## ORIGINAL ARTICLE

# Angiosome-targeted revascularisation in diabetic foot ulcers

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#### Key words

Angiosome; Deep veins; Diabetic foot ulcers; Revascularisation

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## Abstract

Peripheral vascular disease is a common complication of type 2 diabetes and is often more severe and diffuse than in non-diabetic individuals with a higher risk of major amputations in the lower limbs. Diabetic foot revascularisation using both traditional bypass surgery and endovascular therapy are often burdened by the failure and the inevitable subsequent massive amputation. In this study, we examined the clinical response of diabetic patients with critical limb ischaemia and extended ischaemic wounds, treated with a new angiosome-based revascularisation technique. In a 3-year period, nine diabetic patients with imminent amputation threatening and foot ulcers with no feasible arterial revascularisation options were treated by the angiosomebased surgical technique by means of deep vein arterialisation. The postoperative tcPO2 evaluation showed a mean increase in the cutaneous oxygen tension in all patients treated. The overall survival rates were 88.88%, 88.88% and 77.77% at 12, 24 and 36 months, respectively. Limb salvage was 100% at 1 year and steady at 88.88% thereafter. Surgical deep venous arterialisation might be considered as an extreme alternative to attempt tissue preservation in limbs unfit for conventional arterial revascularisations. This technique would give advantages to the patients in terms of better compliance to the minor amputations and thus avoiding major limb amputations.

## Introduction

Diabetes is the most common metabolic disease in industrialised countries and is combined with the rising prevalence of peripheral arterial disease and cardiovascular risk factors (1-3) and it is the leading cause of non-traumatic lower extremity amputation. Consequently, International Guidelines have drawn attention to the need for prevention and treatment of the diabetic foot, particularly to the correct and effective management of the most critical complications of diabetes, such as infection, neuropathy (chronic severe pain) and ulceration (3,4). Pathophysiological events that characterise diabetes and the consequent involvement of the distal regions of the lower limbs are advanced atherosclerosis (5-7) and progressive calcinosis (8-10) of the tunica media and they are responsible for peripheral artery disease (PAD) (11,12). The prevalence of PAD in women and men with diabetes is equal; it rises with age in both men and women (13). The current age-adjusted prevalence is estimated at approximately 12%, affecting men and women equally (14). Approximately 10-20% of patients with PAD identified in epidemiological

## **Key Messages**

- diabetes mellitus 2 is the most common metabolic disease in industrialised countries and is often combined with the rising prevalence of peripheral arterial disease determining high risk of foot ulceration
- diabetic foot revascularisation, using both traditional bypass surgery and endovascular therapy, is often burdened by the failure and the inevitable subsequent major amputation of the limb that affects not only the quality of life, but also represents an important factor related to mortality rate in diabetic patients
- the angiosome model of revascularisation may help the surgeon to better refine vessel selection and specific strategies in the revascularisation of lower limbs with tissue lesions, especially in diabetic patients
- angiosome-targeted surgical technique on diabetic patients gives good results in terms of major amputation-free survival rate compared to traditional revascularisation procedure

studies are symptomatic (mean age 65), and among them classic intermittent claudication was present in only 11%. The prevalence of symptomatic PAD is highest in elderly patients, estimated at 26% in patients with mean age of 81 years among those living in a nursing home. Critical limb ischaemia (CLI), the most advanced form of PAD and usually secondary to severe multilevel PAD, is associated with a high rate of amputation and death. The diagnosis is established when patients present with pain at rest, ulceration or gangrene of the leg associated with evidence of reduced arterial blood flow to the foot (15,16). Diabetic foot revascularisation, using both traditional bypass surgery and endovascular therapy (EVT), is often burdened with failure and the inevitable subsequent massive amputation, which greatly reduces the possibility of retaining the patient's gait.

In this study, we examined the clinical response of CLI diabetic patients with extended ischaemic wounds treated with a new angiosome-based revascularisation technique. It is based on the principle of arterialisation of double deep veins of the foot and surgical ligation of the collaterals.

## **Materials and methods**

In a 3-year period (January 2010–December 2012), nine diabetic patients with imminent amputation threatening and foot ulcers, having no feasible arterial revascularisation options were treated by the angiosome-based surgical technique by means of deep vein arterialisation. Prior approval was obtained from the Institutional Review Board at the University of Catanzaro, in accordance with the Declaration of Helsinki and the Guideline for Good Clinical Practice. The casuistry belonged to the Department of Medical and Surgical Science of University 'Magna Graecia' of Catanzaro and Unit of Vascular and Endovascular Surgery, Regional Hospital of Cosenza. Before the beginning of the study, written informed consent was obtained from all the patients.

Nine patients (5 men and 4 women) with mean age of 72 years (range: 55–86 years) were enrolled in this study. All patients had type 2 diabetes mellitus with PAD. Patient characteristics and risk factors are summarised in Table 1. Severity and extent of foot ulcers were graded using the 1 to 4 Wagner Classification.

The main inclusion criteria (Table 2) expressed the presence of distal foot ulcerations and tissue necrosis (Rutherford categories 5-6) (17) and were assigned to all the treated limbs. Severe ischaemic wounds strictly confined to the foot (Wagner grades 3-4) (18) were noted in six limbs, whereas three others were associated with complex foot and below-the-knee trophic lesions. Following the TASC II stratification (15) of the main infrainguinal lesions, four were of Type B, two Type C and three Type D lesions. Extensive calf vessel calcifications (>5 cm) were present in seven cases. Other inclusion criteria gathered were critical levels of trans-cutaneous oxymetry (tcPO2 < 30 mmHg). On admission, each arterial pulsation was evaluated and the extent of tissue loss was recorded as part of the preoperative vascular assessment. The ankle-brachial index (ABI) and the tcPO2 were used to assess the haemodynamic status of the lower limb, and the tcPO2 was routinely measured at the dorsum and plantar side of the

| Males  | 5 (55.55%)     |
|--|----------------|
| Females                                      | 4 (44.44%)     |
| Mean age                                     | 77-years old   |
|  | (range: 55–86) |
| Coronary artery disease (CAD)                | 6 (66.66%)     |
| Diabetes mellitus                            | 9 (100%)       |
| Peripheral artery disease (PAD)              | 9 (100%)       |
| Hyperlipidemia                               | 7 (77.77%)     |
| Hypertension                                 | 7 (77.77%)     |
| Cerebro vascular disease (CVD)               | 4 (44.44%)     |
| Chronic obstructive pulmonary disease (COPD) | 4 (44.44%)     |
| Osteomyelitis                                | 2 (22.22%)     |
| Chronic renal insufficiency                  | 5 (55.55%)     |
|  |                |

Table 2 Inclusion and exclusion criteria

| Inclusion criteria   |
|--|
| Wagner grade 3 foot lesions<br>Wagner grade 4 foot lesions                         |
| Wagner grades 3 and 4 foot lesions added to calf or ankle trophic defects          |
| Rutherford categories 5–7  |
| TASC II Classification Type B–C–D<br>Calf vessel calcifications<br>tcPO2 < 30 mmHg |
| Exclusion criteria   |
| Wagner grade 5 foot lesions<br>Left ventricular ejection fraction (LVEF) <30%      |

foot. Lower limb arteries were routinely evaluated before the procedure by duplex ultrasound imaging and digital subtraction angiography (DSA). The exclusion criteria were extended and irrecoverable foot gangrene (Wagner grade 5 lesions) (18), severe cardiac insufficiency [left ventricular ejection fraction (LVEF) <30%, appraised by systematic cardiologic evaluation] and eventual disagreement expressed by the patient.

All patients were assessed at 1 week and at 1, 3 and 6 months after the surgical procedure, and those who presented with open ulcers were also followed up by a plastic surgeon. The status of the ulcer and the time until complete healing were recorded. The tcPO2 was measured before and after the procedure.

During our surgical angiosome-based procedures, three transmetatarsal amputations (TMA) and six toe amputations (two major toe amputations and four second/third toe amputations) were carried out.

### **Surgical procedure**

Patient disagreement

The common femoral artery was often the chosen in-flow vessel. Distal anastomosis were realised on one of the paired deep veins (anterior tibial and forefoot, posterior tibial and plantar/heel, peroneal and lateral ankle) in a termino-lateral (n = 7) or termino-terminal (n = 2) manner. In all the cases, 8 mm PTFE armed prostheses were placed. Devalvulation of

the deep veins was performed. Main collaterals of the veins were cut through surgical ligation.

In the postoperative period, patients were assessed by clinical examination, tcPO2 measurements and duplex scan evaluations before discharge and at one month later, and by clinical and duplex assessment every 6 months, thereafter. Mean follow-up was 21.5 months (range: 1-62 months).

## Results

The postoperative tcPO2 evaluation showed a mean increase in the cutaneous oxygen tension with 20 mmHg (12-32 mmHg) in the early postprocedural period in six limbs (66.67%), unchanged values in two patients (22.22%) and decline of the initial level in one case (11.11%). The more relevant increases in tcPO2 were detected in the angiosomes dependent on the posterior tibial versus anterior tibial or peroneal irrigation. Our new surgical angiosome model for deep vein arterialisation was intended in the following orientations: four limbs with trophic lesions of the anterior leg and ankle, the forefoot, toes and dorsum of the foot were treated by preferential anterior tibial deep vein arterialisations (anterior tibial- and dorsalis pedis-dependent angiosomes), four other cases underwent revascularisations via the posterior tibial veins for ulcers in the medial calcaneal, plantar, hallux, medial malleolar and Achillean localisations (angiosomes relying the posterior tibial and plantar vascular bundles), while in the remnant one case, targeted arterialisations of the peroneal deep veins were focused with reference to wounds located in the lateral calcaneal and lateral malleolar territory. It should be noted that for all the successfully treated limbs in this series, either minor amputations (phalanges or forefoot) or intentional mummification of the affected toes were requested. The 30-day perioperative mortality rate was 0%. The survival rates were 100% (all patients), 88.88% (eight patients) and 77.77% (seven patients) at 12, 24 and 36 months, respectively. Limb salvage, applying the same approach, was 100% (nine limbs) at 1 year and steady at 88.88% (eight limbs) thereafter.

## Discussion

In diabetic patients, arterial occlusive disease primarily affects the crural arteries. In most developed countries, the incidence of severe limb ischaemia, which is the presence of tissue loss (ulceration, gangrene) and pain at rest or at night, is estimated to be 50-100 per 100 000 every year and leads to pronounced morbidity and mortality as well as to the consumption of many health care and social-care resources. Ageing populations, the increasing prevalence of diabetes and its lower limb-related complications and the failure thus far to substantially reduce tobacco consumption mean that despite advances in medical therapies the number of patients needing lower limb revascularisation for severe limb ischaemia will probably increase in the foreseeable future. The indications, such as incapacitating claudication, pain at rest and tissue loss that includes gangrene and non-healing ulcers or amputation sites, for diabetic revascularisation are no different as compared to the non-diabetic patient population. The severity of arterial ischaemia should

be confirmed in diabetic patients by physical examination and non-invasive vascular laboratory testing. Physiologic testing is especially important in diabetic patients because superficial ulcerations can heal in the presence of mild ischaemia if infection is eradicated and pressure is off loaded. Revascularisation in CLI is ultimately aimed at preventing limb loss, including major amputation (MA), improving patient quality of life and prolonging survival. MA increases the mortality rate in CLI patients, and although a multidisciplinary approach is recommended by the TransAtlantic InterSociety Consensus (TASC) II guidelines to avoid MA in CLI patients, no pharmacologic therapy ensures limb salvage without revascularisation (15,19). Therefore, revascularisation is the optimal treatment for CLI patients, and bypass therapy remains the standard revascularisation modality because it achieves sufficient arterial perfusion to the foot with associated appropriate high limb-salvage rate and long-term durability (15). However, traditional revascularisation techniques unfortunately fail in large numbers, exposing critical diabetic patients to the risk of MA.

The ultimate goal when caring for a patient with a diseased or injured lower extremity is to salvage the maximum amount of function through revascularisation and minimum amputation. Angiosome-based revascularisation (20) is the optimal treatment for CLI patients. The angiosome concept (21,22) divides the foot into three-dimensional anatomic units of tissue supplied by specific source arteries. Five distinct angiosomes can be identified originating from the three main crural arteries: anterior tibial artery (ATA) and peroneal artery (PA) supply both one angiosome, whereas posterior tibial artery (ATP) supplies three angiosomes. The ATA supplies the dorsal side of the foot and toes, the PA covers the lateral ankle and lateral heel, and the ATP perfuses the plantar surface of the foot and medial heel and ankle. Adjacent angiosomes are connected to each other by a system of collateral arteries, assuring circulation to an angiosome if its source artery is occluded (22). A regular blood flow in previously compromised regions of diabetic foot allows optimisation of foot biomechanics such that subsequent breakdown does not occur (23).

This study showed that the application of our angiosometargeted surgical technique on diabetic patients with foot ulcers, who are likely to undergo major amputation, gives very good results (>90% major amputation-free survival) compared to traditional revascularisation procedures (24–26). Surgical deep venous arterialisation might be considered as an extreme alternative to attempt tissue preservation in limbs unfit for conventional arterial revascularisations. This technique would give advantages to the patients in terms of better compliance to the minor amputation treatments (TMA; 27–31) or toe/ray amputations (23).

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