

## Original Research Article

# Angiosome based revascularization for diabetic foot ulcer

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### ABSTRACT

**Background:** The purpose of this study was to analyze the clinical benefit in wound healing and limb preservation after infrapopliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of diabetic foot ulcers.

**Methods:** This is a prospective controlled study was conducted on 60 patients with critical lower limb ischemia in the form of diabetic foot ulcer and/or gangrene. The study period started from August 2017 until February 2019. Patients included in the study were essentially attending the Vascular Outpatient Clinic at Menoufia University Hospitals and Nasser Institute for Search and Treatment at Cairo treated by infra-popliteal angioplasty.

**Results:** The 60 patients of our study who underwent successful infra-popliteal angioplasty we found that after six months 18 patients in the direct group A (85.71%), 9 patients in indirect group B (42.85%) and 17 patients in combined group C (94.44%) showed complete healing of their wounds and that 18 patients in group A (85.71%), 15 patients in group B (71.42%) and 17 patients in group C (94.44%) have their limbs salvaged total 50 patients (83.33%).

**Conclusions:** We concluded that dilation of angiosome target artery plus any other significant tibial artery lesions should be considered and indirect revascularization should not be denied with acceptable result over time.

**Keywords:** Angiosome, Revascularization, Diabetic foot ulcer

### INTRODUCTION

Peripheral arterial disease (PAD) is a major world-wide health problem affects 12%-14% of the general population. In large observational studies, PAD, ranging from relatively mild disease with limited effects on wound healing to severe limb ischaemia with delayed wound healing, was present in upto 50% of the patients with a diabetic foot ulcer.<sup>1</sup> Atherosclerosis develops at a younger age in patients with diabetes and progresses rapidly. Moreover; atherosclerosis affects more distal vessels in patients with diabetes. Several significant risk factors contribute for the development and progress of PAD including diabetes mellitus, hypertension, hyperlipidemia and smoking.<sup>2</sup> Chronic critical lower limb

ischemia develops when the arterial blood flow is severely reduced to maintain the necessary requirement of normal tissues metabolism. It can be manifested clinically as rest pain, non-healing wounds or tissue loss (necrosis or gangrene). It is usually diagnosed by integrating the clinical exam with non-invasive tests like ankle pressure measurement and ankle brachial index, as well as, transcutaneous oximetry or color-Doppler ultrasound scanning.<sup>3</sup>

Peripheral artery disease in patients with diabetes has a number of characteristics that render it more difficult to treat. The atherosclerotic lesions are multilevel and particularly severe in tibial arteries, with a high prevalence of long occlusions. The predilection for

multiple crural vessel involvement combined with extensive arterial calcification increases the technical challenges associated with revascularization using either open bypass or endovascular techniques.<sup>4</sup> Angioplasty using the angiosome concept is first introduced by Taylor and Paler approximately two decades ago, is considered an important factor in wound healing.<sup>5</sup> An angiosome 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).<sup>6</sup>

Poor vascular connectivity between angiosomes in a diabetic foot can result in treatment failure for ulcers. Because of reduced blood flow to microvascular beds, the trans-atlantic inter-society consensus document on the management of peripheral arterial disease II guidelines state that the amputation rate is higher in diabetic patients than in other patients. Furthermore, patients with diabetic feet have prolonged tissue healing time because of impaired host defense mechanisms against infections. These findings delineate the challenges that doctors face when managing diabetic foot complicated by arterial occlusive disease.<sup>7</sup> For tibial disease, interventional therapy is a critical part of the vascular specialists' armamentarium. The greatest advantage of interventional therapy for tibial disease is that it minimizes the morbidity and mortality typically associated with treating critical limb ischemia (CLI) utilizing open operative therapies. The primary goal in treating CLI is limb salvage and maintenance of quality of life, not patency, making endovascular treatment the ideal approach.<sup>8</sup>

### **Objective**

The object of this study was to analyze the clinical benefit in wound healing and limb preservation after infrapopliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of diabetic foot ulcers.

### **METHODS**

This study was conducted on 60 patients with critical lower limb ischemia in the form of diabetic foot ulcer and/or gangrene. The study period started from August 2017 until February 2019. Patients included in the study were essentially attending the Vascular Outpatient Clinic at Menoufia University Hospitals and Nasser Institute for Search and Treatment at Cairo and treated by infra-popliteal angioplasty.

### **Inclusion criteria**

Patient has tissue loss in the foot and/or the leg in the form of ischemic ulcer and/or gangrene, patient with isolated tibial disease in the form of stenosis and/or total

occlusion and Patients accepted to be included in the study.

### **Exclusion criteria**

Patient with critical lower limb ischemia in the form of rest pain only, patient with acute lower limb ischemia, patients with known history of vasculitis, patient with extensive foot infection, ulceration and/or gangrene beyond salvage, patient with associated supra-genicular arterial disease and patients with elevated serum creatinine levels "poor renal function".

Every patient was subjected to full history taking and full clinical examination. All of patients in our study were diabetic. On examination there is intact popliteal pulse, while posterior tibial and dorsalis pedis pulses were absent.

### **Imaging investigations**

#### *Arterial duplex and ankle/brachial index*

It is an integral part of initial evaluation of the patient with suspected PAOD. Systolic pressure of anterior tibial (AT) and posterior tibial (PT) arteries was measured. The higher of two ankle pressures was divided by highest brachial systolic pressure to yield the arterial duplex and ankle/brachial index (ABI). Repeated measurement of the ABI during serial follow-up was crucial in assessing disease stability, progression, or improvement.

#### *Conventional angiography*

Arteriography or conventional angiography (CT) angiography was done for some patients with critical lower limb ischemia for proper lesion analysis and for detection of stenotic or occluded arterial lesions and for determination of its: location, severity, extent, short or long, eccentric or concentric, and distal run-off.

Patients were categorized according to the successful intervention into three groups: successful intervention to target vessel only (group A); successful intervention to another tibial vessel other than the target vessel (group B); successful intervention to more than one tibial vessel including target vessel (control group).

#### **Follow up**

In all patients the postoperative outcome Follow up was done at 2, 4 and 6 months as regards:

*Clinical:* Ulcer size and appearance.

*Limb salvage rate:* ABI.

*Duplex scanning of dilated segment:* Duplex examination at 2 months, 4 months and at 6 months postoperatively to ensure patency of dilated vessels.

*Angiography*: Done only in case of need.

### Definitions

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.

Technical success is defined as improvement in luminal diameter of more than 50% or less than 30% residual stenosis without any flow limiting dissection.

Limb salvage refers to preservation of functional foot without requirement for prosthesis.

Poor run-off is defined as patients with occlusion of at least two crural arteries.

Restenosis is defined as a reduction in ABI of greater than 0.15 from maximum post-procedure ABI or a stenosis greater than 50% at angiography.

### Statistical methods

Data was recorded in a database sheet which was verified before data entry. SPSS program version 17 was used for data analysis. P value: to find significant relation between two or more percentages for qualitative data: Statistical significance if  $p < 0.05$ , Statistical high significance if  $p < 0.01$ , statistical not significant if  $p > 0.05$ .

### RESULTS

Result in the current study showed that most of direct group aged 40 to 55 years and most of indirect group aged more than 55 years; while, 50% of combined group aged 40-55 years. Also, most of the studied groups were males, all of them had diabetes mellitus followed hypertension. There were no statistically significant differences between the studied groups regarding age, gender and co-morbid factors (Table 1).

**Table 1: Demographic data of the studied groups.**

Demographic data		Direct group A (n=21)	Indirect group B (n=21)	Combined group C (n=18)	P value
		N (%)	N (%)	N (%)	
Age (years)	40-55	12 (57.14)	3 (14.28)	9 (50)	0.606
	>55	9 (42.86)	18 (85.72)	9 (50)	
Gender	Male	15 (71.43)	18 (85.72)	12 (66.67)	0.840
	Female	6 (28.57)	3 (14.28)	6 (33.33)	
Co-morbid factors	DM	21 (100)	21 (100)	18 (100)	1.000
	Smoking	18 (85.7)	15 (71.43)	12 (66.67)	0.559
	HTN	15 (71.43)	15 (71.43)	15 (83.33)	0.974
	Hyperlipidemia	15 (71.43)	15 (71.43)	10 (55.55)	1.00
	IHD	3 (14.28)	6 (28.57)	3 (16.66)	0.769

P>0.05- not significant; \*p<0.05- significant.

**Table 2: Two weeks follow up.**

After 2 weeks	Direct group A (n=21)	Indirect group B (n=21)	Combined group C (n=18)	P value
	N (%)	N (%)	N (%)	
<b>Started granulation tissue formation</b>	18 (85.71)	9 (42.86)	17 (94.44)	0.047
<b>Did not start</b>	3 (14.29)	12 (57.14)	1 (5.56)	

In the current study, after 2 weeks of follow up at the outpatient clinic to the different groups of patients, who underwent infra-popliteal angioplasty, we found that 18 patients in group A (85.71%), 9 patients in group B (42.86%) and one patient in group C (94.44%) started granulation tissue formation. While 3 patients in group A (14.29%), 12 patients in group B (57.14%) and one patient in group C (5.56%) did not start it with presence of more necrotic tissues in their wounds for further debridement (Table 2).

In the current study, after two months of follow up at the outpatient clinic to the different groups of patients, who underwent infra-popliteal angioplasty, we found that 18 patients in group A (14.29%), 9 patients in group B (42.86%) and one patient in group C (94.44%) showed progressive healing and decrease of wound size. 6 patients in group B (28.57%) started to form healthy granulation tissue after proper debridement. While 3 patients in group A (14.29%), 6 patients in group B (28.57%) and one patient in group C (5.56%) underwent

below knee amputation because of increase wound size and progressive gangrene beyond limb salvage, while, after four months of follow up at the outpatient clinic to the different groups of patients, who underwent infra-popliteal angioplasty, we found that 9 patients in group A (42.86%), 6 patients in group B (28.57%) and 15 patients in group C (83.33%) showed complete healing of their wounds. While 9 patients in group A (42.86%), 9 patients in group B (42.86%) and 2 patients in group C (11.11%) showed progressive healing and decrease of wound size.

2 patients in group B (9.5%) and 3 patients in group C (16.66%) showed decrease of ABI and restenosis and consequently re-intervention. After six months of follow up at the outpatient clinic to the different groups of patients, who underwent infra-popliteal angioplasty, we found that 18 patients in group A (85.71%), 9 patients in group B (42.85%) and 17 patients in group C (94.44%) showed complete healing of their wounds. While 6 patients in group B (28.57%) still healing progressively (Table 3).

**Table 3: Two, four and six months follow up.**

	Direct group A (n=21) N (%)	Indirect group B (n=21) N (%)	Combined group C (n=18) N (%)	P value
<b>After 2 months</b>				
Healing	18 (85.71)	9 (42.85)	17 (94.44)	0.8644
Started granulation tissue formation	-	6 (28.57)	-	0.182
BKA	3 (14.29)	6 (28.57)	1 (5.56)	0.297
<b>After 4 months</b>				
Healed	9 (42.85)	6 (28.57)	15 (83.33)	0.757
Healing	9 (42.85)	9 (42.85)	2 (11.11)	0.8139
Re-intervention	-	2 (9.5)	3 (16.66)	0.9847
<b>After 6 months</b>				
Complete Healed	18 (85.71)	9 (42.85)	17 (94.44)	0.8407
Healing progressively	-	6 (28.57)	-	

P>0.05- not significant; \*p<0.05- significant.

## DISCUSSION

CLTI is defined as ischemic rest pain, tissue loss, or gangrene in the presence of peripheral artery disease (PAD) and hypoperfusion of the lower extremity. CLTI is associated with increased mortality, morbidity rates and increased utilization of health care resources. The bypass option for CLTI patients is often compromised by inadequate length of autologous vein and/or significant medical comorbidities. Because of the recent advances in catheter-based technology, there is a great recommendation for angioplasty for CLTI patients especially with infra-popliteal arterial occlusive disease.<sup>7</sup> Direct reperfusion of the artery supplying the wound region depending on the concept of the angiosome is the recent principle. An angiosome is a 3-dimensional blocks of tissue fed by specific arterial and venous drainage. Angiosomes are connected by choke vessels that are able to supply indirect flow to the adjacent angiosome in absence of direct flow. The infra-popliteal main three arteries; the anterior tibial, posterior tibial, and the peroneal artery supply 6 angiosomes of the foot.<sup>6</sup> Our study is concerned with discussing the clinical benefit in wound healing after infra-popliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of ischemic diabetic foot ulcers. Most of patients in our study were above 50 years old. The age of patients in our study ranged from 45-80 years, with a mean age 63.85±11.1 years old. Soderstrom

et al reported in their series that the mean age the studied patients was 71.2±11.8 years old.<sup>9</sup> In the series of Fossaceca et al, the mean age of the patients was 75.5±9.5 years old.<sup>10</sup> Another study that was done by Acin et al who reported in their series that the mean age was 72 years ranging from 64-72 years. In our study of 60 patients, 45 of them (75%) were males being the majority of cases that may reflect that gender is an important determinant risk factor.<sup>11</sup> Soderstrom et al, in their series of 226 patients reported that 60% of the patients were males.<sup>9</sup> Another study was done by Fossaceca et al which revealed that from all of the patients included in the study 136 were males which represent (67.7%).<sup>10</sup> Acin et al, in their series reported that 61.4% of the patients included at the study were of male gender.<sup>11</sup>

The main risk factors in our study were diabetes mellitus in all patients (100%), smoking in 45 patients (75%), hypertension in 45 patients (75%), hyperlipidemia in 40 patients (66.66%) and ischemic heart disease (IHD) in 10 patients (22.22%). On the other hand, the distribution of risk factors in Soderstrom et al, study was as follow, diabetes mellitus (DM) (100%), smoking (21%), and hypertension (76%), and hyperlipidemia (65%).<sup>9</sup> The series of Acin et al showed that risk factors were distributed as follow; DM (100%), smoking (74.3%), hypertension (72.3%), hyperlipidemia (32.7%), cardiac disease (29.7%), and stroke (70%).<sup>11</sup>

In another study done by Fossaceca et al, the distribution of risk factors was as follow; DM (100%), hypertension (61.7%), IHD (32.3%), renal disease on dialysis (7.4%) and obesity (22.8%).<sup>10</sup> The series of Farag et al showed that risk factors were distributed as follow; DM ((65.2%), smoking (28.8%), hypertension (33.3%), hyperlipidemia (25.8%), cardiac disease (22.7%).<sup>12</sup> From the above mentioned distribution of risk factors in our study, diabetes mellitus, smoking and hyperlipidemia are main risk factors for CLTI but in other studies they were DM and hypertension. There was variable distribution of IHD and hypertension as risk factors.

From the 60 patients of our study who underwent infra-popliteal angioplasty we found that the lesion distribution was in AT artery angiosomes in 24 patients which represent (40%), PT artery angiosomes in 32 patients (53.35%) and peroneal artery angiosomes in 4 patients (6.65%). On the other hand, Soderstrom et al showed that infra-popliteal angioplasty in (56.8%) involved the ATA, (20.4%) the PTA and (22.8%) the peroneal artery.<sup>9</sup> In another study by Fossaceca et al, total of 298 stenobstructive lesions were treated; (41.2%) involved the ATA, (34.6%) the PTA and (24.2%) the peroneal artery.<sup>10</sup> Follow up of all patients was conducted at the vascular surgery outpatient clinic after 2 weeks, 2, 4 and 6 months as regarding formation of granulation tissue, healing of wounds and salvaged limbs. During the assessment of the patients of our study within 6 months of continuous follow up, we found that the healing rate of the patients who underwent direct revascularization (DR) (85.71%), indirect revascularization (ID) (42.85%) and combined revascularization (CR) was (94.44%) ( $p=0.8407$ ). Limb salvage rate between CR, DR, IR groups after six months of post-operative follow up was (94.44%), (85.71%) and (71.42%) respectively ( $p=0.9684$ ). It is interesting to note other studies with special concern only on diabetic ischemic ulcer. Soderstrom et al in their study of 226 diabetic patients with CLTI, reported lower complete wound healing rates (72%) in DR vs. (45%) in IR ( $p=0.001$ ) at 12 months.<sup>9</sup> Limb salvage rate between DR, IR groups was (85.9%), (76.7%) respectively. Fossaceca et al in their retrospective study that involved 298 limbs, showed a significant ulcer healing rates for DR that was (97.6%) versus IR that was (85.3%).<sup>10</sup> Limb salvage rate between DR, IR groups at the end of follow up was (90.4%), (91.1%) respectively.<sup>10</sup> In another retrospective study that was done by Acin et al and involved 101 limbs, it was found that the ulcer healing rates for DR was (65.2%) and IR was (41%).<sup>11</sup> Limb salvage rate between DR, IR groups at the end of follow up was (89.1%), (74.3%) respectively.<sup>11</sup> In another study that was done by Farag et al and involved 66 limbs, it was found that CR, DR, and IR has a significant ulcer healing rate at 12-month follow-up (94.7, 66.7, and 57.17%, respectively) with a significant amputation-free survival rate of 94.7, 75.6, and 72.7%, respectively.<sup>12</sup> The improved outcomes seen in some studies based on the use of the angiosome model compared with non angiosome targeted angioplasty could

be explained by the inadequate collateral vessels. When adequate collateral vessels were present, the outcomes of non angiosome procedures were comparable to those consistent with the angiosome concept.<sup>13</sup> 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 multiple angiosome reopening with better ulcer healing rate and limb salvage. With limitations and challenges of angiosome-based strategies, it was found that indirect revascularization should not be denied with acceptable result over time. As technical feasibility is an important limitation for the DR to be the first strategy, future studies should focus on description of angiosomes targeted for reperfusion, their boundaries and the state of choke vessels between inter-angiosomes to provide with the best alternatives to flow to the affected angiosomes.

## CONCLUSION

We concluded that if technically feasible, dilation of angiosome target artery in addition to any other significant tibial artery lesions in the treatment of diabetic feet has shown outstanding outcomes with respect to wound healing and limb salvage rate compared with nonangiosome-targeted angioplasty. With limitations and challenges of angiosome-based strategies, we believe, that IR should not be denied with acceptable results regarding limb salvage over time. Despite successful angioplasty, risks of delayed wound healing and major amputation remain because complex interactions between atherosclerotic vessel disease and microvascular dysfunction in diabetic feet make the outcomes of angioplasty unpredictable.

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## REFERENCES

1. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggese A, Bakker K, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. *Diabetologia.* 2007;50(1):18-25.
2. Misra S. Everflex Stent in SFA peripheral Artery Disease. *J Vas Interven Radiol.* 2012;23(10):1322-3.
3. Varu VN, Hogg ME, Kibbe MR. Critical limb ischemia. *J Vasc Surg.* 2010;51:230-41.
4. Graziani L, Silvestro A, Bertone V, Manara E, Andreini R, Sigala A, et al. Vascular involvement in

- diabetic subjects with ischemic foot ulcer: a new morphologic categorization of disease severity. *Eur J Vascular Endovascular Surg.* 2007;33(4):453-60.
5. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. *Plastic Reconstructive Surg.* 2006;117(7):261S-93S.
  6. Taylor GI, Palmer JH. The vascular territories (angiosomes) of the body: experimental study and clinical applications. *British J Plastic Surg.* 1987;40(2):113-41.
  7. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vascular Surg.* 2007;45(1):5-67.
  8. DeRubertis BG, Faries PL, McKinsey JF, Chaer RA, Pierce M, Karwowski J, et al. Shifting paradigms in the treatment of lower extremity vascular disease: a report of 1000 percutaneous interventions. *Ann Surg.* 2007;246(3):415.
  9. Soderstrom M, Alback A, Biancari F, Lappalainen K, Lepantalo M, Venermo M. Angiosome-targeted infrapopliteal endovascular revascularization for treatment of diabetic foot ulcers. *J Vasc Surg.* 2013;57(2):427-35.
  10. Fossaceca R, Guzzardi G, Cerini P, Cusaro C, Stecco A, Parziale G, et al. Endovascular treatment of diabetic foot in a selected population of patients with below-the-knee disease: is the angiosome model effective? *Cardiovascular Interventional Radiol.* 2013;36(3):637-44.
  11. Acin F, Varela C, Lopez 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.
  12. Farag M, El Alfy K, Roshdy H, Sharaf H. Angiosome-targeted isolated tibial angioplasty for healing of ischemic foot ulcer: a retrospective study. *Egyptian J Surg.* 2016;35(4):433.
  13. Bosanquet DC, Glasbey JC, Williams IM, Twine CP. Systematic review and meta-analysis of direct versus indirect angiosomal revascularization of infrapopliteal arteries. *Eur J Vasc Endovasc Surg.* 2014;48(1):88-97.

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