications of peripheral arteriography: a new system to identify patients at increased risk. *J Vasc Surg*. 1995;22(6):787-794.

22. Igari, K, Kudo T, Toyofuku T, et al. Quantitative evaluation of the outcomes of revascularization procedures for peripheral arterial disease using indocyanine green angiography. *Eur J Vasc Endovasc*. 2013;46(4):460-465.

23. American Diabetes Association. Peripheral arterial disease in people with diabetes. *Clinical Diabetes*. 2004;22(4):181-189.