Angiosome-targeted isolated tibial angioplasty for healing of ischemic foot ulcer: a retrospective study

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Purpose
On the basis of the angiosome concept in critical limb ischemia patients who presented with isolated tibial lesions and foot ulcers, we evaluated and compared clinical outcomes, ulcer healing, and amputation-free survival between patients with successful angiosome-targeted tibial angioplasty alone [direct revascularization (DR)], patients with indirect revascularization (IR) in whom the dilated vessels successfully were the nonangiosome target, and those who underwent combined revascularization (CR) (both DR and IR were achieved).

Patients and methods
We retrospectively analyzed a total of 66 critical limb ischemia patients who presented with ischemic foot ulcer with isolated tibial vessel lesions at Mansura University Hospital during the period from January 2014 to January 2016. DR of the ischemic angiosome was performed in 37.8% (n=25), IR in 33.3% (n=22), and CR in 28.7% (n=19) of patients. All patients were evaluated for the status of wound healing and limb salvage at 1, 3, 6, 9, and 12 months. The study endpoints were major amputation or death, limb salvage, and ulcer epithelialization at 12 months.

Results
The mean follow-up was 11.08±3.2, ranging from 3 to 13 months. On Kaplan–Meier analysis, 65% of patients were diabetic. Ulcer healing rate at 12-month follow-up based on angiosome hypothesis among groups CR, DR, and IR was 94.7, 66.7, and 57.17%, respectively, with a significant P value (0.013) between CR and DR and a significant P value (<0.001) between CR and IR. However, on comparing the DR and the IR group, mean time to complete ulcer healing was not statistically significant (P=0.222). Amputation-free survival rate was 94.7, 75.6, and 72.7% in CR, DR, and IR, respectively.

Conclusion
If technically feasible, dilation of angiosome target artery plus any other significant tibial artery lesions should be considered. We should orient procedures toward multiple angiosome reopening with better ulcer healing rate and limb salvage. However, with limitations and challenges of angiosome-based strategies, especially in diabetic patients with depletion of choke vessels, we believe that IR should not be denied with acceptable result over the time.

Keywords:
angioplasty, angiosome, ischemia, tibial

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Introduction

Although a multidisciplinary approach is recommended by the Trans-Atlantic Inter-Society Consensus II guidelines to avoid major amputation in critical limb ischemia (CLI) patients [1], no medical therapy ensures limb salvage without revascularization [1,2]. Therefore, revascularization is the backbone modality for limb salvage in CLI.

Taylor was the first to introduce the concept of angiosome. Anangiosome is an anatomic unit (consisting of skin, subcutaneous tissue, fascia, muscle, and bone) fed by a specific artery and drained by specific veins. The foot contains six angiosomes, fed by the anterior tibial artery (one angiosome), the peroneal artery (two angiosomes), and the posterior tibial artery (three angiosomes) [3].

There are studies endorsing angiosome-targeted revascularization in CLI due to more favorable outcome compared with non-angiosome-targeted angioplasty [4,5]. However, other studies did not find a significant difference between angiosome-targeted and non-angiosome-targeted angioplasty for revascularization and healing of foot ulcers. The proposed explanation for these contradicting studies is that blood flow can be restored to the foot either through interangiosomal choke vessel connections or through the pedal arch [6].

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However, the angiosome concept has not been systematically studied in endovascular therapy and in associated factors affecting limb salvage for CLI patients with pure, isolated tibial lesions.

Aim

The aim of this study was to evaluate and compare clinical outcomes and ulcer healing between patients in whom angiosome target vessel revascularization alone was performed successfully [direct revascularization(DR)], patients with indirect revascularization (IR) in whom the dilated vessels successfully were the nonangiosome target, and patients in whom combined DR and IR was achieved [combined revascularization (CR)]. This study included patients with CLI due to isolated tibial vessel disease presenting with foot ulcers.

Patients and methods

All patients' records were evaluated during the period from January 2014 to January 2016. IRB/Ethics committee approval was taken from our faculty committee it is no (16/03/34). A total of 66 CLI patients presented with ischemic foot ulcer with isolated tibial vessel lesions at Mansoura University Hospital. Patients with associated proximal lesions, associated severe infection, and those who presented with acute limb ischemia requiring emergency revascularization or functionally unsalvageable limbs and cases of technically failed dilation of any tibial vessel were excluded from the study. All 66 patients evaluated were in the Rutherford–Becker category 5–6 ischemia.

Before posterior tibial artery (PTA), all patients were subjected to thorough general and local examination, including pulse assessment, ankle brachial index measurement, and ulcer measurement, location, and whether or not associated with infection. Any previous vascular medication, including its type and duration, was recorded. Previous endovascular intervention and vascular surgery were also documented.

All patients were subjected to full laboratory investigations, including complete blood count, blood glucose level, kidney functions, liver functions, coagulation profile, and lipid profile.

Duplex and computed tomography angiography were performed for the diagnosis and characterization of the lesions before PTA. Initial magnetic resonant angiography (MRA) was not standard practice in our department and was restricted only to cases in which computed tomography angiography was contraindicated.

Assessment of the extent of the disease and identification of the crural vessel crossing the ankle to perfuse the foot ulcer were carried out, as well assessment of the need for arterial reconstructive procedure confirming the location of nonhealing ulceration/gangrene and the angiosome-based favorable target lesion. We then generally attempted an angiosome-based intervention of the target lesion (the DR group; group A). However, if treatment of the angiosome-based target lesion was unsuccessful, a non-angiosome-based lesion was treated (the IR group; group B), and in some cases an angiosome-based and non-angiosome-based revascularization was achieved (the CR group; group C).

Angiographic information on diseased segment location and degree of stenoses or occlusion and extent of distal runoff were available for all patients before angioplasty. All patients received periprocedural medications with oral antiplatelet in the form of salicylic acid 150 mg twice daily and cilostazol 100 mg twice daily and good hydration with normal saline for 6 h before and after the procedure.

The procedure was performed under local anesthesia in most of the cases, and, in few cases with noncooperative patients, spinal anesthesia was the choice. Ipsilateral antegrade femoral arterial puncture was used in all cases. All patients received 5000 IU heparin intravenous after sheath insertion. Selective angiography of the infrapopliteal arteries was performed with a 4 Fr multipurpose diagnostic catheter.

Afterwards, a 0.018 and or 0.014 guidewire with a steerable soft atraumatic tip was then used to pass culprit lesion in an antegrade direction. Revascularization was classified as DR if the ischemic area was perfused by its source artery, which was the first trial in all cases, as IR if the artery perfusing the foot was other than the source artery of the specific angiosome, and as CR if both DR and IR were performed. In patients with large ischemic ulcers involving more than one region of the foot (e.g. midfoot and heel or forefoot and midfoot) and if the revascularization was indirect, the region of the foot that was the farthest away in terms of perfusion from the vessel being perfused was considered as the primary angiosome.

After crossing the lesion, dilation using low-profile balloons with a diameter of 2.5–3 mm and a length of 40–150 mm with 6–10 atm for 30–60 s was performed.

Following deflation, routine angiography was performed with the guidewire remaining across the lesion, and procedure outcome was recorded. Technical success was achieved with residual stenosis less than 30%.

Postinterventional medication of 150 mg of acetylsalicylate indefinitely on a lifetime basis plus 75 mg of clopidogrel once daily for 1 month and cilostazol 100 mg twice daily for 1 year was prescribed. Antibiotics were routinely administered if the ulcer was complicated with infection according to culture sensitivity test; serial debridement with appropriate topical wound care was performed until granulation tissue showed a sign of healing.

Study outcome

The wounds were photographed and ulcer size was calculated preoperatively and immediately after debridement and was followed up at 1, 3, 6, 9, and 12 months. All wounds were classified as either fully epithelialized, granulating, or worsening at the time of each visit. Limb salvage is defined as no amputation beyond tarsometatarsal amputation. Ulcer healing was considered successful if the ulcer/gangrenous segment had healed completely, or if at the end of the follow-up period the ulcer persisted but with a significant reduction in size. All patients were followed up to the endpoints of limb salvage at 12 months.

The risk factors were compared between the three groups. Patients were also assessed for the need for adjuvant wound healing measures such as split skin grafting if the wounds did not show signs of adequate epithelialization despite improved vascularity after revascularization.

Definitions

Success, failure, complications, and ulcer healing were analyzed according to the guidelines provided by the Society of Vascular Surgery and the International Society for Cardiovascular Surgery [7,8].

Technical success was defined as obtaining at least one straight-line flow in one crural vessel without any flow-limiting dissection.

The follow-up period ranged from 3 to 13 months with a mean follow-up period of 11.08+3.2 months. Follow-up was carried out in the vascular surgery outpatient clinic at 1, 3, 6, and 12 months as regards ulcer size and appearance. Clinical success of PTA was defined as disappearance of necrotic and inflammatory signs and partial or total healing of the ulcer without bypass grafting or major amputation and limb salvage rate.

Results

Baseline patient characteristics in the overall population and in the three groups are reported in Table 1. A comparison between groups showed no significant differences in patient status, atherosclerotic risk factors, and presence of cardiovascular disease.

Most of the patients were categorized as Rutherford V, with minor tissue loss in 38 (57.5%) patients, and there were no statistically significant differences in lesion characteristics and ankle brachial index between groups (Table 2).

As regards lesion distribution, heel and plantar ulcerations were the most common, with a nonsignificant statistical difference between groups (Table 3).

Table 1 Demographic data

	Total (*n*=66) [*N* (%)]	DR group (*n*=25)	IR group (*n*=22)	CR group (*n*=19)
Age (mean±SD)	62.58±8.36	61.40±9.61	62.41±7.42	64.32±7.75
Sex				
Male	38 (57.6)	14 (56)	13 (59.1)	11 (57.9)
Female	28 (42.4)	11 (44)	9 (40.9)	8 (42.1)
DM	43 (65.2)	18 (72)	17 (77.2)	14 (73.6)
ESRD	14 (21.2)	4 (16)	6 (27.3)	4 (21.1)
Smoker	19 (28.8)	10 (40)	4 (18.2)	5 (26.3)
Coronary heart disease	15 (22.7)	8 (32)	3 (13.6)	4 (21.1)
HTN	22 (33.3)	10 (40)	7 (31.8)	5 (26.3)
Hyperlipidemia	17 (25.8)	8 (32)	3 (13.6)	6 (31.6)

CR, combined revascularization; DR, direct revascularization; ESRD, end stage renal disease; HTN, hypertention; IR, indirect revascularization.

Table 2 Rutherford categorization

	Total (*n*=66) [*N* (%)]	DR group (*n*=25) [*N* (%)]	IR group (*n*=22) [*N* (%)]	CR group (*n*=19) [*N* (%)]
Rutherford				
V	34 (51.5)	15 (60)	12 (54.5)	11 (57.9)
VI	32 (48.5)	10 (40)	10 (45.5)	8 (42.1)
ABI	0.58±0.17	0.58±0.17	0.56±0.18	0.61±0.15

ABI, ankle brachial index; CR, combined revascularization; DR, direct revascularization; IR, indirect revascularization.

Table 3 Ulcer sites

	DR group (*n*=25) [*N* (%)]	IR group (*n*=22) [*N* (%)]	CR group (*n*=19) [*N* (%)]
Toe	4 (16)	4 (18.2)	4 (21.1)
Heal	10 (40)	5 (22.7)	4 (21.1)
Dorsum	4 (16)	4 (18.2)	2 (10.5)
Plantar	6 (24)	8 (36.4)	5 (26.3)
Ankle	1 (4)	1 (4.5)	4 (21.1)

CR, combined revascularization; DR, direct revascularization; IR, indirect revascularization.

The posterior tibial artery was the more frequently diseased artery in all groups. After statistical adjustment, there were no statistically significant differences in limb in target vessel PTA between groups (Table 4).

Overall, two (3%) patients died and two (3%) patients were lost to follow-up.

Discussion

Effective revascularization is a cornerstone in the treatment of ischemic foot ulcer. The angiosome anatomy and angiosome overlap have been described extensively by Attinger *et al.* [9–11]. Intuitively, DR is preferable for specific ischemic ulcer and IR is preferable for nonspecific ulcer. This, however, may not always be possible. Berceli *et al.* [12] reported on the efficacy of dorsalis pedis artery bypass for ischemic forefoot and heel ulceration. In this study, the 86% limb salvage for heel ulcerations relying on either of the two perfusion routes indicates that ulcer healing and limb salvage are possible even in the absence of an intact pedal arch, thus relying on interangiosome connections for perfusion.

To the best of our knowledge, this is the first study to divide patients into three groups, including the combined group (CR) in which both DR and IR were achieved.

In our retrospective assessment, of the 66 patients, 65% of them were diabetic. Revascularization based on angiosome hypothesis suggests that CR, DR, and IR if technically achievable has a significant ulcer healing rate at 12-month follow-up (94.7, 66.7, and 57.17%, respectively) (Fig. 1 and Table 5) with a significant amputation-free survival rate of 94.7, 75.6, and 72.7%, respectively (Fig. 2 and Table 6).

On comparing the DR and IR groups, the mean time to complete healing and amputation-free survival were comparable, with no statistically significant difference.

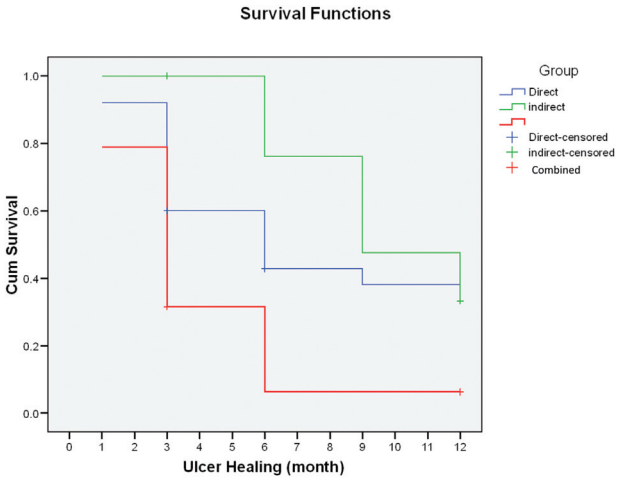
Our results on the DR and IR groups analysis are consistent with other studies such as that of Neville *et al.* [4], who analyzed CLI ischemic ulcer in 48 CLI patients; 87% of them were diabetic with a healing rate of 91 versus 62% and an amputation rate of 9 versus 38%

Table 4 Target vessel angioplasty

	DR group (*n*=25) [*N* (%)]	IR group (*n*=22) [*N* (%)]	CR group (*n*=19) [*N* (%)]
ATA	8 (32)	11 (50)	12 (63.2)
PTA	13 (52)	8 (36.4)	13 (68.4)
Peroneal	4 (16)	3 (13.6)	9 (47.4)

ATA, anterior tibial artery; CR, combined revascularization; DR, direct revascularization; IR, indirect revascularization.

Figure 1



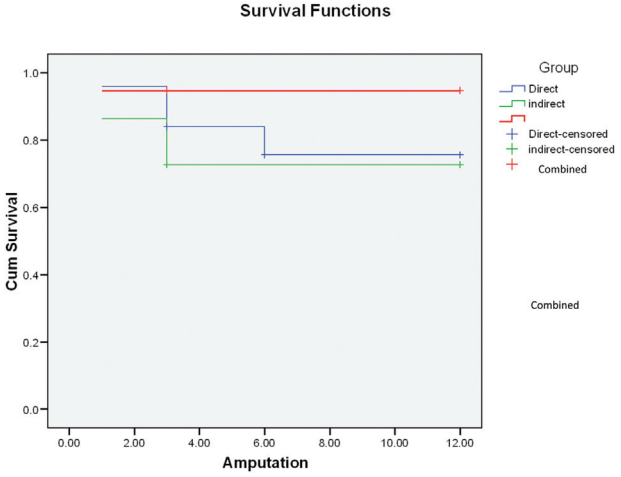
Ulcer healing rate.

Table 5 Ulcer healing rate

	Median±SE	95% CI	Test of significance
DR (group A)	6±1.76	2.55–9.46	P_1=0.222
IR (group B)	9±1.53	6.01–11.91	P_2=0.013*
CR (group C)	3±0.45	2.12–3.88	P_3<0.001*

CR, combined revascularization; CI, confidence interval; DR, direct revascularization; IR, indirect revascularization. P_1: DR versus IR. P_2: DR versus CR. P_3: IR versus CR. *Significant, P<0.05.

Figure 2



Amputation free survival.

Table 6 Amputation free survival

	Mean±SE	95% CI	Test of significance
DR (group A)	9.98±0.74	8.53–11.42	P_1=0.707
IR (group B)	9.27±0.96	7.40–11.15	P_2=0.109
CR (group C)	11.42±0.56	10.32–12.53	P_3=0.070

CR, combined revascularization; CI, confidence interval; DR, direct revascularization; IR, indirect revascularization. P_1: DR versus IR. P_2: DR versus CR. P_3: IR versus CR.

between DR and IR, respectively. There was no statistically significant difference between groups with regard to mean time of healing, whereas there was a significant difference (P=0.03) with regard to complete wound healing time. Consistent with these reports, in a prospective series that included 64 CLI patients, Kabra *et al.* [13] found that ulcer healing was 96.4 and 83.3%, which was significant with regard to the rate of healing (P=0.021), whereas limb salvage rate was nonsignificant (84 vs 75% in DR and IR, respectively), with 39% of their cases managed by endovascular therapy.

It is interesting to note other studies with special concern only on diabetic ischemic ulcer. A study by Alexandrescu *et al.* [14] on 208 ischemic foot ulcers treated with below knee angiosome-oriented angioplasty revealed significantly better wound healing (P<0.018) and limb salvage (P<0.03). Belvins and Scneider [15] reported a statistically significant increase in $TcPO_2$ value at follow-up compared with baseline (P<0.05) between DR and IR in diabetic patients with ischemic ulcer.

The effect of Diabetes mellitus (DM) on inter-angiosomal communicating vessel and outcome on target revascularization could be explained by, firstly; presence of specific calcification which represent one of major technical challenges for vascular surgeon [15]. Diabetic crural vessels atherosclerosis affecting medial layer in concentric continuous manner on the arterial wall (Monkerberg sclerosis or type II calcification) [16] with consequence collateral depletion (choke vessels depletion) in comparison to non diabetic calcification type I which is eccentric and patchy [13].

Another challenging factor in diabetic patients is local neuropathy causing microcirculatory impairment by autonomic denervation. These specific diabetic foot challenges indicate the need to treat ischemic diabetic foot areas with more specific vascular angiosome-oriented reconstruction.

Conclusion

We can conclude from this study that, if technically feasible, dilation of angiosome target artery plus any other significant tibial artery lesions should be considered; we should orient procedures toward tandem or multiple angiosome reopening with better ulcer healing rate and limb salvage.

The strategy of revascularization has to be shifted, whenever possible, from 'which artery is most suitable to revascularize' to 'which region governed by which artery should be managed'.

With limitations and challenges of angiosome-based strategies, we believe, however, that IR should not be denied with acceptable result over time.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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