Evaluation of wound healing after angiosome-directed infrapopliteal endovascular angioplasty in critical limb ischemia

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Background

Because of delayed healing duration of variable foot wounds, techniques for identifying methods to expedite wound healing process were needed. Angiosome concept divides the foot into three-dimensional zones of tissue supplied by specific arterial source.

Patients and methods

This study included 40 patients (40 limbs) who presented with Rutherford class (5 and 6) foot wounds, with infrapopliteal arterial disease, without significant proximal arterial disease with good run-in and run-off tibial segments and patent foot arch and underwent successful primary tibial angioplasty. Patients were recruited from January 2018 till June 2018 and were followed up till 2 years from July 2018 till July 2020 for the effect of angiosome-directed angioplasty on wound healing and limb salvage rates.

Results

Direct angiosomal arterial flow to the wound zone was accomplished in 27 (67.5%) patients, with better and faster wound healing rate at 1.4 months (SD: 0.41) and high limb salvage rate, compared with indirect nonangiosomal arterial flow, which was accomplished in 13 (32.5%) patients with delayed wound healing rate at 7.8 months (SD: 1.7) and low limb salvage rate. Age, sex, and different comorbitities were statistically insignificant in wound healing rates.

Conclusion

The study established that direct angiosomal tibial angioplasty had a considerable role in improving foot wound healing rate, with higher limb salvage rate than the indirect nonangiosomal tibial angioplasty. Obtaining direct arterial supply based on the angiosome technique of perfusion to different foot ulcers or post minor toes amputation ulcer (gangrenous toes) seemed to be significant for wound healing rates in patients with critical limb ischemia.

Keywords:
angiosome-directed infrapopliteal endovascular angioplasty, critical limb ischemia, wound healing

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Introduction

Patients with critical limb ischemia are at great hazard of limb loss. Different foot wounds are one of diabetes greatest complications. Neuropathy, infection, and ischemia are variable reasons that could cause foot wound complications and usually found together. The major factor preventing healing of different foot wounds is usually inadequate blood supply [1].

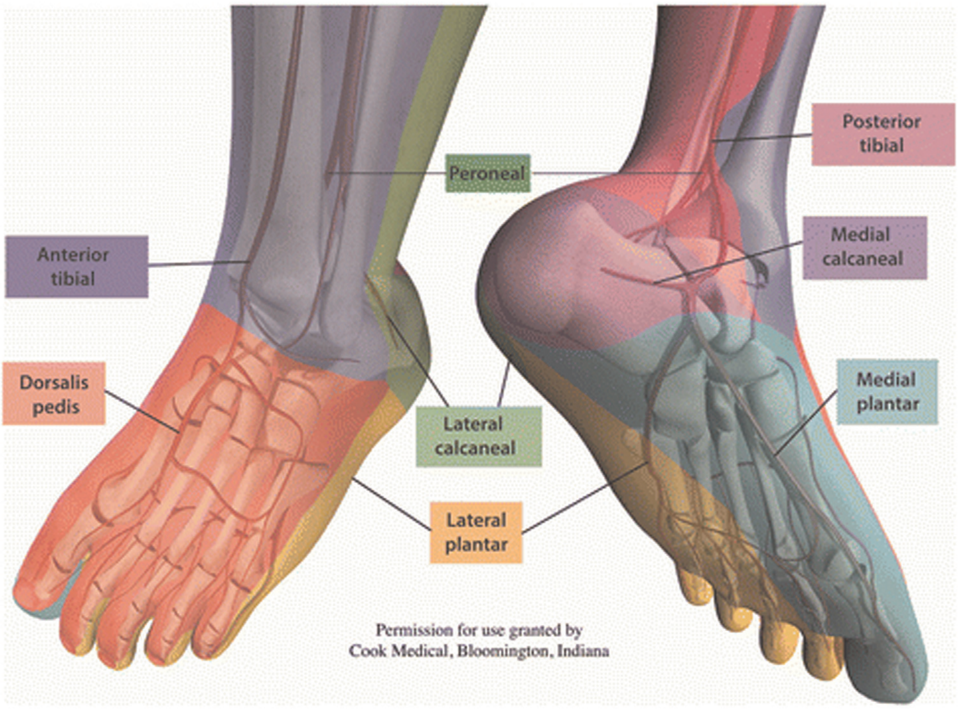
Different foot wounds might fail to heal because of insufficient arterial blood supply to the specific wound zones. The purpose of recent studies was to evaluate if infrapopliteal endovascular revascularization guided by angiosome concept of perfusion had an effective role on the healing of different foot wounds compared with indirect nonangiosomal perfusion [2].

Angiosome is considered as a three-dimensional anatomic distribution of tissues (skin, subcutaneous tissue, tendons and fascia, muscle, and underlying bone) supplied by certain artery and drained by certain vein. Foot and ankle arterial angiosomes were clarified on topographic map, which was categorized into six regions, each region being supplied by three major arteries (Fig. 1) [4].

Patients and methods

The study plan was accepted by the Ethical Committee of Ain Shams University Hospital. The study was held at Ain Shams University Hospitals.

Figure 1



Topographic map that shows the angiosomal-six territories of foot and ankle and their specific blood supply, according to Attinger *et al*. [3].

This is a prospective nonrandomized interventional cohort study done on 40 patients with critical limb ischemia owing to infrapopliteal disease to evaluate the role of direct angiosomal angioplasty compared with the indirect nonangiosomal angioplasty with respect to different foot wound healing and limb salvage rates. Patients who successfully underwent primary tibial angioplasty were selected to be included in the study. They were categorized according to the anatomy of the foot wound and targeted vessel into two groups: angiosomal directed and nonangiosomal indirect flow. To be considered in the nonangiosomal group, we aimed to open as much tibials as we could and we corrected any pedal arch stenosis to give the patient the best chance for revascularization wound healing was followed up within 2 years from July 2018 till July 2020 at 1, 6, 12, and 24 months after the procedure.

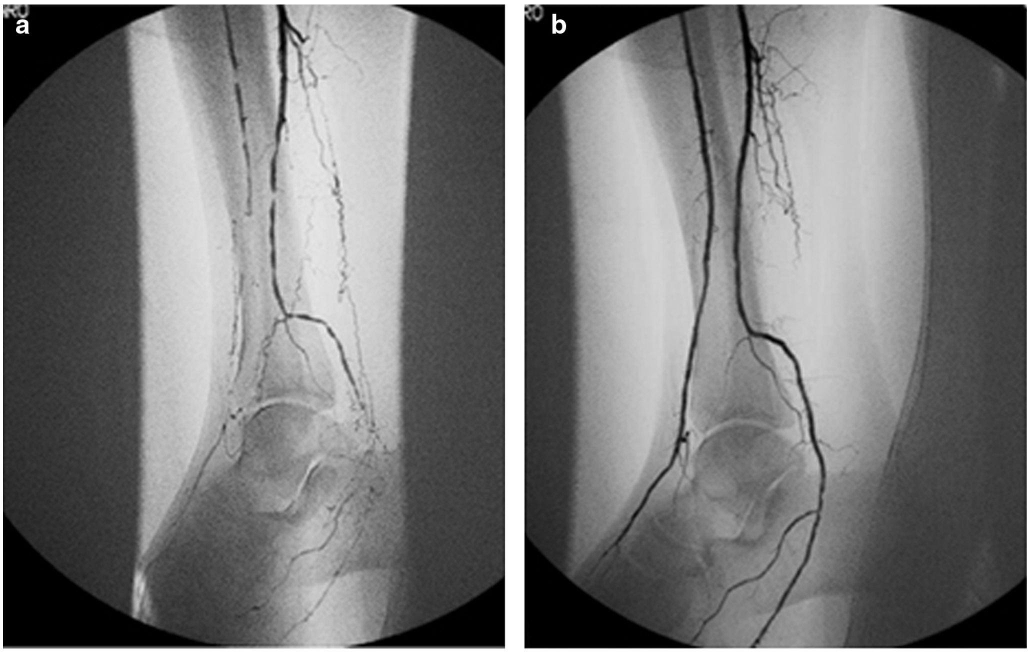
40 patients were selected randomly from the vascular out patients clinic between January 2018 till June 2018 and then followed up within 2 years from July 2018 till July 2020 for this prospective cohort after assessing the sample size using PASS version 11 program, setting the type 1 error (α) at 0.05 and power at 80%.

Criteria for the patients' selection included all symptomatic patients with critical limb ischemia grade 5 or 6 according to Rutherford classification (Rutherford *et al.*, 1997) [27] with or without rest pain, with different wounds distributed all over foot or toes gangrene due to infrapopliteal disease (stenotic lesions or total occlusion), detected radiologically by arterial duplex or computed tomography angiography with intact popliteal pulse (no proximal lesion), with good run in and run off and with good foot arch. However, patients with supramalleolar ulcers and severely infected wound with lost limb (nonsalvagable) and high total leukocytic count, or patients with acute charcot joint, acute arterial thrombosis, or proximal significant arterial disease to the tibial vessels, and with any contraindication to contrast media were excluded.

A total of 40 patients who met the inclusion criteria were included in the study and according to European Society of Vascular and Endovascular Guidelines 2018. Full detailed history (e.g. age, sex, smoking, medical history like diabetes, hypertension, ischemic heart disease, renal insufficiency, obesity, history of claudication pain, and rest pain), full local vascular examination [e.g. preprocedural ankle-brachial index (ABI) measurement, pulse examination, ulcer examination], and preoperative laboratory examination and investigations were done.

Foot ulcer was known as a full-thickness skin defect distal to the malleolar level present for a minimum of 2 weeks. University of Texas Wound Classification System was used to classify depth of foot ulcer:

Figure 2



Intraoperative angiography showing diseased posterior tibial artery (PTA). Photograph a: stenotic PTA and anterior tibial artery (ATA) with stenosed foot arch. Photograph b: patent PTA, ATA, and foot arch after balloon angioplasty.

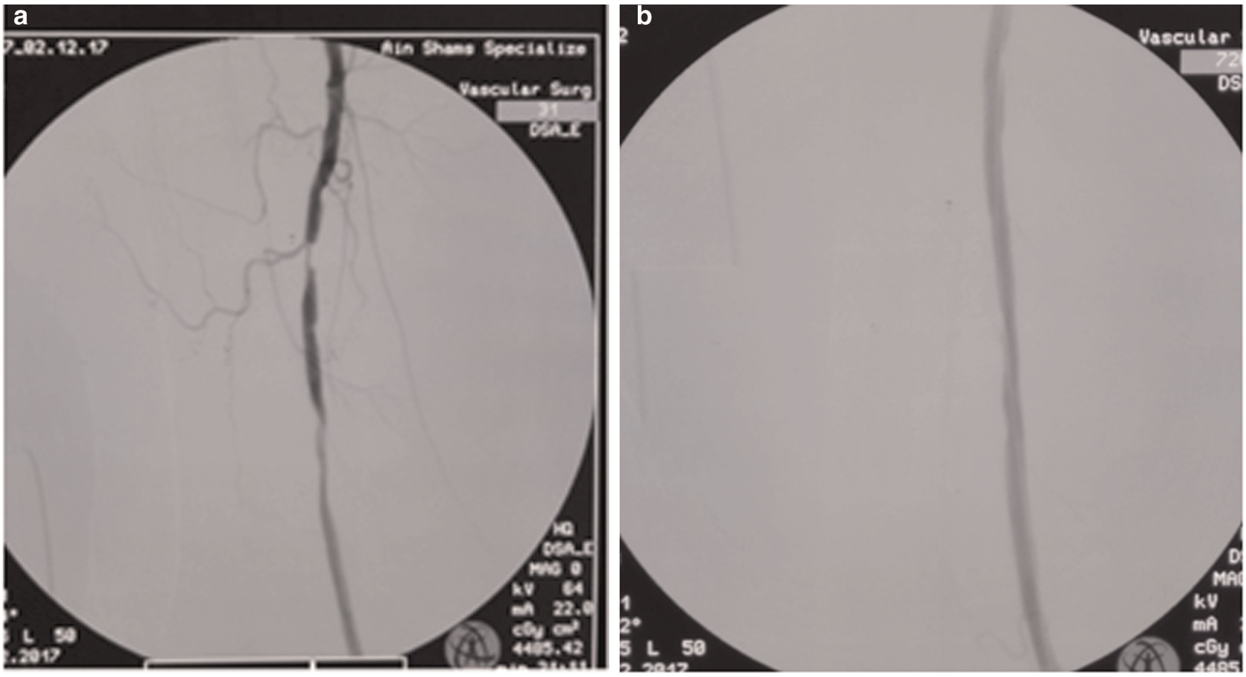
grade 1: superficial ulcer; grade 2: ulcer reaching the muscle, tendon, or capsule of joint; and grade 3: ulcer reaching the bone or joint, as well as to classify existence of infection: grade A: nonischemic, noninfected ulcer; grade B: nonischemic, infected ulcer; grade C: noninfected, ischemic ulcer; and grade D: infected ischemic ulcer [5,29].

Preoperative foot ulcer assessment was done and classified according to previous classification. Culture and sensitivity swab was taken from the wound, and dressing was done by betadine. All patients with infected foot wounds were kept on broad-spectrum antibiotics in the form of third-generation cephalosporins till swab results were revealed. However, patients with dry gangrene were kept on daily dressing by betadine only without systemic antibiotics. Preprocedural ABI was measured for all patients and recorded.

The primary end point was complete wound healing, and the secondary end points were limb salvage and amputation-free survival rate.

All patients went for tibial angioplasty using C-arm devices (Siemens device in 23 patients out of 40 cases in vascular OR room, whereas Ziehm device was used in 17 patients out of 40 cases in catheter laboratory theater). Ipsilateral antegrade access site was done in all 40 patients performed under local anesthesia, by infiltration of 10 ml (2%) xylocaine diluted in 10 ml of saline, around common femoral artery in groin area under ultrasound guidance. Puncture was done using puncture needle IN 18, 18 G, 7 cm in length under ultrasound guidance, followed by insertion of 6-french sheath. A total of 32 (80%) patients underwent ipsilateral antegrade access only, whereas eight (20%) patients needed ipsilateral retrograde access at different tibial vessel using micropuncture sheath after failure of ipsilateral antegrade access to cross the lesion, though retrograde access may be exceptionally done directly without a sheath, as sheathless access. Bolus of 5000 units of heparin was given after sheath insertion routinely in all patients. Preoprocedural intraoperative angiography was done to locate the site of lesion, run in and the run off, type of lesion (stenosis or total occlusion), and foot arch patency. It revealed ten patients had total occlusion lesion (25%), 26 patients had stenotic lesions (65%), and four patients had both (10%). The operator succeeded to pass the lesion transluminal in 65% of the patients, whereas in 35% managed to pass the lesion through subintimal track without causing any significant dissection using different types of wires for manipulation, like hydrophilic wire (0.035) by Medtronic and (V18) and (V14) wires by Boston Scientific (Fig. 2a and b). Once the operator crossed the lesion by the wire, balloons ranging in size of 3, 2.5, and 2 diameters (admiral balloons (Medtronic, USA) and sterling balloons (Boston Scientific, USA) were used to dilate the lesion with good postdilatation results, with no significant dissection or distal thrombosis or perforation (Fig. 3).

Figure 3



Intraoperative angiography showing diseased anterior tibial artery (ATA). Photograph a: stenotic ATA. Photograph b: patent ATA after crossing lesions, after balloon angioplasty.

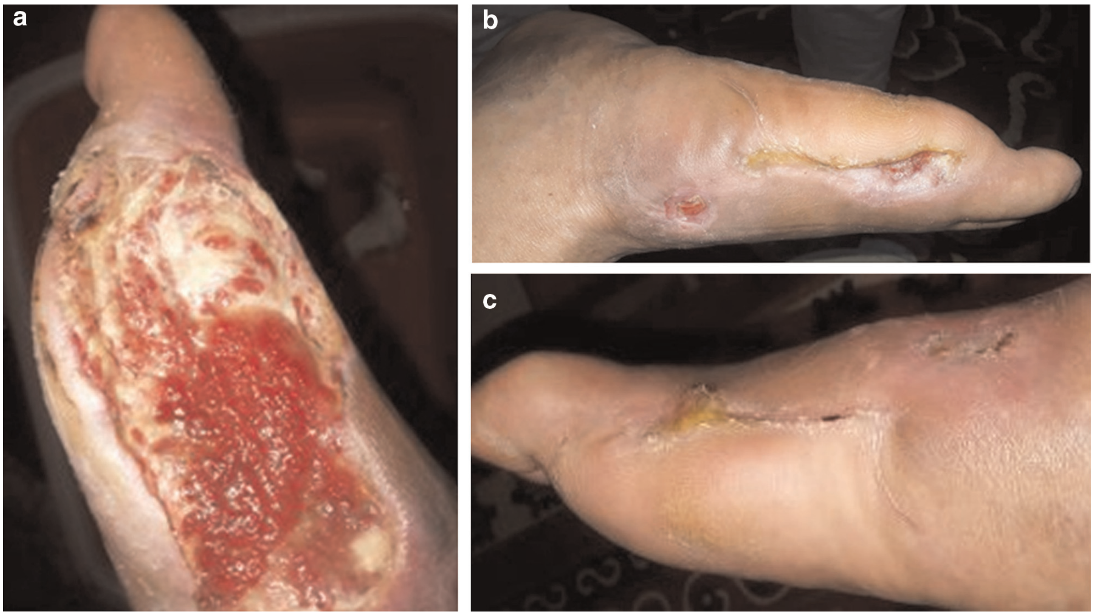
Postprocedural technical success was defined as percutaneous angioplasty of infrapopliteal arterial lesion without residual stenosis of more than 50%. After the procedure, the 40 patients were divided into two groups according to the angiosome model depending on the anatomy of the foot wounds of each patient into direct group where the foot ulcer/toe gangrene got its arterial flow from direct angiosomal artery, and indirect group where foot wound was fed by collaterals from other angiosomes.

Procedural-related adverse effects like groin hematoma, superficial groin area and perineal area ecchymosis, and contrast-induced nephropathy were recorded if present. Immediate hemodynamic improvement and postprocedural ABI were recorded and evaluated. All patients were kept after the procedure on single antiplatelet medication clopidogrel (75 mg tabs once daily for 1 year) according European Society of Vascular and Endovascular Guidelines, unless it was contraindicated owing to any general causes.

Postprocedural (angioplasty) wound care for the study patients was categorized into either minor amputation of wet gangrenous toe or surgical wound debridement to remove infected necrotic ischemic tissues, which was done either on the same day of procedure (if the wound needed urgent debridement or due to wet gangrenous toe) or after the procedure by one or two days (if the patient needed general anesthesia and needed to be prepared). Local wound care postoperatively (surgical debridement or toe amputation) was in form of daily dressing done by betadine at first week to act as local antiseptic, then starting from second week, daily dressing was done by Iruxol Mono 1.2 U/g ointment (containing clostridiopeptidase A and protease) to enhance granulation tissues and improve epithelization.

The patients were followed up at the vascular outpatient clinic. The first follow-up visit was 1 week after percutaneous angioplasty and debridement or minor amputation, and then at intervals of 1, 6, 12, and 24 months (Fig. 4). The surveillance continued until the wound totally healed. Wound healing was defined as complete epithelialization of the tissue defect by secondary intention or after any additional local wound surgery (Fig. 5). The foot wound was considered nonhealed if it did not heal during follow-up or certain period of time. In addition to the clinical status, follow-up visits included ABI measurements. Duplex scanning and/or angiography were performed in patients with clinical deterioration corroborated by ABI. Re-percutaneous transluminal angioplasty was considered for restenosis. For this study, follow-up ended 2 years after the primary infrapopliteal percutaneous transluminal angioplasty, or death, whichever occurred first.

Figure 4



Post-big toe amputation wound, post-angiosome-directed angioplasty, (a) first week post amputation, day 7, (b) 4 weeks after amputation, and (c) 6 weeks after amputation.

After completion of study period, the data was collected and analyzed by the Statistical Package IBM SPSS Statistics version 26 (IBM Corp., Armonk, New York, USA) for statistical analysis. Comparisons of univariate continuous variables between the two groups were computed via the Student *t*-test (normal distribution). Kaplan–Meier survival curve univariable analysis was used to estimate cumulative ulcer healing, leg salvage survival, and amputation-free survival. Survival rates are reported as proportion (SE). Life tables between groups were compared with log-rank test. To test the hypothesis of the study, the duration of wound healing was measured in months between the two groups and detect if there is any difference in the duration if the patient went through angiosome-directed or indirect tibial angioplasty with comparison of limb salvage rates between two groups.

Outcome and evaluation

The main target of this study was to evaluate if achievement of direct angiosomal arterial flow to different foot wounds had significant effect on wound healing rate compared with indirect nonangiosomal perfusion according to the angiosome principle. The secondary target was to assess the rate of limb salvage in both groups. We had treated the patients in their best interests, so we at first treated the angiosome-related tibial artery to the foot wound, and when this failed, we treated the nonangiosomal tibial artery perfusing the foot wound indirectly.

Results

Out of the 40 patients of the study sample, 19 patients (47.5%) were females and 21 (52.5%) patients were males. The mean age was 58.9±7.81 years (40–71). Of the 40 patients, 26 (65%) were smokers and 14 (35%) patients were nonsmokers (Table 1).

Of the 40 patients who underwent infrapopliteal percutaneous angioplasty, 27 (67.5%) patients achieved direct flow to the foot wound based on the angiosome concept, and 13 (32.5%) patients achieved indirect perfusion flow to the foot ulcer. Of the 27 patients of the direct angiosomal group, we approached posterior tibial artery in 10 patients for heel and big toe ulcers, anterior tibial artery in 11 patients for dorsum of foot ulcers and different toes ulcers, and peroneal artery in six patients for lateral aspect of the foot ulcers. In comparing the demography and different comorbidities and measuring their significance between the two groups of the study, regarding age, sex, smoking, and other comorbidities as diabetes, hypertension, renal insufficiency, ischemic heart disease and obesity, there was no significant difference between the two groups of the study (Table 2).

Of 40 patients, 17 patients were Rutherford class 5 (11 patients in the direct angiosomal group whereas seven patients in the indirect nonangiosomal group), and 23 patients were Rutherford class 6 (16 patients in the direct group, whereas seven patients in the indirect

Figure 5

Infected ischemic heel wound. (a) Preprocedural, (b) post-angiosome-directed angioplasty and surgical debridement by 2 weeks, (c) follow-up at fourth week, and (d) follow-up 6 weeks after intervention.

Table 1 Demography of the whole study sample

Initial data	*N*=40 [*n* (%)]
Age	
Mean±SD	58.90±7.81
Range	40–71
Sex	
Female	19 (47.5)
Male	21 (52.5)
Current smoking	
Smoker	26 (65.0)
Nonsmoker	14 (35.0)

nonangiosomal group). The preprocedural ABI was measured for all the 40 patients and compared between the two groups of the study; it showed no significant difference (Table 3).

All the study sample patients were intervened through ipsilateral antegrade access. Of those 40 patients, 32 (80%) patients were intervened successfully through ipsilateral antegrade only using 6-F sheath, and eight (20%) patients failed to pass the lesion through the ipsilateral access only and needed ipsilateral retrograde intervention using micropuncture set through one of the tibials, which was through posterior tibial artery in five patients and through anterior tibial artery in three patients.

All the study sample patients showed immediate hemodynamic improvement, with technical success proved by intraprocedural angiography and hand-held Doppler signals. Postprocedural ABI

Table 2 Comparison between the two groups of the study as regard demography and different comorbidities

Initial data	Direct angiosomal group [*n* (%)] *N*=27	Indirect nonangiosomal group [*n* (%)] *N*=13	Test value	*P* value	Significance
Age					
Mean±SD	58±8.31	60.77±6.57	−1.051•	0.300	NS
Range	40–70	51–71			
Sex					
Female	12 (44.4)	7 (53.8)	0.311*	0.577	NS
Male	15 (55.6)	6 (46.2)			
Smoking					
No	15 (55.6)	11 (84.6)	3.257*	0.071	NS
Obesity					
No	9 (33.3)	4 (30.8)	0.026*	0.871	NS
Yes	18 (66.7)	9 (69.2)			
		DM			
No	1 (3.7)	0	0.494*	0.482	NS
Yes	26 (96.3)	13 (100.0)			
Type of DM					
Non diabetic	1 (3.7)	0			NS
Type 1	2 (7.4)	0	1.562*	0.458	
Type 2	24 (88.9)	13 (100.0)			
HTN					
No	10 (37.0)	7 (53.8)	1.015*	0.314	NS
Yes	17 (63.0)	6 (46.2)			
Hyperlipidemia					
No	5 (18.5)	3 (23.1)	0.114*	0.736	NS
Yes	22 (81.5)	10 (76.9)			
IHD					
No	17 (63.0)	10 (76.9)	0.780*	0.377	NS
Yes	10 (37.0)	3 (23.1)			
Renal Insufficiency					
No	23 (85.2)	12 (92.3)	0.407*	0.523	NS
Yes	4 (14.8)	1 (7.7)			

DM, diabetes mellitus; IHD, ischemic heart disease.

Table 3 Comparison between the two study groups as regard the preprocedural ABI

Site of the lesion	Direct angiosomal group *N*=27	Indirect non angiosomal group *N*=13	Test value	*P* value	Significance
Preoperative ABI					
Mean±SD	0.42±0.09	0.47±0.11	−1.640•	0.109	NS
Range	0.3–0.55	0.3–0.6			

ABI, ankle-brachial index.

measurements showed marked improvement in both of the study groups, as in the direct angiosomal group showed mean±SD 1.06±0.13, with range: 0.9–1.2, whereas in the indirect nonangiosomal group showed mean±SD 1.05±0.14 with range: 0.9–1.3, both showing significant improvement compared with the preprocedural ABI but without significant difference between the two study groups.

All the 40 patients showed sustained haemodynamic improvement during the first month postprocedural proved by arterial duplex. Regarding the comparison between the two study groups with respect to the maintained patency at the 6 months, restenosis rates and the required re-intervention are shown in Table 4, revealing no significant difference between the two groups.

Only three (7.5%) patients out of 40 patients (all of them in the direct group) developed procedural-related adverse effects, in the form of dye-induced nephropathy, which occurred after 3 days from the procedure, and dye anaphylaxis and dyspnea owing to volume overload, both occurred at the same setting of the procedure and managed carefully. Neither 30-day mortality nor procedural-related mortality occurred in the entire study sample, but there was an overall mortality of three (7.5%) patients owing to different causes. The first patient died owing to heart failure

Table 4 Comparison between the two study groups regarding the maintained patency at 6 months, restenosis rates, and the required re-intervention

	Direct angiosomal group [*n* (%)] *N*=27	Indirect nonangiosomal group [*n* (%)] *N*=13	Test value	*P* value	Significance
Re-do angioplasty after 6 months					
Negative	19 (70.4)	5 (38.5)	3.723*	0.054	NS
Positive	8 (29.6)	8 (61.5)			
Follow-up duplex after 6 months					
Patent	19 (70.4)	5 (38.5)	3.723*	0.054	NS
Restenosis	8 (29.6)	8 (61.5)			

Table 5 Comparison between the two study groups regarding the minor amputation and its time of occurrence

	Direct angiosomal group [*n* (%)] *N*=27	Indirect nonangiosomal group [*n* (%)] *N*=13	Test value	*P* value	Significance
Minor amputation					
No	10 (37.0)	6 (46.2)	0.304*	0.581	NS
Yes	17 (63.0)	7 (53.8)			
Duration of minor amputation occurrence					
Same setting of procedure	13 (48.1)	5 (38.5)			
After 1 day	5 (18.5)	3 (23.1)			
After 2 days	6 (22.2)	4 (30.8)	4.052*	0.542	NS
After 1 week	0	1 (7.7)			
After 2 weeks	2 (7.4)	0			
After 1 month	1 (3.7)	0			

after 6 months from the procedure. The second patient died due to acute myocardial infarction after 5 months from the procedure, whereas the third patient died due to respiratory failure (due to sever pneumonia) after 8 months from the procedure.

Minor amputation in form of toes amputation occurred in 24 (60%) of 40 patients; 16 (40%) patients needed surgical debridement [10 (37%) patients in the direct group, whereas six (46.2%) patients in the indirect group]. Table 5 shows the comparison between the two study groups regarding the occurrence of minor amputations and its time of occurrence. A total of 18 patients went for minor toe amputation or surgical debridement at the same setting of procedure owing to active infection; eight patients on the first day postoperatively; 10 (25%) patients on the second day after procedure, as it took time to prepare the patients under general anesthesia as they refused local anesthesia (owing to the fear to be painful procedure); only one patient at the first week after the procedure, as the patient developed infection on top of dry gangrene; two patients at the second week after the procedure, as gangrenous toe became sharply demarcated; and one patient at 1 month after the procedure, as the toe was semiamputated. The comparison showed no significant difference between the two groups. Only one (2.5%) patient went for major amputation (below amputation), which occurred after 6 months from the procedure owing to spreading of infection and uncontrolled DM.

Of 40 patients, 37 (92.5%) achieved the primary end point (total wound healing) and completed the study duration, whereas the remaining three (7.5%) patients died before the end of study duration, where one of them lost his limb and went for below-knee amputation. Overall, 26 patients (all of them were direct-angiosomal group) of 37 patients (70.2%) achieved total complete foot wound healing within very short period of time (mean±SD: 1.48±0.41 in months with range 1–2 months) compared with 11 patients (all of them were indirect nonangiosomal group) of 37 (29.8%) patients who achieved total complete foot ulcer healing within longer period of time (mean±SD: 7.82±1.72 in months with range 6–12 months) (Table 6). On comparing the wound healing duration between the two groups of the study, it showed high significance difference between the two groups (P=0.000) (Table 6). The primary end point was compared between the two study groups, represented by Kaplan–Meier curves, and showed high significance (P<0.001), as shown in Fig. 6.

Regarding the patients who achieved the secondary end point (limb salvage rate), 26 (96.3%) patients survived from amputation in direct (angiosomal) group and 11 (84.6%) patients from the indirect group. By

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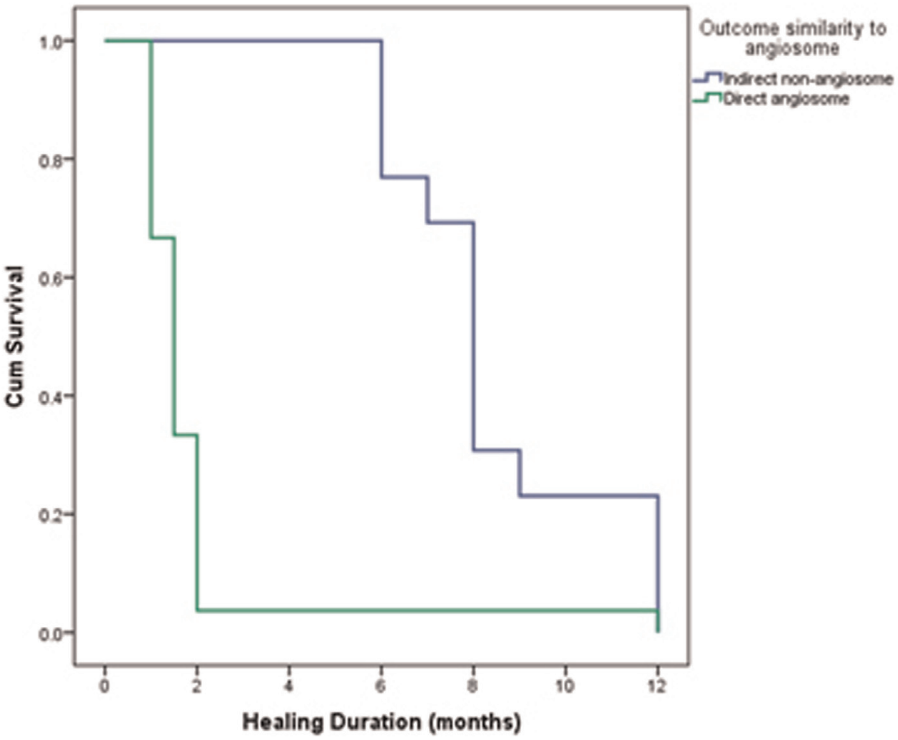
Table 6 Comparison between the two groups of the study regarding the wound healing duration (in months)

	Direct angiosomal group *N*=27	Indirect non angiosomal group *N*=13	Test value	*P* value	Significance
Healing duration (months)					
Mean±SD	1.48±0.41	7.82±1.72	−17.909•	0.000	HS
Range	1–2	6–12			

HS, highly significance.

Figure 6



Kaplan–Meier curve showing high significance between the two groups regarding wound healing rate (duration in months).

Table 7 Comparison between the two groups of the study regarding limb salvage rate

	Limb salvage (months)		95% CI		Test value	*P* value	Significance
	Mean	SE	Lower	Upper			
Indirect nonangiosome	12.462	0.756	10.979	13.944			
Direct angiosome	20.370	0.447	19.494	21.247	39.831	<0.001	HS
Overall	17.800	0.706	16.415	19.185			

CI, confidence interval; HS, highly significance.

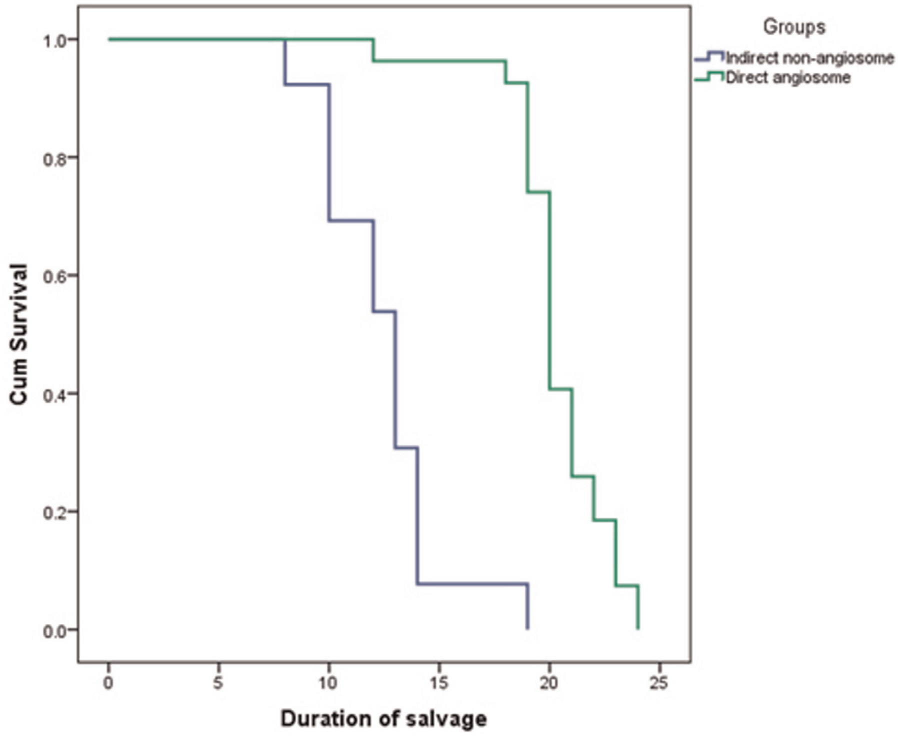
comparing the limb salvage rate between the two groups of the study, it showed high significance ($P<0.001$) (Table 7) and was represented also by Kaplan–Meier curve (Fig. 7).

Discussion

Knowing the boundaries of angiosome principle and variable vascular connections between its arterial sources provided the cornerstone for logically more than empirically designed map for tissue perfusion and to design reconstructions or amputations that eventually preserve blood supply for different foot wounds to heal [6].

Attinger and colleagues declared 9% wound healing failure rate when foot wounds were managed by angiosome principle obtaining direct arterial flow compared with 38% wound healing failure rate when arterial flow perfusion was obtained via indirect arterial flow. Some recent papers stated that limb salvage rates were also superior when direct angiosomal blood flow was achieved. Iida and colleagues studied 203 patients with critically ischemic lower limbs Rutherford class 5

Figure 7



Kaplan–Meier curve showing high significance between the two groups regarding limb salvage rates.

and 6, attaining limb salvage rate of 86% with direct angiosomal flow vs 69% with indirect nonangiosomal flow, with results proven by Varela and colleagues [7,8].

A paper was published in *Journal of Vascular Surgery*, at February 2012, Department of Cardiovascular Medicine, at Shinshu University School of Medicine, showing the clinical outcomes that were compared between direct angiosomal and indirect nonangiosomal endovascular perfusion depending on angiosome concept in 369 patients with critical limb ischemia with isolated below-the-knee tibial arterial disease, Rutherford class 5 and 6. They first identified the foot nonhealing ulceration/gangrene site and the angiosome-related target tibial artery lesion by intraoperative digital subtraction angiography, and then they tried an angiosome-related intervention of the targeted lesion in 200 patients, while they achieved indirect nonangiosomal arterial flow to 169 patients. During follow-up visits (mean: 18 months), the total limb salvage rate was 81% (300 out of 369), and the re-intervention rate was 31% (114 out of 369), whereas limb salvage rate was 82% which was significantly higher in the direct angiosomal group than in the indirect nonangiosomal group reaching up to 4 years after procedure. The study proved that attaining direct angiosomal arterial flow by angioplasty based on the angiosome principle in patients with critical lower limb ischemia with isolated tibial arterial lesions was clinically significant for faster wound healing rates, and limb salvage rates appeared to be higher in patients with direct flow from the feeding artery than those patients with indirect flow [9,10].

In recent decades, there was a debatable discussion regarding the most significant factors for rapid foot wound healing rates in patients with critical lower limb ischemia. Recently, it was agreed that restoring direct pulsatile arterial flow to ischemic foot wounds depending on the angiosome principle seemed to be critical step in revascularization and progression of the microperfusion of different foot wounds and its healing rates. So, a prospective study was held in Germany, March 2016, at vascular surgery department, to evaluate the angiosome principle on tibial vascular interventions. A total of 30 patients with tibial angioplasty were included in the study, and their macrocirculation was assessed by measurement of the ABI, and there was a significant total improvement in foot ulcers perfusion directly after tibial angioplasty according to angiosome model [11,12].

Another study was done in Egypt, December 2017, at Vascular and Endovascular Surgery Department, and was published in the *European Journal of Vascular and Endovascular Surgery* at 2018, to evaluate wound healing rates and limb salvage rates in patients with critical lower limb ischemia with different foot ulceration/toe gangrene who were subjected to direct angiosomal infrapopliteal angioplasty. Direct angiosomal arterial flow to different foot wounds based on angiosome principle was attained in 117 (55.2%) patients vs 95 (44.8%) patients included in the indirect nonangiosomal group. At 12 months after tibial angioplasty, total wound healing rates were 80.8% in the direct group and 63.0% in the indirect group (P=0.02), and limb salvage rates were 90.4% in the direct group and 82.2% in the indirect group (P=0.148). Finally, the study proved that the wound healing rate was faster and better in case that target foot wounds received direct angiosomal perfusion depending on the angiosome principle, whereas limb salvage rates were not significantly different between the two groups [13,14].

In comparison with wound healing rates in our study, it revealed that the angiosome-directed tibial angioplasty group had very short wound healing duration within less than 2 months with better outcome, whereas the indirect nonangiosomal tibial angioplasty group has longer wound healing duration, within 6–9 months, and one patient required 12 months with slower healing rates, whereas limb salvage rates were significantly different between the two groups of the study, as limb salvage rates were higher in the direct angiosomal group.

A recent study was held in China, Department of Interventional and Vascular Surgery, Tongji University, which was published in its journal of vascular surgery 2018, to explore the predictors of delayed foot wound healing rates after effective isolated below-knee angiosome-directed endovascular angioplasty in patients with ischemic foot wound Rutherford class 5 and 6. The total wound healing rates were 13.9, 43.8, 57.7, and 65.7% at 3, 6, 9, and 12 months, respectively. It was proven through this study by multivariate Cox proportional hazards analysis that predictors of foot wound nonhealing after effective tibial angioplasty depending on the angiosome principles of foot wounds were patients with end-stage renal disease receiving dialysis, serum albumin level, C-reactive protein level, major tissue loss, sever wound infection, wet gangrene, wound depth, ulcer onset and its duration, and lack of patent foot arch runoff [15,16].

In comparison with the predictors of delayed wound healing and the effect of different comorbitities on limb salvage rates in our study, it was revealed that there was no marked significant difference between their effect on both groups of the study, but smoking and high-total leucocytic count (TLC) delayed the wound healing in general, and patients with end stage renal disease (ESRD) required re-do angioplasty, and we excluded patients with severely infected foot wounds or extensive foot wet gangrene from our study.

Another study was done in China at Department of Vascular Surgery of the First Affiliated Hospital School of Medicine, Zhejiang University, in 2016, to evaluate the clinical significance of presence of collaterals during the application of angiosome principle for treatment of patients with infrapopliteal critical limb ischemia, Rutherford classes 5 and 6. The study included 486 patients with unilateral tibial arterial disease treated at two hospitals from January 2005 to December 2014. According to angiosome principle, patients were divided into three groups: direct angiosomal group, indirect nonangiosomal group through collaterals, and indirect nonangiosomal group without collaterals. All data from the first year of follow-up after primary angioplasty were collected and analyzed for the three groups. According to angiosome concept of revascularization for endovascular intervention, direct angiosomal blood flow through the feeding artery and indirect arterial flow attaining perfusion through collaterals can effectively improve foot wound healing rates and lower the amputation. Collateralizations of foot arch played a critical role in treatment of ischemic foot wounds [17,18].

Recent studies proved that angiosome-targeted endovascular angioplasty was more important in improving the wound healing rates of ischemic foot wounds than surgical intervention in patients with infrapopliteal tibial lesions. A study done in Finland, University of Helsinki, Department of Vascular Surgery, in 2017, stated that in diabetic patients, indirect nonangiosomal endovascular perfusion led to significantly worse wound healing and leg salvage rates compared with direct angiosomal revascularisation. So, endovascular intervention ought to be targeted depending on the angiosome principle. Moreover, during surgical bypass procedures, the tibial artery with the more preferable runoff ought to be chosen as outflow artery [19,20].

Regarding the role of multivessel vs single-vessel angioplasty for foot ulcers revascularization, with irrespective of angiosome principle, a report from Darling and colleagues showed that multivessel angioplasty had no effect on limb salvage, and angiosome principle should be respected as it had major effect on wound healing rates. The inconsistent results in the literature could be referred to the variable patient populations included in the different studies.

One efficient variable that could influence wound healing, not frequently mentioned in these studies, was the pedal arch status and collateral circulation patency. Rashid and colleagues showed that the wound healing and its duration rate were directly affected by the quality of the pedal arch. In case of pedal arch patency or well-developed collaterals, sufficient perfusion to the angiosome of interest could be attained even through single vessel [21–23].

A complete computed tomography angiogram, with pedal angiogram, ought to be performed to detect the arterial patency before intervention options. Angiosome-directed angioplasty should be done if technically could be done. This was in line with the recent 2017 European Society of Cardiology/European Society for Vascular Surgery Guidelines on peripheral arterial disease. However, it seems reasonable to consider multivessel angioplasty in patients with incomplete pedal arch and inadequate collaterals until we could have more reliable and practical means to evaluate perfusion at foot ulcer site [24–26]. That is why in our study, we excluded the patients with poor runoff or insufficient foot arch.

Conclusion

In our study, we focused on the role and the significance of angiosome-directed infrapopliteal endovascular angioplasty of patients with foot ulceration and gangrene in enhancing wound healing rates. The study proved that the angiosome-directed tibial angioplasty had a better foot wound healing rate and limb salvage rate than the nonangiosomal indirect flow. Attaining a direct arterial flow based on the angiosome concept of perfusion to the foot ulcer or post minor toe amputation ulcer (gangrenous toes) appeared to be important for better wound healing and higher limb salvage rate.

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Conflicts of interest

There are no conflicts of interest.

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