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Review Article

Advanced limb salvage: Pedal artery interventions

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ABSTRACT

Chronic limb-threatening ischemia (CLTI) is on the rise due to the increasing prevalence of diabetes, which is a significant cause of morbidity and mortality worldwide. Due to diabetes, many patients with CLTI present with a predominance of tibial and pedal artery disease. Despite best care, limb amputation cannot always be prevented. Surgical bypass has always been the mainstay in distal revascularization and limb salvage; however, many patients with CLTI have comorbidities, insufficient vein, and anatomic abnormalities that prevent them from undergoing surgery. As a result, endovascular therapies have increased over the last 2 decades and are providing revascularization options in these patients. Although most of the current endovascular literature has focused on above-ankle arterial interventions, recent studies have highlighted the feasibility, safety, and clinical importance of pedal artery interventions. These endovascular techniques hold promise in relieving ischemic pain, healing foot ulcers, reducing rates and extent of amputation, and improving patient functionality and quality of life. This review aims to comprehensively detail pedal artery interventions in terms of anatomy, technique, intraprocedural imaging, and outcomes. In addition, suggestions of when to perform pedal artery interventions and post-intervention surveillance options will be discussed.

1. Introduction

Chronic limb-threatening ischemia (CLTI) results in increased mortality, amputation, and poor quality of life. As defined by the Global Vascular Guidelines, CLTI is the presence of lower limb peripheral artery disease concurrently with rest pain, gangrene, or ulceration of longer than 2 weeks [1]. Diabetes is the most significant nontraumatic risk factor for the development of CLTI. As rates of metabolic disease increase throughout the developing world, so too does the need to develop evidence-based approaches to managing patients with CLTI [2,3]. CLTI presents a significant burden to the patient with >73% of those diagnosed progressing to amputation within 1 year [4,5]. Limb salvage is critical as primary amputation is associated with shorter survival and a greater risk for subsequent future major amputation [5]. Although the mainstay for the initial management of CLTI is risk factor modification and medical management, many patients will progress and require endovascular therapy or surgery. The choice of intervention remains complex [6–8], however, immediate revascularization is key in preventing functional limb deficits and limb loss [6–10]. Given the prevalence of diabetes in patients with CLTI, these patients often present with more distal disease with diffuse and severe tibial and pedal artery disease [11]. When significant coexisting pedal artery disease is left untreated, clinical trials have demonstrated suboptimal wound

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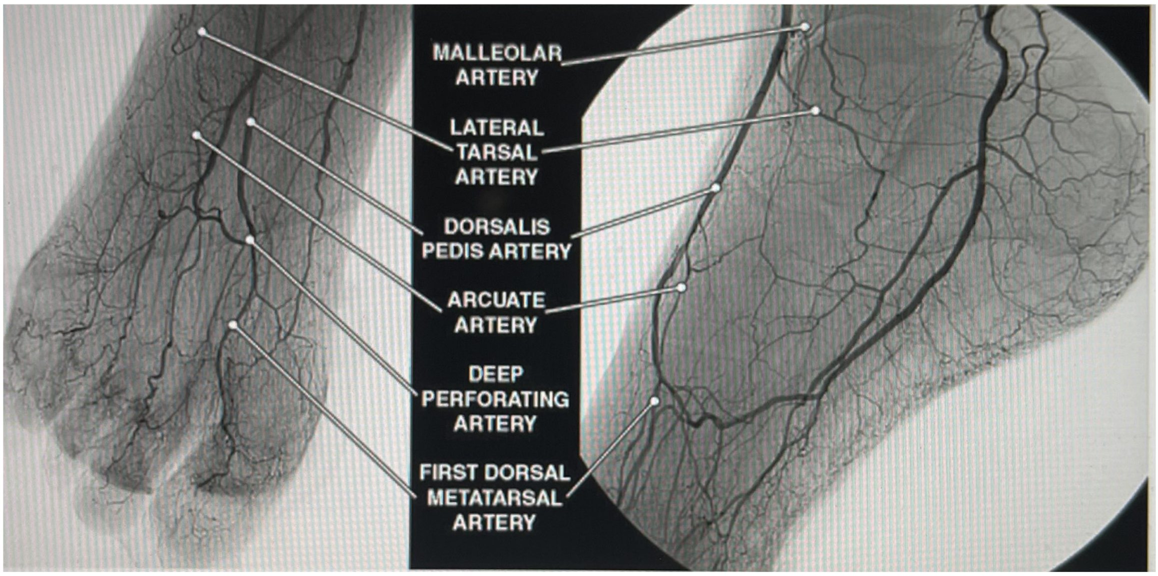


Fig. 1 – Anterior circulation of the foot. Anterior-posterior view (left image) and lateral view (right image). From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

healing and increased rates of amputation [12–17]. Such outcomes lower patient quality of life and represent significant driving forces in hospital and financial resource expenditures [13,17–19]. The last decade has resulted in improved endovascular equipment, including support catheters, guidewires, and angioplasty balloons. In addition, advanced endovascular techniques and devices have improved. These factors have resulted in improved outcomes of previously unreconstructable pedal artery disease [20]. Consequently, there has been a renewed interest in pedal artery interventions. In this review, we discuss the many facets of pedal artery interventions, including anatomy, technique, optimal intraprocedural imaging, outcomes, suggestions of when to perform pedal artery interventions, and post-intervention surveillance.

2. Anatomy

The arterial supply to the foot is composed of anterior and posterior circulatory pathways. These anterior and posterior pathways are supplied predominantly by the anterior tibial (ATA) and posterior tibial (PTA) arteries, respectively. Although the peroneal artery supplies both territories of the foot, especially in the setting of ATA and PTA occlusive disease, in general it is not a significant artery when discussing pedal artery interventions. In the anterior circulation (Fig. 1), the ATA becomes the dorsalis pedis artery (DPA) at the ankle joint, which then travels distally and supplies the dorsum of the foot. The DPA gives rise to a number of branches, including the medial and lateral malleolar arteries, medial and lateral tarsal arteries, and the arcuate artery and deep perforating artery, both at the first metatarsal space. The arcuate artery, when present, forms an anastomotic loop with the lateral tarsal artery and gives rise to the small dorsal digital arteries of the second through fourth toes. The next branch of the DPA is the deep perforating artery, which courses medial to lateral and joins the posterior circulation via the lateral plantar artery [21–23].

In the posterior circulation (Fig. 2), the PTA supplies the medial ankle and the plantar surface of the foot. The PTA gives rise to the common plantar artery and the medial calcaneal artery. The common plantar artery bifurcates at the calcaneal body into the medial and lateral plantar arteries with the lateral plantar artery forming an anastomosis with the deep perforating artery forming the plantar arch of the foot.

As a result of this complex anatomy, three anastomotic loops are often described and are useful when considering pedal artery interventions. The most common is the pedal plantar loop formed by the DPA, deep perforating artery, lateral plantar artery, and PTA (Fig. 3). This loop is also referred to as the "pedal arch" or the "pedal loop" and is most commonly referred to when discussing endovascular pedal loop interventions. This loop is complete in approximately 90% of cases, which is advantageous when performing pedal plantar loop reconstructions. Another loop in the foot called the "deep pedal arch" is a more proximal communication between the superficial branch of the medial plantar artery and the medial tarsal artery (Fig. 4). Although this loop is typically narrow and difficult to navigate with guidewires, catheters, and balloons, it may become the dominant connection in patients after forefoot amputations or occlusion of the pedal plantar loop. Finally, a loop formed by an anastomosis of the arcuate artery with the lateral tarsal artery is only seen in a small percentage of patients [21–23].

Of course, pedal artery variations exist and are common. These anatomic variants are well described and make pedal artery interventions in patients with CLTI challenging, especially in the setting of significant occlusive disease when anatomy is difficult to determine [22].

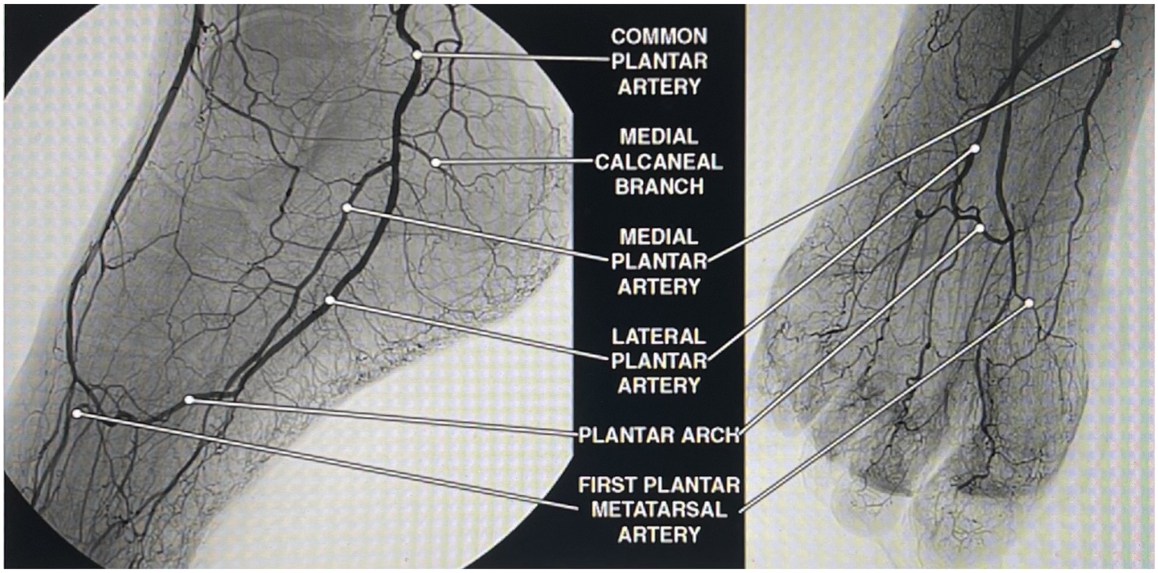


Fig. 2 – Posterior circulation of the foot. Lateral view (left image) and anterior-posterior view (right image). From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

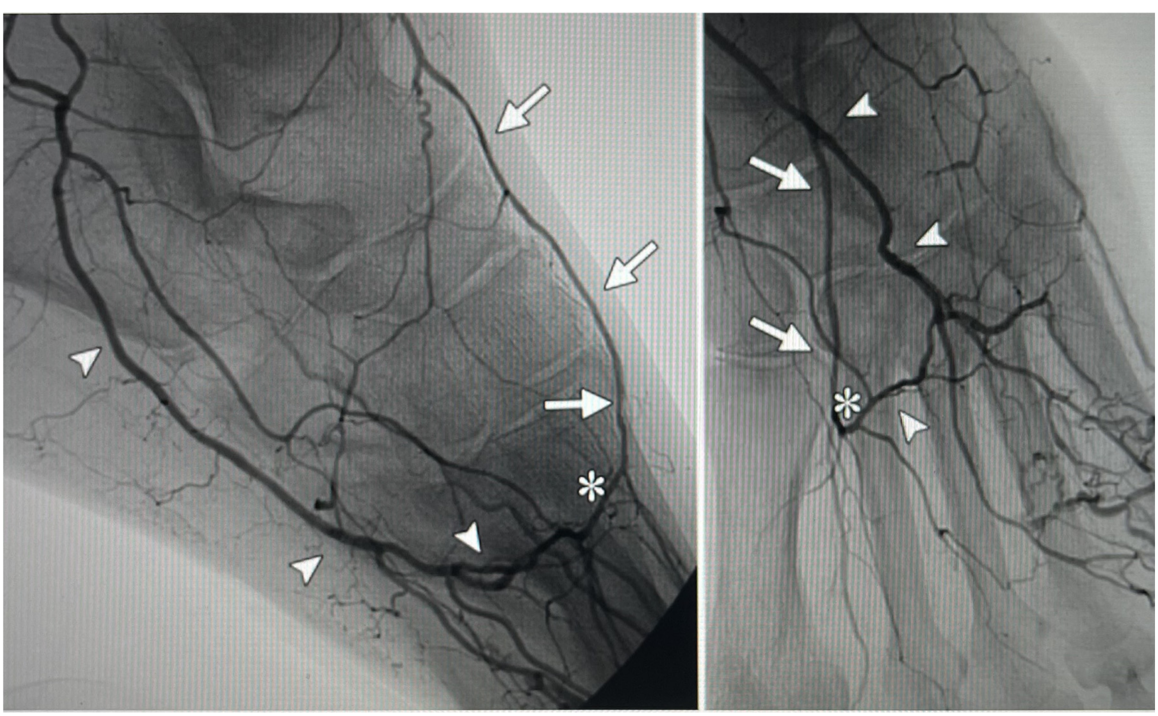


Fig. 3 – Lateral oblique view (left image) and anterior-posterior view (right image) show the pedal-plantar loop. The dorsalis pedis artery (arrows) is connected via the deep perforating artery (*) in the first metatarsal space with the plantar arch and lateral plantar artery (arrowheads). From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

Fig. 4 – The deep pedal arch is a proximal communication between the superficial branch of the medial plantar artery and the medial tarsal artery. From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

3. Technique

Over the last decade, there have been improvements in endovascular equipment, which are used during pedal artery interventions. These include improved 0.014-inch support catheters, guidewires, and low-profile angioplasty balloons. In addition, advanced endovascular techniques, such as retrograde pedal and digital artery access, controlled antegrade and retrograde subintimal tracking, reverse controlled antegrade and retrograde subintimal tracking, and subintimal arterial flossing with antegrade-retrograde intervention have been perfected [20,24–29].

In general, pedal artery interventions are best performed using antegrade access into the common femoral or proximal superficial femoral artery. Once access is obtained with ultrasound guidance, a 6Fr vascular sheath is introduced as distal as possible, typically in the P2 or P3 segment of the popliteal artery [30]. A 6Fr sheath optimizes imaging and allows the use of two 0.014-inch guidewires, catheters, and balloon systems, if needed. In addition, the distal position of the sheath optimizes visualization of chronic total occlusion cap morphology, collaterals, and reconstitution points. Antegrade access also allows for more pushability, torqueability, and a shorter distance to travel to treat disease below the ankle. Ergonomics is improved and radiation exposure to the operator's arms and hands is also reduced significantly, regardless of which leg is being treated. There are times when safe ipsilateral antegrade femoral access is unattainable. In this case, retrograde contralateral femoral access is achieved and may be used as well [22]. However, sheath position as distal as possible in the P2 or P3 segment of the popliteal artery is still recommended for the reasons described above.

4. Intraprocedural imaging

Once optimal access is achieved, imaging is important to the success of any pedal artery intervention. Digital subtraction angiography including antero-posterior and lateral oblique views of the foot are essential. Manzi et al. [22] established general criteria for optimal positioning and evaluation of the pedal arteries. The antero-posterior view (Fig. 5) should include the proximal first metatarsal interspace and forefoot in order to show the pedal-plantar loop passing from the dorsal portion to the plantar portion, as well as the origins of the tarsal and metatarsal arteries. It is also important that the lateral oblique view (Fig. 6) project the fifth metatarsal bone outward from the base of the foot and include the heel and proximal forefoot. This projection allows optimal imaging of the common planter artery bifurcation into the medial and lateral plantar arteries and optimizes visualization of the DPA and the pedal plantar loop [22]. This initial evaluation is of paramount importance to visualize chronic total occlusion caps, collateral flow, variant anatomy, determine the need for alternative access sites, and helps to plan a treatment strategy.

Fig. 5 – Anterior-posterior view should include the proximal first metatarsal interspace and forefoot (left image) in order to show the pedal-plantar loop passing from the dorsal portion to the plantar portion (arrowhead). From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

Fig. 6 – Lateral oblique view (left image) should project the fifth metatarsal bone outward from the base of the foot and include the heel and proximal forefoot. This projection (right image) allows optimal imaging of the common planter artery bifurcation into the medial and lateral plantar arteries and optimizes visualization of the dorsalis pedis artery and the pedal plantar loop. From Manzi M, Cester G, Palena LM, et al. Vascular imaging of the foot: the first step toward endovascular recanalization. Radiographics 2011;31:1623–36 [22], adapted with permission.

Despite optimal technique and imaging and a well-formulated treatment plan, there is still a >20% failure rate using access from above only. As a result, other alternative access sites are often needed, including direct antegrade access into the ATA, PTA, DPA, and/or retrograde access into the lateral plantar and common planter arteries. In some instances, the first metatarsal artery is accessed in retrograde fashion. In addition, a myriad of well-described chronic total occlusion crossing and pedal plantar loop techniques and newer endovascular devices increases the odds of treatment success. When the above are combined, successful intervention is achieved in up to 85% of cases [20,29,31,32].

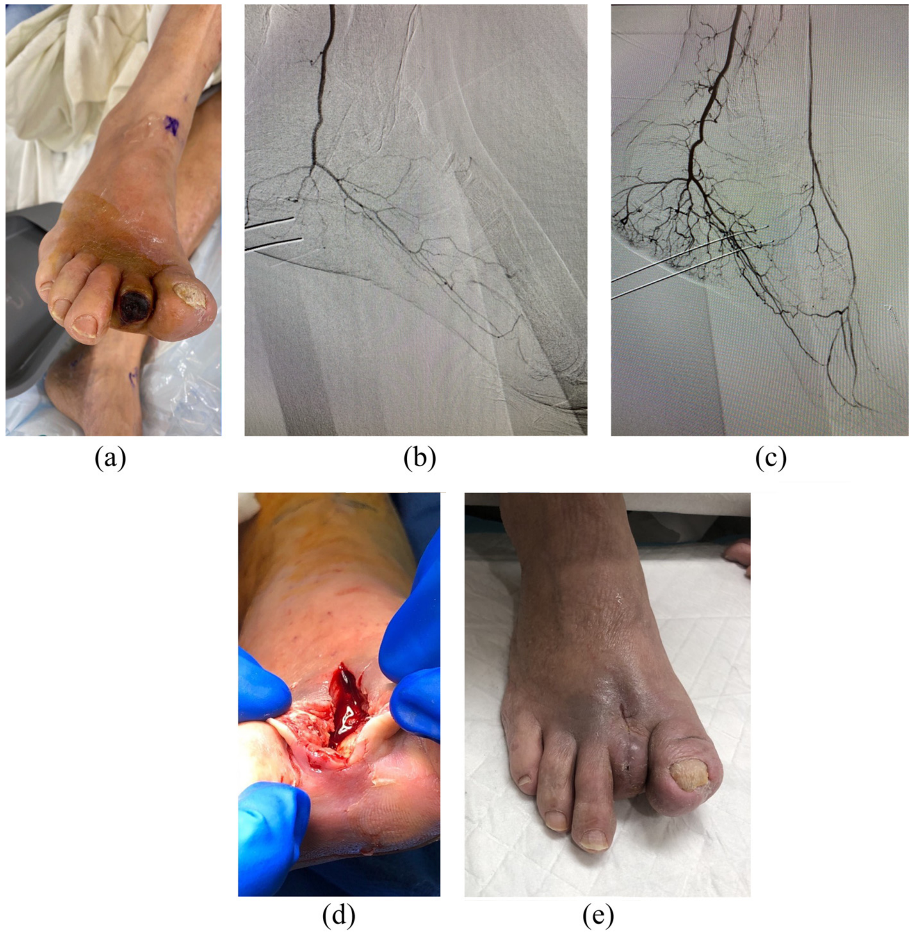


Fig. 7 – Patient status post–second toe resection for nonhealing ulcer and associated osteomyelitis with development of gangrene at the operative site (a). Preintervention angiogram (b) shows incomplete pedal loop and suboptimal digital flow. After successful pedal artery intervention (c), robust intraoperative bleeding was seen during surgery (d) with subsequent complete healing (e).

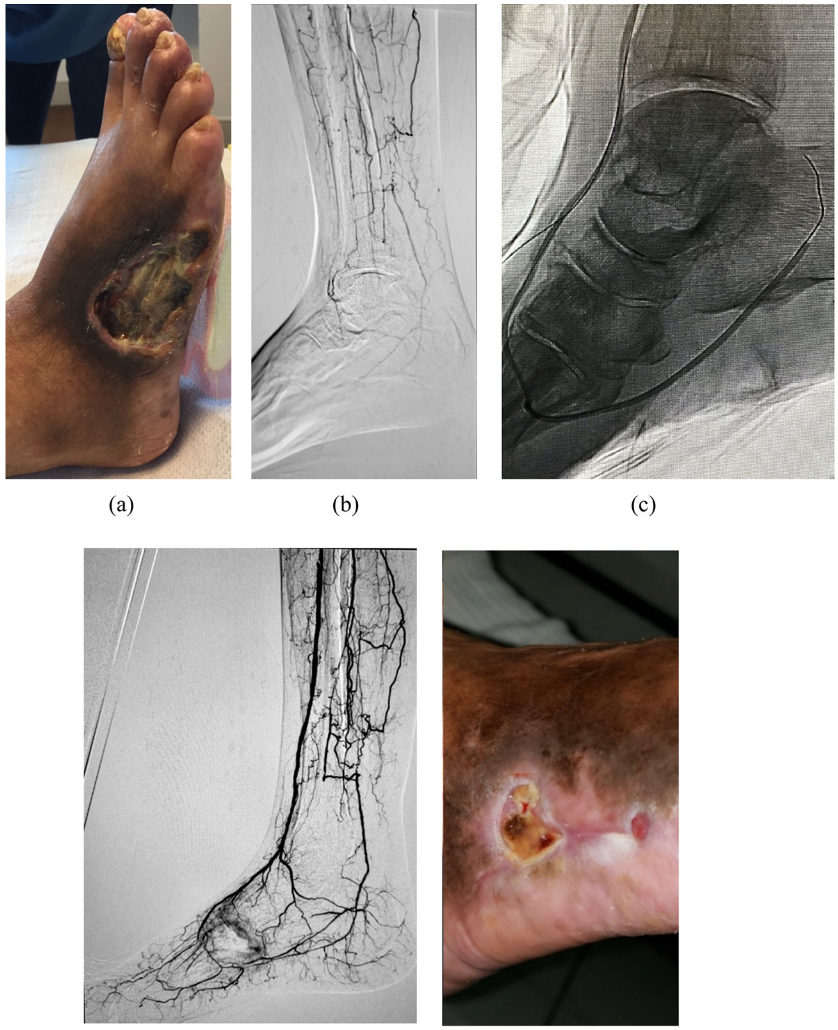
5. Pedal artery intervention data (feasibility, safety, and outcomes)

In 2009, Manzi and his colleagues [20] first described the pedal-plantar loop technique. In their prospective trial of more than 1,300 patients with CLTI (10.1% were pedal artery interventions), pedal artery interventions were safe and technically feasible in 85% of cases and provided positive clinical results at 12 months.

Later, Kawarada and his colleagues [12] were the first to describe a practical pedal arch classification system and also showed that pedal arch status was an independent predictor of wound healing. At that time, his team suggested that revascularization to establish a pedal arch was vital to facilitate complete wound healing.

A few years later, the RENDEZVOUS trial found a direct correlation between rate and extent of wound healing after pedal artery intervention [33,34]. In this multicenter prospective study including 5 Japanese institutions, 257 patients with CLTI with infrapopliteal and pedal artery disease were divided into two cohorts: those receiving pedal artery angioplasty (PAA) (n = 140) and those who did not (n = 117). Patients were also classified into low risk, moderate risk, and high risk on the basis of a delayed wound healing score that was determined by a number of independent predictors described in the study. In the low-risk population, those who underwent PAA had increased rates of wound healing compared with those who did not (93.3% *v* 69.2%; P = .184), but the result was not statistically significant. In the moderate-risk population, the PAA group had a significantly higher rate of wound healing (59.3% *v* 33.9%; P = .001) and shortened healing times (211 *v* 365 days; P = .008). However, in the high-risk population, additional PAA did not demonstrate efficacy (29.4% *v* 35.7%; P = .477) [33]. A subset analysis also showed that the wound healing rate was improved at 1 year, irrespective of the degree of pedal artery disease [34]. Further studies have built on the importance of an intact pedal arch on wound healing, limb salvage, minor amputation-free survival, and overall survival in patients with CLTI.

The single-center retrospective study by Troisi et al. [36] subdivided 137 patient with CLTI with nonhealing foot ulcers after endovascular therapy into three groups based on pedal arch status: complete pedal arch (CPA, n = 42 [30.7%]), in-



(a) (b) (c) (d) (e)

Fig. 8 – Large area of nonhealing ulceration in the foot (a). Preintervention angiogram shows severe tibial and pedal artery disease (b). After tibial intervention and pedal artery intervention (c), final angiography showed in-line flow in the anterior tibial and dorsalis pedis arteries, patent pedal plantar loop, robust filling of the posterior tibial artery via collaterals, and an angiographic wound blush (d), which resulted in significant healing (e).

complete pedal arch (IPA, n = 60 [43.8%]), and an absent pedal arch (APA, n = 35 [25.5%]). The CPA cohort demonstrated a higher rate of wound healing (50%) compared with the IPA and APA cohorts (28.3% and 20%, respectively; $P = .01$), improved 1-year limb salvage rates (100% *v* 93.8% and 70.1%), improved 1-year minor amputation-free rates (84.1% *v* 82.4% and 48.9%; $P = .001$), and improved overall survival rates (90% *v* 80.8% and 62.7%; $P < .001$) [36].

In a similarly designed and parallel study, Ismail and Ahmed [37] studied a cohort of 60 consecutive diabetic patients with CLTI with CPA (n = 15 [25%]), IPA (n = 26 [43.3%]), or APA (n = 19 [31.7%]). Their study identified increased rates of limb salvage (CPA 100% *v* IPA 88.5% *v* APA 68.4%; $P = .01$) and healing time (CPA 3.4 months *v* IPA 4 months *v* APA 6.1 months; $P = .02$) in those patients who had a CPA compared with those who did not [37].

Around the same time, Huizing et al. [38] performed a systematic review and meta-analysis of PAA in patients with CLTI. Their analysis evaluated the safety and effectiveness of PAA and assessed whether additional PAA after tibial artery intervention would improve clinical outcomes. This review included 10 articles, 478 patients, and 524 legs treated with PAA. The pooled 1-year limb salvage and amputation-free survival rates were 92% and 78%, respectively. Although there was no statistically significant difference when tibial plus pedal artery angioplasty was compared with tibial artery intervention alone, the wound healing rates were better in patients who had both tibial and pedal artery disease treated successfully [38].

An additional retrospective analysis by Jung and colleagues [39] demonstrated that patients undergoing successful pedal artery intervention had higher rates of wound healing (76% *v* 67%; $P = .031$) and a lower major amputation rate (96.3% *v* 84.2%; $P = .009$) at 1 year compared with those who did not. Major adverse limb events, freedom from reintervention, and overall survival were not significantly different between those

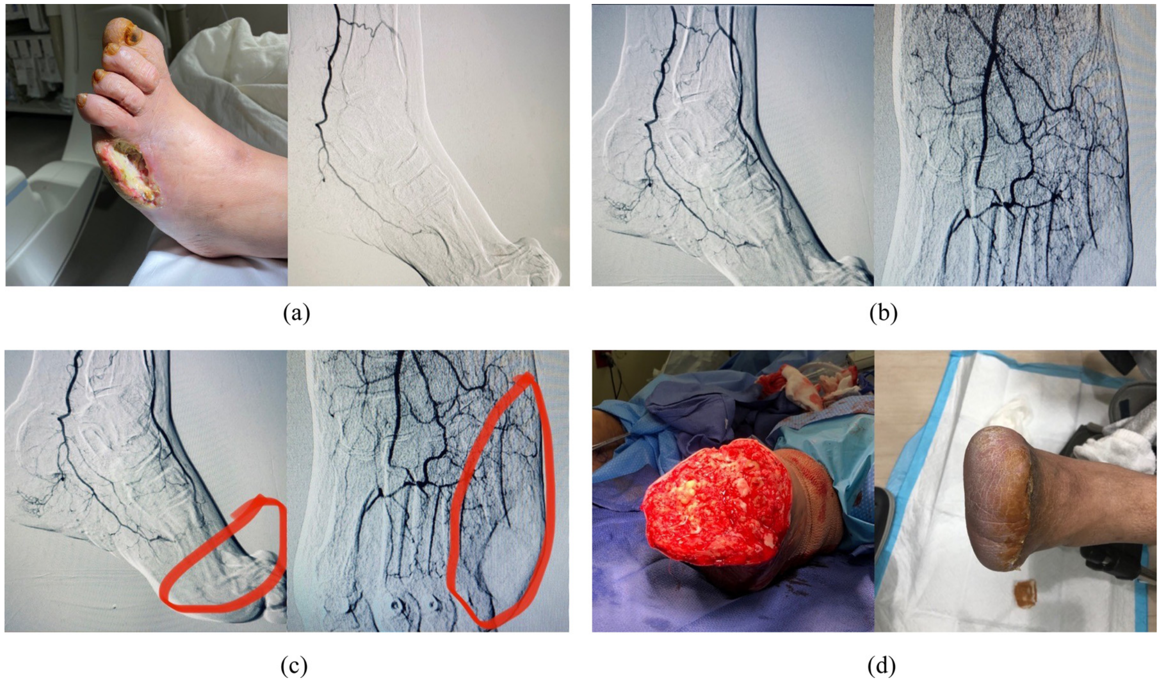


Fig. 9 – Diabetic patient with wound dehiscence and infection at left fifth toe amputation site (a). Despite successful pedal artery intervention with intact pedal plantar loop (b), there was no healing at the amputation site due to diabetic microcirculation disruption (red circles) (c). However, pedal artery intervention allowed healing of a transmetatarsal amputation (d).

who underwent a successful pedal artery intervention and those who did not [39].

6. Pedal artery interventions in practice

Although the feasibility and safety of pedal artery interventions has been demonstrated and the positive impact of pedal artery interventions has been shown, there are still limited data and a lack of widespread adoption. This is due to the lack of randomized controlled trials (RCTs), lack of societal guidelines of when to intervene and the extent of reconstruction needed, and the lack of expertise by many vascular specialists today. More RCT data may lead to incorporation of these interventions into societal guidelines. This would then allow vascular training programs to incorporate these techniques and therapies more robustly into their training programs, thus increasing the numbers of experts in this type of complex intervention. As with any CLTI treatment, the goal of pedal artery interventions is to relieve ischemic pain, heal ulcers, prevent limb loss, improve patient function and quality of life, and prolong survival [40]. In general, pedal artery interventions should only be performed in the setting of CLTI and limb salvage. Patients who are nonambulatory, wheelchair bound, or have no hope for functional recovery of their limb despite revascularization should not undergo pedal artery intervention.

Currently, non-RCT data and expert opinion support common scenarios in which pedal artery interventions may be necessary. These include patients with CLTI with both tibial and pedal artery disease if optimal healing does not occur after successful tibial artery intervention, patients with gangrene/tissue loss (Figs. 7 and 8), and those with post-surgical ischemic wounds from forefoot amputations, as surgery may separate the anterior and posterior circulations of the foot (Fig. 9). In these patients, direct in-line flow based on angiosome and angiographosome revascularization can optimize blood flow to the ischemic wound or surgical flap [20,23,35,38,41–46].

7. Post-intervention surveillance

After a successful pedal artery intervention, surveillance is an important part of patient management. To ensure a successful outcome, timing based on the patient's comorbidities, overall clinical scenario, and risks of limb amputation if the treated arteries close prematurely must be considered. However, assessment of the pedal arteries and determination of foot perfusion is challenging due to limited techniques and published data in this vascular territory. Commonly, ankle-brachial index (ABI), toe-brachial index (TBI), duplex ultrasound, transcutaneous oxygen pressure, and toe photoplethysmography are used for noninvasive testing. Although these are excellent studies, there are limitations. Specifically, most patients with CLTI have diabetes or chronic kidney disease, which often results in erroneous ABI and TBI measurements. In addition, small-diameter vessels, vessel tortuosity, calcification, bone-related artifacts, and prior amputations limit assessment of the pedal arteries using duplex ultrasound, transcutaneous oxygen pressure, and toe photoplethysmography.

Recently, a new technique to determine foot perfusion in patients with CLTI called pedal acceleration time has been described. This technique uses duplex ultrasound to directly visualize the pedal arch, map the pedal artery anatomy, and determine pedal flow hemodynamics. It is an objective measurement of foot perfusion in the pedal arteries and has been shown to correlate with ABI/TBI measurements and predict wound healing [47–49]. Clearly, more study and data are needed, but this technique is showing promise in patients with CLTI.

8. Conclusions

The benefits of pedal artery interventions are becoming clearer. Although non-RCT data and expert opinion are helping to support common scenarios in which pedal artery interventions may be beneficial, challenges remain. These include the need for more RCT data, better tools, and more vascular specialists trained in this complex intervention.

Declaration of Competing Interest

Srini Tummala is a course faculty, speaker, and consultant for Abbott Vascular, Cardiovascular Systems Inc, and Terumo. The remaining author discloses no conflicts.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1053/j.semvascsurg.2022.04.007.

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