Impact of pedal arch revascularization on clinical outcomes of diabetic patients with critical limb ischemia

Osama A. Ismail[a], Ahmed A. Ahmed[b]

[a]Department of Vascular Surgery, Sohag University, Sohag, [b]Department of Radiology, Alazhar University, Cairo, Egypt

Correspondence to Ahmed A. Ahmed, MD Radiology, Department of Radiology, Alazhar University, Cairo, 82524, Egypt.
Tel: 00201005781485;
E-mail: dr_ahmedazkool@yahoo.com

Received: 1 December 2019
Accepted: 25 December 2019
Published: 27 April 2020

The Egyptian Journal of Surgery 2020, 39:344–351

Aim
The aim was to evaluate the effect of pedal arch revascularization in diabetic patients suffering from critical limb ischemia (CLI) on wound healing, time to heal, and limb salvage.
Materials and methods
The study was carried out from March 2016 to February 2019 at Sohag University Hospitals on 60 diabetic patients diagnosed with CLI. Pedal arch revascularization was combined with traditional management. Patients were divided into complete pedal arch (CPA), incomplete pedal arch (IPA), and absent pedal arch (APA) groups. Wound healing, time to heal, limb salvage, and freedom from minor amputations were evaluated and compared among the patient groups.
Results
The patients were classified into CPA group (15 patients, 25%), IPA (26 patients, 43.3%), and APA group (19 patients, 31.7%). There were no statistical difference between groups in age, sex, or risk factors. CPA patients showed a significantly higher rate of wound healing and shorter time-to-heal than other patient groups, 93.3% in CPA, 73.1% in IPA, and 52.6% in the APA group (P=0.003). Time to heal was 3.4±2.5 months in CPA patients, 4.0±2.9 in IPA, and 6.1±3.2 in APA group (P=0.02). Limb salvage rate was significantly better in CPA patients (100% in CPA, 88.5% in IPA, and 68.4% in APA group; P=0.01). Freedom from minor amputation was 86.6, 76.9, and 47.4% (P=0.086) in CPA, IPA, and APA group, respectively.
Conclusion
Pedal arch patency has a positive clinical impact on wound healing rate, time to heal, and limb salvage in the management of diabetic patients with CLI undergoing endovascular intervention.

Keywords:
critically limb ischemia, diabetic patients, pedal arch, revascularization

Egyptian J Surgery 39:344–351

1110-1121

Introduction

Critical limb ischemia (CLI) is an undesirable clinical consequence of peripheral arterial disease (PAD) [1]. It affected ~8 million people in the USA and affects 12–20% of American people aged more than 65 years. Within 1 year of PAD diagnosis, 25% of those patients progress to a major amputation and the other 25% die due to co-morbid conditions [2].

CLI is not usually a candidate for surgery because of advanced age, associated comorbidities, for example, diabetes, smoking, or hypertension as well as the nature of atherosclerotic pathology characterized by diffuse vessel involvement and high rates of restenosis and multilevel occlusion. On the contrary, endovascular intervention with its recent dedicated tools, novel techniques, and progressing clinical experience is another key to establish adequate blood flow to the wound especially when the limb is threatened and jeopardized. It has become more popular because of its less invasiveness and reasonable limb salvage rate compared with surgery [3].

The aim of treatment of CLI is avoidance of limb amputation, first, and then gaining complete wound healing in a relatively short time. It was reported that discrepancy between limb salvage and delay in achievement of reasonable wound healing affected the quality of life and hold up the social activities [4]. So complete wound healing should be considered as another goal in treatment after prevention of major amputation [5].

From the beginning of this century, there was increasing attention to the pedal arch patency in diabetic and nondiabetic patients with CLI [6]. Also, Ciavarella *et al.* [7] confirmed the involvement of foot vessel occlusions in diabetic patients which affect their outcomes. Several clinical trials have reported that pedal vessel disease resulted in worse

wound healing and recommended adjunctive procedures for pedal arch revascularization to improve the rate of wound healing [3]. Kim *et al.* [8] appreciated this concept when the technical results of proximal angioplasty were unsatisfactory and the foot was risky especially in end-stage renal disease and diabetic patients to accelerate healing of trophic ulceration and relieve ischemic pain. Also, Manzi [9] had reported that it is essential to recanalize both pedal and plantar vessels and their anatomical anastomoses in cases of extensive trophic wounds to achieve maximum blood flow.

Materials and methods

This prospective study was carried out from March 2016 to February 2019 at Sohag University Hospitals on 60 diabetic patients complaining of CLI, Rutherford category 5, caused by infrapopliteal arterial occlusive disease. Patients were treated with pedal arch revascularization added to the traditional strategy of their management.

Exclusion criteria were patients with nonsalvageable limb or those with life-threatening infection, totally occluded tibial segments that cannot be crossed by a wire, developing acute thrombosis, dissection, or perforation in infrapopliteal vessels prior to treatment of the arch.

All patients were admitted and signed a written informed consent. This series was approved by the Hospital Ethics Committee. Patients were assessed clinically including history of other risk factors other than diabetes mellitus (DM), for example, smoking, hypertension, cardiovascular, cerebrovascular diseases, renal insufficiency and previous endovascular intervention or bypass surgery. All patients were examined carefully including the level of occlusion, ankle brachial pressure index (ABI), and duplex ultrasound. Computed tomography angiography was performed in all cases. All patients were subjected to full laboratory investigations with special concern to renal functions and coagulation profile.

Procedure details

Preprocedural medications with dual antiplatelet therapy in the form of salicylates 75 mg and clopidogrel 300 mg as a loading dose followed by daily maintenance dose of clopidogrel 75 mg continued postoperatively for at least 3 months in all cases. The procedure was done under local anesthesia in all cases through ipsilateral femoral access. A measure of 70–100 U/kg of unfractionated heparin was injected intra-arterially after sheath insertion. Preintervention angiography was performed to assess lesion characteristics: length, stenosis/occlusion, distal runoff vessels, and angiosome pattern possibility.

V-18 guidewire (Boston Scientific, Massachusetts, Boston, USA) was used to cross the lesion. After crossing the lesion, dilatation with 2.5 mm low-profile balloons (sterling balloon; Boston Scientific) was performed for 1–2 min. The target crural artery was decided based on the angiosome concept. When the angiosome revascularization was difficult accessed or failed, indirect revascularization was performed as an alternative. Strategy of multivesselrevascularization of more than one vessel was the aim to gain maximum perfusion to the foot. Nitroglycerin 100–200 μg was helpful to overcome vessel spasm in some cases.

Angiographic assessment was performed to evaluate the technical success prior to the foot revascularization procedure.

Pedal arch revascularization

A 0.014-inch hydrophilic guidewire (PT2; Boston Scientific) was advanced and supported by a balloon (Amphirion Deep Balloon, Invatec; Medtronic, Minneapolis, Minnesota, USA). After crossing the lesion by wire, occluded pedal arch was dilated with 2 mm balloon in its nominal pressure.

After completion angiography of the foot, patients were divided into three groups according to the pedal arch patency as classified by Kawarada *et al.* [10]: complete pedal arch (CPA), incomplete pedal arch (IPA) and absent pedal arch (APA) group (Figs 1–3).

Follow-up was conducted daily during the period of admission and then in vascular surgery outpatient clinic at 3, 6, 9, and 12 months of follow-up period. During follow-up visits, reassessment of the regained pulse, ankle brachial index (ABI), disappearance of rest pain, wound healing, and time to heal were calculated and any observed complications were recorded.

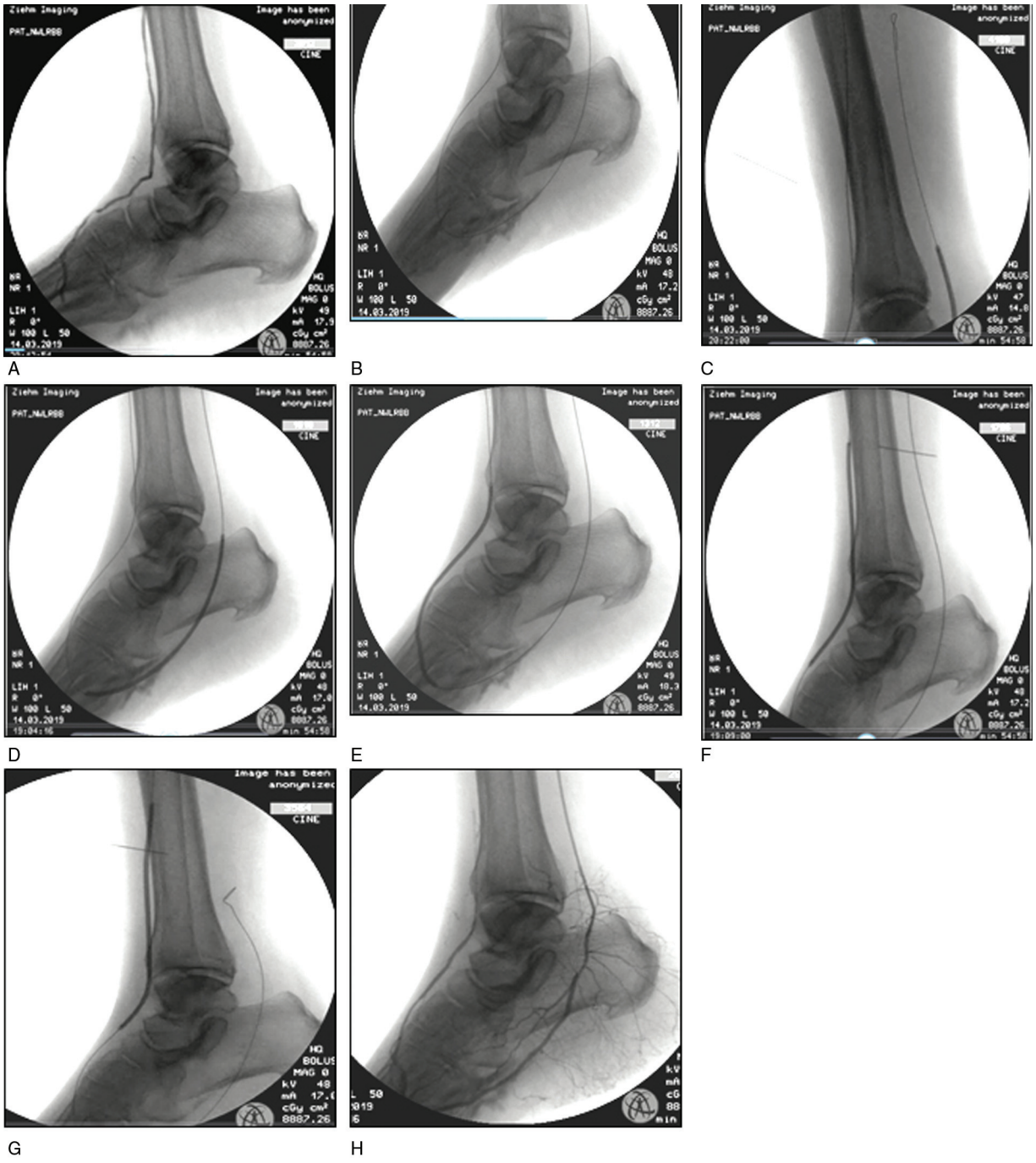
Wound management

Patients with ischemic ulcers or gangrene received standard wound care, for example, debridement, toe amputation, and/or midtarsal amputation.

Definitions

Successful pedal arch revascularization was considered when at least one vessel either dorsal or plantar artery was recanalized.

Figure 1



(a) Stenosis of dorsalis pedis artery and absent planter artery; (b) crossing the arch by 0.014 wire; (c–g) balloon dilatation of pedal arch; (h) completion angiography showing complete pedal arch revascularization.

Complete arch revascularization

Both dorsal and plantar arteries were patent and connected to each other.

Complete wound healing

Achievement of complete epithelialization of the wound without major amputation.

Time-to-heal

Time needed to achieve complete wound healing calculated per month.

Limb salvage

Freedom from above ankle amputation.

Major amputation means above ankle amputation.

Minor amputation

Absence of any type of amputation except for toe amputation or midtarsal amputation.

Study outcome

Included rate of wound healing at 1 year, time-to-heal, and limb salvage rate.

Statistical analysis

Continuous variables are expressed as mean±SD. Categorical variables are expressed as percentage. Unpaired Student's *t*-test was used to compare continuous variables. χ^2-testand Fisher's exact test were used for categorical variables. Kaplan–Meier method was applied to the study outcome. Groups were compared using log-rank test. Statistical significance was defined as *P* value less than 0.05.

Results

A total of 60 patients with CLI, Rutherford category '5' underwent pedal arch revascularization. CPA revascularization was successful in 15 (25%) patients, IPA in 26 (43.3%) patients, and APA occurred in 19 (31.7%) patients.

All patients had DM. The most common risk factors other than diabetes were smoking and hypertension in both groups. Baseline characteristics are shown in Table 1. In the CPA group, the mean age was 55 (48–72) years, and 10 (66.6%) patients were men. In the IPA group, the mean age was 52 (49–68) years, and 16 (61.5%) patients were men. In the APA group, the mean age was 54 (48–75) years, and 14 (73.7%) patients were men. There were no significant differences in patient baseline characteristics between the three pedal arch groups.

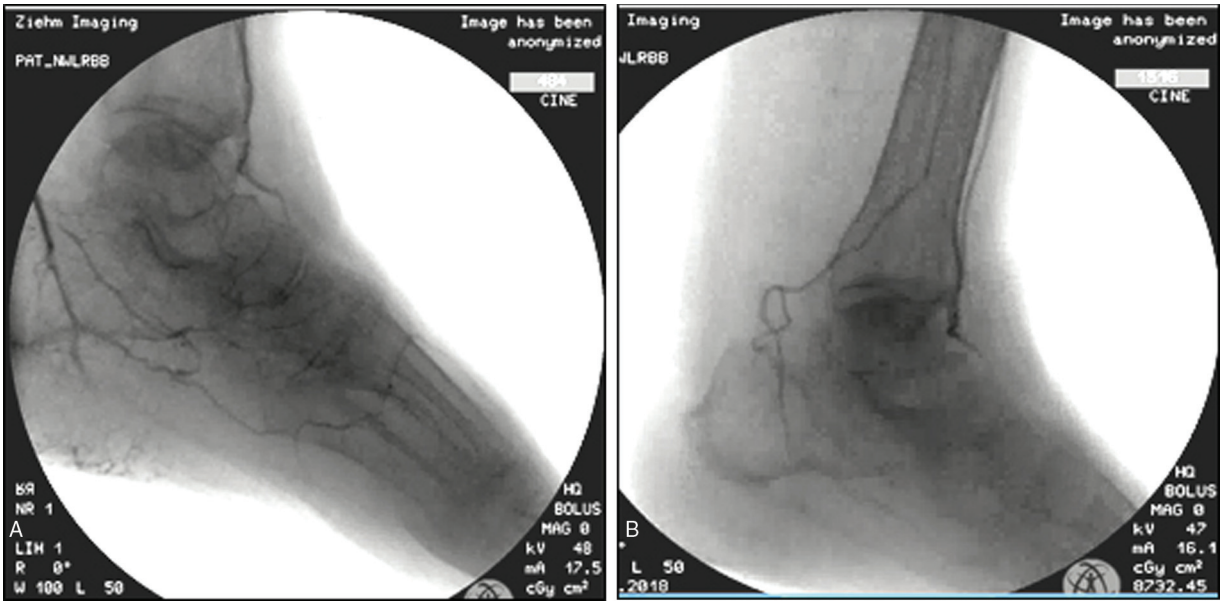
Most of the patients in both groups (80, 84.6, and 89.5%, respectively), had more than one vessel distal runoff to the foot. The most common site of ischemic wound/ulcer was toes in the CPA group and the APA group (53.3 and 63.1%), while it was planter area (57.7%) in the IPA group. There were no significant differences between groups (Table 2).

Patients with CPA revascularization showed a significantly higher rate of wound healing and

Figure 2

Incomplete pedal arch: recanalized planter artery without dorsalis pedis artery.

Figure 3



Absent pedal arch: failed canalization of either dorsalis pedis artery or planter artery.

Table 1 Demographic data and risk factors

	CPA group (*n*=15)	IPA group (*n*=26)	APA group (*n*=19)
Age	55 (48–72)	52 (49–68)	54 (48–75)
Male/female	10/5	16/12	14/5
Risk factors [*n* (%)]			
Smoking	12 (80)	21 (80.7)	16 (84.2)
Hypertension	11 (73.3)	20 (76.9)	14 (73.7)
Ischemic heart disease	6 (40)	10 (38.4)	8 (42.1)
Renal impairment	3 (20)	5 (19.2)	4 (21.1)
Cerebral stoke	2 (13.3)	4 (15.4)	3 (15.8)

APA, absent pedal arch; CPA, complete pedal arch; IPA, incomplete pedal arch.

Table 2 Baseline patients' criteria

	CPA group (*n*=15) [*n* (%)]	IPA group (*n*=26) [*n* (%)]	APA group (*n*=19) [*n* (%)]
Runoff vessels			
One vessel	3 (20)	4 (15.4)	2 (10.5)
Two vessels	10 (66.7)	17 (65.1)	12 (63.2)
Three vessels	2 (13.3)	5 (19.2)	5 (26.3)
Site of the wound/ulcer			
Toes	8 (53.3)	7 (26.9)	12 (63.1)
Planter surface	4 (26.7)	15 (57.7)	5 (26.3)
Heel area	1 (6.7)	2 (7.7)	1 (5.3)
Extended ischemic area	2 (13.3)	4 (15.4)	1 (5.3)

APA, absent pedal arch; CPA, complete pedal arch; IPA, incomplete pedal arch.

shorter time-to-heal than other patient groups. Healing rate was 93.3% in the CPA group, 73.1% in the IPA group, and 52.6% in the APA group (P=0.003). Time to achieve wound healing was 3.4 ±2.5 months in CPA patients, 4.0±2.9 in IPA, and 6.1 ±3.2 in APA (P=0.02) (Fig. 4).

Limb salvage rate was statistically significant (P=0.01); 100% in CPA patients, 88.5% in IPA, and 68.4% in APA (Fig. 5). Freedom from minor amputation was achieved in 86.6, 76.9, and 47.4% in CPA, IPA, and APA group, respectively (P=0.086). It was noted that the occurrence of debridement and minor amputation might be attributed to the ischemic wound lesion in the foot prior to revascularization especially when all patients enrolled in this study were Rutherford category '5'.

Wound management

In CPA patients, 13 cases were treated by debridement, two patients had minor amputation, and no major amputation was recorded in this group. In IPA patients, 14 cases were treated by debridement, nine patients had minor amputation, and two had major amputations. In the APA group, three cases had debridement, 10 patients had minor amputation, and four cases had major amputation. Indication of major amputation was sepsis.

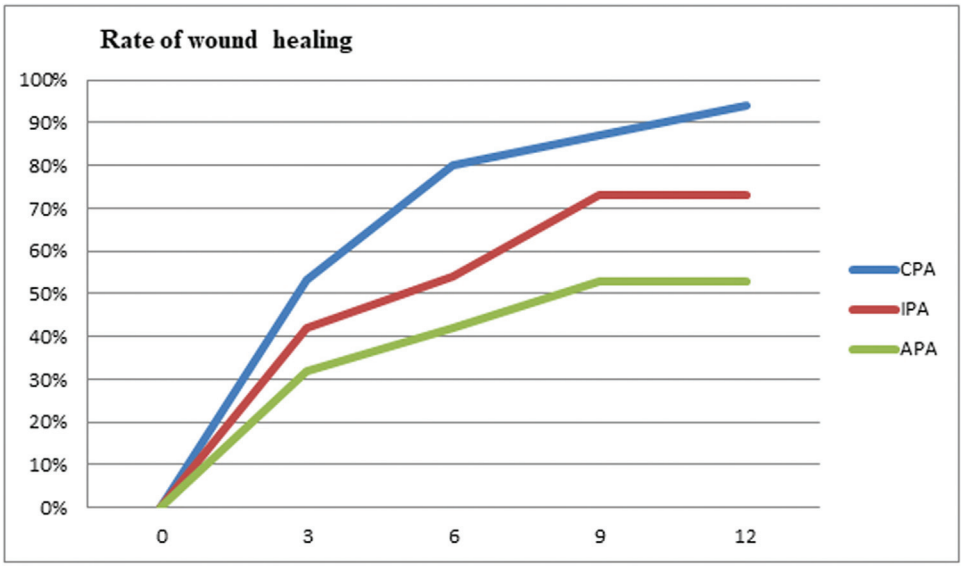
Regarding procedure-related complications, access site hematoma was recorded in 7/60 (11.7%) patients among all patient cohorts of this study and was resolved spontaneously. Death occurred in 3/60 (5%) patients from associated comorbidities.

Discussion

Diabetic patients with ischemic wounds represent a serious clinical problem and a majority of those patients will end by some sort of amputation. Standard endovascular techniques for limb ischemia are inadequate and the incidence of technical failure reaches up to 20%. Recent advanced techniques, for example, retrograde access, transcollateral recanalization, and pedal plantar loop techniques are beneficial in improving the success rate. However, these strategies may also fail when the foot vessels are diseased [11].

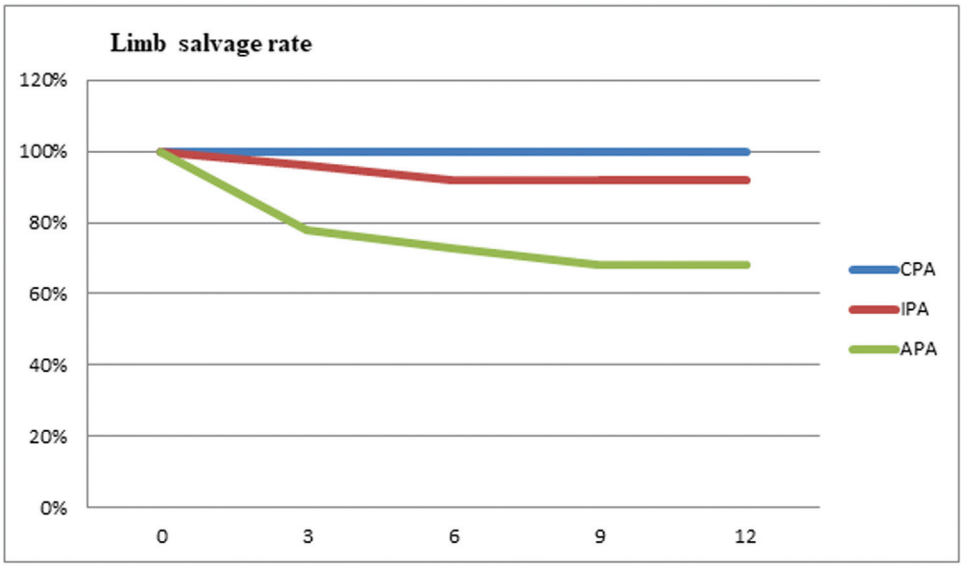
Angiosome concept of revascularization is a widespread strategy although its effectiveness is a controversy. This concept is not almost right especially in patients with pedal arch disease as the blood flow through the recanalized vessels cannot reach the target area of the wound directly with optimal flow and perfusion. So, pedal arch reconstruction might be considered a salvageable and beneficial option to

Figure 4



Complete pedal arch group showed highly significant healing rate and short time-to-heal in comparison to other patient groups.

Figure 5



Limb salvage rate differed significantly between complete pedal arch group and absent pedal arch group.

improve wound healing. Acin *et al.* [12] reported that the angiosomal concept is no longer of great value as the blood supply toward the target wounds depends on the patency of artery-to-artery connections and collateral circulation. This opinion was agreed with Higashimori *et al.*[13] and attributed this reason as the angiosome structure might be altered or mixed in a complex manner by collaterals. In this series, the strategy of revasularization respected the angiosomal concern as the target crural vessel was accessed first whenever possible. Multivessel revascularization was an effective and wise decision to gain sufficient perfusion to the foot. Although this procedure was approved by others [4,10], other clinical trials showed little effect of this strategy [3,12]. Higashimori *et al.* [13] reported that in cases of single-vessel runoff to the foot, it was highly important to create patent pedal arch to improve limb salvage rate.

Most of diabetic foot ulcers are found in the distal foot. Vessels in this area are terminal branches and thus their revascularization is of great value in limb salvage [8].

Kawarada *et al.* [10] had classified pedal arch disease into three types: type 1 patent both dorsal and lateral plantar vessels, type 2 had patent either the dorsal (type 2A) or lateral plantar (type 2B) artery, and type 3 absent both dorsal and lateral plantar vessels.

Nakama *et al.* [1] had reported that the indications of additional pedal arch revascularization were absence of sufficient pedal flow, relatively large foot wounds or limb-threatening infection requiring large amounts of blood flow for achievement of limb salvage and wound healing. Wound blush which is a contrast opacification around the wound was another indicator reported by Utsunomiya *et al.* [14] that depended on the angiographic evidence during the procedure. They reported that when wound blush was insufficient, additional pedal artery revascularization was indicated and recommended.

Manzi [9] had created a special technique in pedal vessel revascularization, pedal plantar loop technique and concluded that this method made the angiographic results and clinical outcome better and improved the local oxygen tension. He used a low-profile balloon, amphirion deep balloon and appreciated it because it helps to tackle very challenging angles and tortuosity of the foot. In this series, procedure technique was tackling the arch either by the same technique as the Manzi method or from the dorsalis pedis artery. This balloon by chance was also used in this study.

In 19/60 (31.7%) patients, pedal revascularization failed and inadequate pedal flow occurred. This was due to difficulty in crossing the occluded segment, occurrence of flow-limiting dissection, or vessel perforation. These cases were treated conservatively and were followed-up.

Technical success was achieved in 41/60 (68.3%) patients. The Manzi technique [9] reported technical success achieved in 85% of cases in his thesis and defined it as diameter stenosis of less than 50% in the treated vessel without flow-limiting dissections.

It is well known that preserving the threatened limb and avoidance of major amputation is the hope and considered the main goal in the management of CLI. The second priority is achievement of complete and rapid wound healing to decrease undesirable events, for example, frequent debridement with or without minor amputation, improved patient quality of life, and decreased financial costs. Delayed wound healing is still an important clinical entity after endovascular intervention. Reed *et al.* [15] reported in his series that there was about 20% difference between limb salvage rate and rate of wound healing, so a considerable number of patients still suffered from unhealed wounds in spite of limb preservation and avoidance of major amputations.

Patients who underwent CPA revascularization showed a significantly higher rate of wound healing and shorter time-to-heal than other patient groups. Healing rate was 93.3% in the CPA group, 73.1% in the IPA group, and 52.6% in the APA group (P=0.003). Time to achieve wound healing was 3.4 ±2.5 months in CPA patients, 4.0±2.9 in IPA, and 6.1 ±3.2 in APA (P=0.02). Rashid *et al.* [16] reported that there was a significant difference in healing rate and time to healing between CPA, IPA, and APA (P=0.0264). Also, Troisi *et al.* [6]and Nakama *et al.* [1] had reported in their studies that diabetic patients with CPA and IPA had better outcomes in terms of wound healing and limb salvage and thus confirmed the great effect of additional pedal revascularization. On the contrary, Higashimori *et al.* [13] compared wound healing rate in patients with and without pedal arch revascularization and recorded 89.4 and 80.6%, respectively, which was statistically insignificant (P=0.11).Kawarada *et al.* [10] reported that DM, wound infection, and pedal arch disease should be considered as prognostic factors of delayed wound healing. Conversely, Shiraki *et al.* [5] denied the pedal arch disease as a predictor of delayed healing. Kobayashi *et al.* [3] added the importance of ulcer depth and volume as another significant parameter.

In this series, limb salvage rate was 100% in CPA, 88.5% in IPA, and 68.4% in APA (P=0.01). Troisi *et al.* [6] had reported nearly similar results in his series; CPA 100% vs IPA 90.9% *vs* APA 76.1% (P=0.02). Nakama *et al.* [1] had reported that limb salvage and amputation-free survival were similar between patients with and without pedal arch revascularization.

Freedom from minor amputation was achieved in 86.6, 76.9, and 47.4% in CPA, IPA, and APA group, respectively (P=0.086). Nearly similar results were reported by others [6,17].

Finally, it is of great value to highlight the paramount importance of additional pedal arch revascularization in improving clinical outcomes regarding wound healing rate, time-to-heal, and limb salvage rate in diabetic patients with CLI undergoing endovascular intervention.

Conclusion

Pedal arch patency has a positive clinical impact on wound healing rate, time to healing, and limb salvage in the management of diabetic patients with CLI undergoing endovascular intervention.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Nakama T, Watanabe N, Haraguchi T, Sakamoto H, Kamoi D, Tsubakimoto Y, *et al.* Clinical outcomes of pedal artery angioplasty for patients with ischemic wounds. Cardiovasc Interv 2017; 10:79–90.

2 Dua A, Rothenberg KA, Lee JJ, Gologorsky R, Desai SS. Six-month freedom from amputation rates and quality of life following tibial and pedal endovascular revascularization for critical limb ischemia. Vasc Endovasc Surg 2019; 53:212–215.

3 Kobayashi N, Hirano K, Nakano M, Muramatsu T, Tsukahara R, Ito Y, *et al.* Predictors of non-healing in patients with critical limb ischemia and tissue loss following successful endovascular therapy. Catheter Cardiovasc Interv 2015; 85:850–858.

4 Iida O, Soga Y, Yamauchi Y, Hirano K, Kawasaki D, Yamaoka T, *et al.* Clinical efficacy of endovascular therapy for patients with critical limb ischemia attributable to pure isolated infrapopliteal lesions. J Vasc Surg 2013; 57:974–981.

5 Shiraki T, Iida O, Takahara M, Soga Y, Yamauchi Y, Hirano K, *et al.* Predictors of delayed wound healing after endovascular therapy of isolated infrapopliteal lesions underlying critical limb ischemia in patients with high prevalence of diabetes mellitus and hemodialysis. Eur J Vasc Endovasc Surg 2015; 49:565–573.

6 Troisi N, Turini F, Chisci E, Ercolini L, Frosini P, Lombardi R, *et al.* Impact of pedal arch patency on tissue loss and time to healing in diabetic patients with foot wounds undergoing infrainguinal endovascular revascularization. Korean J Radiol 2018; 19:47–53.

7 Ciavarella A, Silletti A, Mustacchio A, Gargiulo M, Galaverni MC, Stella A, Vannini P. Angiographic evaluation of the anatomic pattern of arterial obstructions in diabetic patients with critical limb ischaemia. Diabete Metab 1993; 19:586–589.

8 Kim S, Choi D, Shin S, Shin DH, Kim JS, Kim BK, *et al.* Dorsal-plantar loop technique using chronic total occlusion devices via anterior tibial artery. Yonsei Med J 2013; 54:534–537.

9 Manzi M. Pedal-plantar loop technique: a new method for revascularization of foot vessels. Endovasc Today I 2009; 62–64.

10 Kawarada O, Fujihara M, Higashimori A, Yokoi Y, Honda Y, Fitzgerald PJ. Predictors of adverse clinical outcomes after successful infrapopliteal intervention. Catheter Cardiovasc Interv 2012; 80:861–871.

11 Palena LM, Brocco E, Manzi M. The clinical utility of below-the-ankle angioplasty using 'transmetatarsal artery access' in complex cases of CLI. Catheter Cardiovasc Interv 2014; 83:123–129.

12 Acin F, Varela C, Lípez de Maturana I, de Haro J, Bleda S, Rodriguez-Padilla J. Results of infrapopliteal endovascular procedures performed in diabetic patients with critical limb ischemia and tissue loss from the perspective of an angiosome-oriented revascularization strategy. Int J Vasc Med 2014;2014:270539.

13 Higashimori A, Iida O, Yamauchi Y, Kawasaki D, Nakamura M, Soga Y, *et al.* outcomes of one straight-line flow with and without pedal arch in patients with critical limb ischemia. Catheter Cardiovasc Interv 2016; 87:129–133.

14 Utsunomiya M, Nakamura M, Nakanishi M, Takagi T, Hara H, Onishi K, *et al.* Impact of wound blush as an angiographic end point of endovascular therapy for patients with critical limb ischemia. J Vasc Surg. 2012; 55:113–121.

15 Reed GW, Salehi N, Giglou PR, Kafa R, Malik U, Maier M, Shishehbor MH. Time to wound healing and major adverse limb events in patients with critical limb ischemia treated with endovascular revascularization. Ann Vasc Surg 2016; 36:190–198.

16 Rashid H, Slim H, Zayed H, Huang DY, Wilkins CJ, Evans DR, *et al.* The impact of arterial pedal arch quality and angiosome revascularization on foot tissue loss healing and infrapopliteal bypass outcome. J Vasc Surg 2013; 57:1219–1226.

17 Troisi N, Turini F, Chisci E, Ercolini L, Frosini P, Lombardi R, *et al.* Pedal arch patency and not direct-angiosome revascularization predicts outcomes of endovascular interventions in diabetic patients with critical limb ischemia. Int Angiol 2017; 36:438–444.