# Target Vessel Revascularization of Diabetic Foot According to Angiosomes

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## ABSTRACT

***Introduction:*** *Peripheral arterial disease (PAD) is a major world-wide health problem. It affects about 12%–14% of the population. The international consensus to define chronic limb threatening ischemia (CLTI) is that any patient with chronic ischemic rest pain, ulcers, or gangrene for more than two weeks with proven PAD.* ***Aim of the Work:*** *To assess the outcome of target vessel revascularization according to angiosome concept on the healing process of ischemic diabetic foot ulcers.* ***Patients and Methods:*** *This is a prospective study conducted at Ain Shams University Hospitals and Nasser institute Hospital in Cairo on 45 patients complaining CLTI in the form of ulcer &/or gangrene. The patients of successful angioplasty were classified into three groups. Group (**A**) direct revasularization, group (**B**) indirect revascularization and group (**C**) combined revascularization.* ***Results:*** *During the assessment of the patients of our study after 6 months of continuous follow up, we found that the healing rate of the patients who underwent direct revascularization (DR), indirect revascularization (ID) and combined revascularization (CR) were (91.67%), (75%) and (92.86%) respectively (p=0.769).* ***Conclusion:*** *Angioplasty of more than one tibial vessel including the target vessel has the best results and more preferable. Direct revascularization of the target artery depending on angiosome model leads to better wound healing rates than indirect revascularization.*

***Key words:*** *Tibial vessel revascularization, diabetic foot, angiosomes.*

## INTRODUCTION

Peripheral arterial disease (PAD) is a major world-wide health problem. It affects about 12%–14% of the population. There are several risk factors that contribute for the development and progress of PAD including Diabetes Mellitus, hypertension, hyperlipidemia and smoking **(1).** The international consensus to define chronic limb threatening ischemia (CLTI) is that any patient with chronic ischemic rest pain, ulcers, or gangrene for more than two weeks with proven PAD **(2).**

CLTI due to infra-popliteal arterial disease is associated with higher rate of limb loss due to minor and major amputations. This will lead to loss of mobility and social interaction, as well as higher mortality rates compared to patients whose limbs can be saved. Therefore, limb salvage by means of aggressive attempts of revasularizations either by vascular surgery or endovascular procedures are justified in CLTI patients **(3).**

The diagnosis of peripheral arterial occlusive disease (PAOD) is usually made clinically depending on medical history and ankle to brachial index (ABI) measurements. According to Fountaine classification, stage I PAOD is asymptomatic. Stage II patients have intermittent claudication. Rest pain and ulcerations are the clinical manifestations of stages III and IV, respectively **(4).**

In diabetics, PAD usually affects the infra-popliteal arteries **(5).** Foot ulcers are a common complication of diabetes. Ischemia, neuropathy, and infection are the causes that lead to diabetic foot complications and they frequently occur together. The basic factor preventing healing of a diabetic foot ulcer is often insufficient perfusion. **(6)**

Healing of foot ulcers is so important because complications of foot ulcers are the most important and leading cause of hospital staying and amputation among diabetic patients **(7).** Also, foot ulcers have important effects on quality of life **(8).** On the contrary, despite successful revascularization attempts, ulcer healing is a very slow process, especially in diabetics **(9).**

There are different modalities of treatment of chronic lower limb ischemia. Firstly, best medical

treatment (BMT) which includes regular exercise, smoking cessation, blood pressure control, good control of blood sugar, regulation of lipid level and pharmacologic medications that improve the peripheral blood flow [(2)].

Surgical re-vascularization is the other option for treating chronic lower limb ischemia patients. Usually the infra-popliteal arterial disease is not suitable for surgical bypass option which lead us to another option of revascularization. Angioplasty is an expanding era that can be achieved by dilatation of narrowed or occluded arterial segment with minimal invasive procedure [(2)].

Infra-popliteal angioplasty has acceptable rates of limb preservation in patients with CLTI who have a high risk for surgery. These procedures have low morbidity, mortality and lower costs compared with surgical revascularization. Therefore, aggressive angioplasty attemps should be an option when primary amputation would be the other available one [(10)].

The main problem is to find a way to provide a sufficient blood flow to the ischemic area of the foot. This may lead to either direct revascularization of the ischemic area or indirect reperfusion depending on collaterals surrounding the diseased region. The arterial connections between different zones of the foot may not be sufficient to provide healing and to prevent amputation of the limb [(11)].

All this debate made us think about other alternative strategy called the angiosome model. It is target vessel reperfusion, depending on the pioneering work of Taylor and coworkers who performed detailed dissections with injection of dye in the vessels. They identified that the foot and ankle consist of six angiosomes. An angiosome is a three-dimensional blocks of tissue which is perfused and drained by a specific artery and vein [(12)].

**Aim of the Work**

The aim of this work is to discuss the clinical benefit in wound healing and limb preservation after infra-popliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of diabetic foot ulcers.

## PATIENTS & METHODS

This is a prospective study that was conducted at Ain Shams University Hospitals and Nasser institute Hospital in Cairo on 45 patients from June 2017 till June 2018 complaining CLTI in the form of ulcer &/or gangrene of foot and ankle. Patients suitable for endovascular therapy were chosen according to certain criteria:

**Inclusion criteria:**

1. Patients who have tissue loss in the foot &/or the leg in the form of ischemic ulcer &/or gangrene.
2. Patients with isolated tibial disease in the form of stenosis &/or total occlusion.

**Exclusion criteria:**

1. Patients with CLTI in the form of rest pain only.
2. Patients with acute lower limb ischemia.
3. Patients with known history of vasculitis.
4. Patients with extensive foot infection, ulceration &/or gangrene beyond salvage.
5. Patients with associated supra-genicular arterial disease.
6. Patients with elevated serum creatinine levels "Poor renal function".

**All patients were subjected to the following:**

- Careful history taking with special consideration to the complaint of the patient, history of present illness, past medical history of the patient and previous surgical interventions.
- Careful clinical examination including general and local examination in the form of full pulse examination of the lower limb arterial system for all patients, recording ankle to brachial Index (ABI) and description of ulcer &/or gangrene if present.
- CT angiography for all patients according to the patients' condition and renal function (serum creatinine).
- Endovascular intervention for his tibial disease then the patients were categorized according to successful intervention into three groups:
  1. Successful intervention to target vessel only***. (group A)***
  2. Successful intervention to a tibial vessel other than the target vessel***. (group B)***
  3. Successful intervention to more than one tibial vessel including target vessel. ***(control group)***

Endovascular procedures were done under local anesthesia in all patients, but with proper sedation in irritable patients. We used antegrade femoral approach. Seldinger needle was inserted and slowly advanced until it reached the artery and when tip is inside the arterial lumen, an immediate jet of pulsatile blood escapes from the hub.

After successful arterial puncture, the guide wire was cautiously advanced to avoid dissection of the artery. The sheath was introduced over the guide wire. Diagnostic angiogram was done to select the area for intervention using non-ionic contrast material to evaluate the lesion and to be sure that it is within the criteria for intervention.

We manipulate the guide wire to pass the lesion as much as possible distal to the occlusion. This negotiation with the lesion was done by a 0.018 guide wire supported by 4 or 5 french guiding catheter. After crossing the lesion the balloon was introduced. We should assess proper balloon sizing as regard to length and diameter. The balloon catheter was advanced into position over the guide wire using fluoroscopy. The balloon was slowly inflated by diluted contrast solution under fluoroscopy, using an inflation device.

Inflation pressure ranging from 6-10 atmospheres was repeated once if there was persistent or residual stenosis after the initial inflation. Intra-arterial injection of heparin (5000 IU) as a bolus and heparinized saline is done (5000 IU on 500 cm saline) (10 cm after any of the previous steps). Intra-arterial injection of a vasodilator agents such as tridil was given in selected cases especially if spasm has occured. Completion angiography postoperatively was done for evaluation of angioplasty results.

Technical success is defined as improvement in luminal diameter of more than 50% or less than 30% residual stenosis. If significant residual stenosis was present despite full inflation of the angioplasty balloon; slightly higher pressure was cautiously attempted. Re-evaluation of the sizing of the angioplasty balloon selected was done to ensure that the selected balloon was optimum. After removal of the sheath immediately after the procedure Compression of the puncture site was done.

**Follow up:**

***All patients were followed up in regards to:***

1. Technical success in the form of restoring arterial flow immediately after the interventional arteriography.
2. Clinical success in the form of granulation tissue formation after amputation or debridement with decrease in the size of the wound till complete healing.
3. Follow up at 2, 4 and 6 months.

**Definitions:**

- Primary patency is defined as a patency not requiring additional procedure.
- Primary assisted patency is defined as angioplasties that needed an additional procedure after occlusion.
- Technical success is defined as restoring of blood flow angiographically.
- Clinical success is formation of granulation tissue after amputation and/or debridement with decrease in the size of the wound till complete healing.

**Ethical consideration:**

- The data were confidential.
- A written consent was obtained from all patients after explaining the procedure and its complications.

## RESULTS

Baseline characteristics of the patient of the total population are reported in table (1).

Baseline characteristics of the patient in the three groups are reports in table (2)

Based on angosiome model, the distribution of the lesions, is showed in table (3).

From the 45 patients of the study, we have 43 patients (93.33%) who underwent successful infra-popliteal angioplasty and they were classified into the three groups of the study.

Follow up of all patients was conducted at the vascular surgery outpatient clinic after one, 2 weeks, 2, 4 and 6 months regarding formation of granulation tissue with decrease in wound size, showed in table (4).

**Table (1):** Demographic data of the patients.

| | | No | % |
|---|---|---|---|
| **Gender** | **Male** | 29 | 64.44 |
| | **Female** | 16 | 35.56 |
| **Age (in years)** | **30-50 years** | 4 | 8.89 |
| | **> 50 years** | 41 | 91.11 |
| **Co-moribd factors** | **Diabetes** | **45** | 100 |
| | **Smoking** | **29** | 64.44 |
| | **Hypertension** | **27** | 60 |
| | **IHD** | **10** | 22.22 |

**Table (2):** Demographic data of the groups.

| | | **Group (A) (n=12) No (%)** | **Group (B) (n=16) No (%)** | **Group (C) (n=14) No (%)** | ***P* value** |
|---|---|---|---|---|---|
| **Age** | **30 – 50 ys** | 2 (16.66) | 1 (6.25) | 1 (7.14) | $x^2$=1.022 (p=0.606) |
| | **> 50 ys** | 10 (83.33) | 15 (93.75) | 13 (92.86) | |
| **Gender** | **Male** | 9 (75) | 11 (68.75) | 9 (64.3) | $x^2$=0.348 (p=0.840) |
| | **Female** | 3 (25) | 5 (31.25) | 5 (35.7) | |
| **Comorbid factors** | **DM** | 12 (100) | 16 (100) | 14 (100) | $x^2$=0.000 (p=1.000) |
| | **Smoking** | 9 (75) | 9 (56.25) | 11 (78.57) | $x^2$=1.163 (p=0.559) |
| | **HTN** | 8 (66.67) | 10 (62.5) | 9 (64.3) | $x^2$=0.052 (p=0.974) |
| | **IHD** | 2 (16.66) | 4 (25) | 4 (28.57) | $x^2$=0.525 (p=0.769) |

*p-value >0.05 NS*

**Table (3):** Angiosome based lesion.

| | **No** | **%** |
|---|---|---|
| **PTA** | 18 | 40 |
| **ATA** | 20 | 44.44 |
| **Peroneal** | 7 | 15.56 |

**Table (4):** Follow up of the groups of patients.

| | | **Group (A) (n=12) No (%)** | **Group (B) (n=16) No (%)** | **Group (C) (n=14) No (%)** | ***P* value** |
|---|---|---|---|---|---|
| **After 2 weeks** | Started granulation tissue formation | 11 (91.67) | 10 (62.5) | 13 (92.86) | *$x^2$=5.713 (p=0.047*)* |
| | Did not start | 1 (8.33) | 6 (37.5) | 1 (7.14) | |
| **After 2 months** | Wound size decrease > 50% | 9 (75) | 8 (50) | 12 (85.7) | *$x^2$=4.735 (p=0.094)* |
| | Wound size decrease < 50% | 2 (16.67) | 2 (12.5) | 1 (7.14) | *$x^2$=0.568 (p=0.753)* |
| | Started granulation tissue formation | 0 (0%) | 2 (12.5) | 0 (0%) | *$x^2$=3.412 (p=0.182)* |
| | BKA | 1 (8.33) | 4 (25) | 1 (7.14) | *$x^2$=2.431 (p=0.297)* |
| **After 4 months** | Complete healing | 9 (75) | 8 (50) | 12 (85.7) | *$x^2$=4.735 (p=0.094)* |
| | Wound size decrease > 50% | 2 (16.67) | 2 (12.5) | 1 (7.14) | *$x^2$=0.387 (p=0.824)* |
| | Wound size decrease < 50% | 0 (0%) | 2 (12.5) | 0 (0%) | *$x^2$=3.412 (p=0.182)* |
| **After 6 months** | Complete healing | 11 (91.67) | 12 (75) | 13 (92.86) | *$x^2$=2.431 (p=0.297)* |

*p-value >0.05 NS; *p-value <0.05 S*

## DISCUSSION

Our study is concerned with discussing the clinical benefit in wound healing and limb preservation after infra-popliteal endovascular revascularization guided by an angiosome model of perfusion in the healing process of ischemic diabetic foot ulcers.

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), indirect revascularization (ID) and combined revascularization (CR) was (91.67%), (75%) and (92.86%) respectively ***(p=0.297)***.

It is interesting to note other studies with special concern only on diabetic ischemic ulcer. A study by Alexandrescu *et al* on 208 ischemic foot ulcers treated with infra-popliteal angiosome based angioplasty revealed significantly better wound healing rates for direct and indirect revascularization were (73%) and (69%) respectively **[(13)].**

Our results on the DR analysis are consistent with other studies such as that of Neville *et al* who analyzed ischemic ulcer in 48 CLTI patients with a healing rate of 91% in DR versus 62% in IR. **[(14)].** Soderstrom *et al* in their study of 226 diabetic patients with CLTI, reported lower complete wound healing rates (72%) in DR versus (45%) in IR (p = 0.001) at 12 months **[(15)].**

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%) **[(16)].** In another retrospective study by Acin *et al* involved 101 limbs, showed that the ulcer healing rates for DR and IR were (65.2%) and (41%) respectively **[(17)].**

The better outcomes shown in studies depended on the angiosome model compared with non angiosome targeted angioplasty can be explained by the inadequate collateral circulation. When sufficient collateral circulation was present, the results of the non angiosome targeted procedures were comparable to those followed the angiosome model **[(18)].**

There are some challenges that face direct revascularization based on angiosome model in diabetic patients with infra-popliteal arterial disease that limit its effectiveness and lead to indirect revascularization. In addition to that, in spite of successful infra-popliteal angioplasty attempts, risks of delayed wound healing and major amputation remain **[(13)].**

Angiosome targeted reperfusion may be more relevant for endovascular procedures than for bypass surgery. During the intervention, it is better to attempt DR then IR according to technical feasibility and state of foot vascularity**[(19)].**

As technical feasibility is an important challange 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 angiosomes to provide with the best options to flow to the affected angiosome **[(20)].**

## CONCLUSION

We can conclude from this study that, angioplasty of more than one tibial vessel including the target vessel is more preferable and must be considered if technically feasible. Direct revascularization of the target artery leads to better wound healing rates than indirect revascularization, so the former is more preferable than the later. We can't deny the role of indirect revascularization in wound healing process especially with the limitations and challenges that face direct revascularization.

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**Conflicts of interest**
There are no conflicts of interest.

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