Review Article

The Role of the Angiosome Model in Percutaneous Intravascular and Surgical Reperfusion Treatment of Peripheral Artery Disease of the Lower Limbs

Athanassios G. Antonopoulos[1,2], Matthaios Thomopoulos[1], Athanasios Trikas[1]

[1]Cardiology Department, "Elpis" General Hospital, Athens, Greece; [2]Dipartimento Cardio Medico Chirurgico, Toraco Vascolare, Hesperia Hospital, Modena, Italy

Key words: **Direct and indirect reperfusion, anatomy of the pedal arteries, diabetic vascular disease, ankle brachial index.**

Manuscript received: June 23, 2013; *Accepted:* August 30, 2013.

Address: Athanassios G. Antonopoulos

59 Alexandras Ave. 114 74 Athens, Greece e-mail: *athadon@gmail.com*

The increase in average age has led to an increase in the population of patients who suffer from ischemic vascular disease of the lower limbs (lower limb arterial disease, LLAD), a major cause of amputation in the developed countries of the world.[1] Reperfusion provides an opportunity to save the limb through a bypass procedure, with artificial or venous grafts, or a percutaneous intravascular intervention.

During revascularization procedures of the lower limbs the usual approach, as recommended by the current guidelines, is reperfusion of the best vessel that passes beyond the level of the base of the foot. In this way, indirect restoration of blood flow will be obtained to the foot, mostly via the development of collateral circulation (best target vessel theory, or indirect reperfusion).[1] Nevertheless, the arterial anastomoses developed between different regions of the limb may not guarantee limb salvage after revascularization, or the avoidance of amputation.[2]

The aforementioned strategy does not appear to fully satisfy the anatomical needs of an ischemic foot in these patients. Recently, a different reperfusion strategy has been described, which takes into account a division of the body into three-dimensional vascular territories supplied by specific source arteries. This concept is called the "angiosome model".[3] Thus, for example, targeted reperfusion of the artery that is distributed at the boundaries of a trophic lesion will result in optimum treatment (direct reperfusion). The inflow and outflow of blood between angiosomes may also pass through bridging vessels, or through newly developed collateral vessels—which, however, are less effective than direct blood supply to the angiosome.[4] From a practical point of view, the application of the angiosome treatment concept to LLAD (below-the-knee) disease, relates to a concept used in cardiology, in which a discrimination of areas with reversible ischemia is made, and the respective vessels leading to these areas are treated in a distinctive way.

This strategy is particularly important in plastic or corrective procedures,[5] but it has not attracted much attention in the past for the treatment of LLAD.

The aim of this review is to present and discuss the role of the angiosome model in the treatment strategy of ischemic LLAD.

Peripheral vascular disease

Peripheral vascular disease has a variety of clinical manifestations and is categorized according to the classification of Fontaine or Rutherford (Table 1). The most typical clinical picture is one of intermittent claudication (stage Fontaine II, Rutherford I). The presence of ulcer or gangrene (stage Fontaine IV, Rutherford III) is an indication of critical ischemia. Arterial ulcers are painful, but the absence of pain may be due to peripheral neuropathy, especially in diabetic patients.

The cornerstone of treatment in these patients is, of course, an attempt to obtain a good flow in the affected vessel region. This should be implemented as soon as possible, as long as there are no contraindications.[6] During the last decade, intravascular interventional procedures, with or without the use of stents, have gained ground as a first choice strategy, because of their fewer complications, higher success rates, and good long-term results.[7] This approach was also supported by the results of a multicenter, randomized study that compared surgical bypass with intravascular angioplasty (BASIL trial).[8] Thus, in patients with severe lower limb ischemia due to stenosis of the infra-popliteal arteries (which both vascular surgeons and interventionists judge to be a gray zone as regards the best means of reperfusion), both the former and the latter approach have equivalent results in terms of amputation-free survival, although the cost of surgical treatment is clearly greater. Nonetheless, when it comes to choosing a reperfusion method, it should be tailored to each case individually, taking account of anatomical peculiarities, the extent of the disease, any comorbidities, expected survival, as well as the patient's own preference. More specifically, as was shown by the BASIL trial,[8] in patients with expected survival greater than two years surgical treatment should be preferred as first-line choice, whereas in patients with shorter expected survival treatment with angioplasty is likely to be better. The rationale is that the latter patients will not be able to benefit from the better long-term results of surgical treatment, are more likely to experience morbidity or possible mortality associated with the surgical procedure itself, while in the short term angioplasty is less costly than surgery.

We can therefore understand that the anatomical approach to the treatment of peripheral vascular disease, based on the distribution of perfusion of supplying vessels (the angiosome model), may be an important tool in the treatment of both chronic critical and acute ischemia of the lower limbs.

Description of the angiosome model

Anatomy of the arteries of the foot (Figure 1)

Blood is supplied to the foot via three main arteries, the anterior tibial, the posterior tibial, and the peroneal artery. These branch into six final arteries, each of which perfuses an angiosome:

1. **The anterior tibial artery** supplies the anterior portion of the base of the foot (ankle) and continues as the *dorsalis pedis* artery. It branches into the lateral tarsal artery and the arcuate artery.[9]

   The **posterior tibial artery** divides into three branches:
2. The *calcaneal branch*, which supplies the interior and plantar surfaces of the heel.
3. The *internal plantar artery*, which is distributed over the inner-outer region of the sole and the big toe.
4. The *external plantar artery,* which supplies the distal part of the external sole.

   Together, the two plantar arteries form the dorsal and plantar arch, via which the remaining four toes are perfused.

Table 1. Classification of peripheral vascular disease by Fontaine and Rutherford.

Fontaine		Rutherford		
Stage	Clinical picture	Degree	Class	Clinical picture
I	Asymptomatic	0	0	Asymptomatic
IIa	Mild intermittent claudication	I	1	Mild intermittent claudication
IIb	Moderate to severe intermittent claudication		2	Moderate intermittent claudication
			3	Severe intermittent claudication
III	Ischemic pain at rest	II	4	Ischemic pain at rest
IV	Ulceration or gangrene	III	5	Mild tissue loss
			6	Severe tissue loss

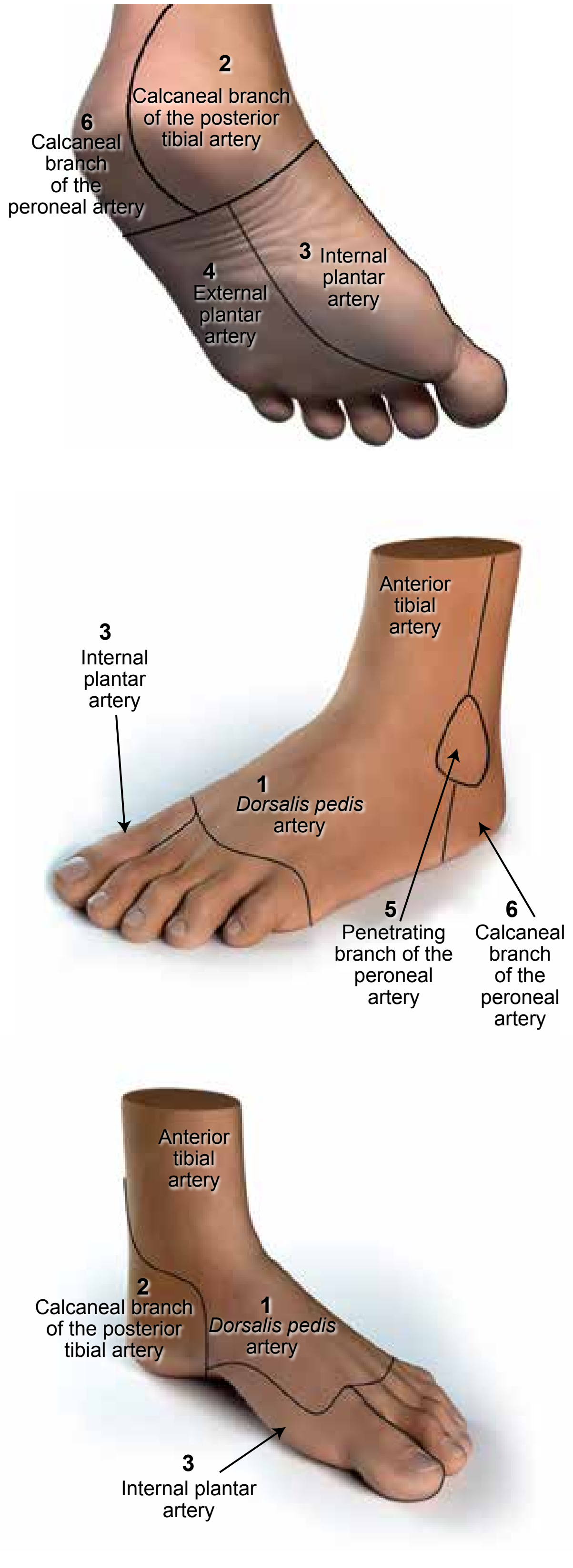

Figure 1. Distribution of the angiosomes of the foot and the arteries that supply them.

The **peroneal artery** branches into:

5. An *anterior penetrating branch*, which supplies the upper-lateral ankle.
6. A *calcaneal branch*, which distributes to the external and plantar surfaces of the heel.

Angiosome connections with bridging and collateral vessels (choke vessels)

The angiosomes of the foot are interconnected by anastomotic arteries, which exist *a priori* but with the progression of LLAD may come to be occluded.[10] These include:

- A connection between the anterior tibial and peroneal arteries, via the external malleolar artery.
- A connection between the anterior tibial and the posterior tibial arteries, via the plantar arterial arch. The internal plantar artery is connected with the anterior tibial via cutaneous branches.
- A connection between the peroneal and the posterior tibial arteries, via branches from the internal and external calcaneal arteries within the Achilles tendon.
- There are no connections between the internal and external calcaneal arteries.

If there are no connections between the angiosomes, or under conditions of ischemia, a small-diameter vascular net (*choke vessels*) is created that allows interconnections.[3] The vessels in question, however, allow satisfactory blood supply only to non-atheromatous and non-diabetic limbs.[10]

Intravascular intervention based on the angiosome model

Definitions

Procedural success is defined as reperfusion with direct blood flow from the aorta to the sole (i.e. to the site of the lesion), and residual stenosis less than or equal to 20%. Clinical success is defined as an increase in the ankle-brachial index greater than 0.10, or rapid healing of the trophic lesions in the affected limb. Salvage of the limb is defined as complete functional autonomy of the patient (walking), without major amputation.[6]

Clinical experience – contemporary applications of the angiosome model

There are already a large number of applications of the angiosome model to treatment in several medical fields, such as myocardial reperfusion,[12] elective embolization of the splanchnic artery,[13] and plastic or corrective procedures.[14] Only during the last decade has this approach been introduced to lower limb salvage treatment; however, a few studies have compared it with intravascular techniques or surgical arterial bypass, with encouraging results as regards the main endpoint, namely the healing of the ulcer.

Healing of the ulcer: This is the most frequent endpoint in most studies concerning reperfusion of the lower limbs. In 2006, Attinger et al,[10] in an initial study of 52 infra-popliteal revascularization procedures, found that patients who were treated with an intravascular strategy based on the angiosome model showed failure to heal the ulcer in only 9% of cases, compared with 38% of those who underwent indirect (surgical) reperfusion. The probability of amputation varied around the same levels.[10] In a study of 203 patients with ischemic ulcerations under intravascular treatment, Iida et al[15] observed salvage of the limb in 86% of cases in the angiosome strategy group, compared with 69% for indirect treatment. More recently, the same investigators[16] studied 369 patients with Rutherford stage III LLAD (50% with end-stage renal disease), of whom 200 were treated with direct and 169 with indirect reperfusion. The results of the study indicated that amputation-free survival was clearly superior in the group that underwent direct reperfusion (49% versus 29%, respectively), even after four years' follow up.

The preventive significance of the presence of collateral circulation was studied by Valera et al in 2010,[17] in a mixed group of patients with ischemic ulcers who were treated either with venous grafts or using intravascular techniques. When collateral circulation was present (as determined by Doppler ultrasound), similar healing rates were observed for indirect and direct reperfusion (92% versus 88%, respectively, over 12-month follow up). In the absence of collateral circulation during indirect reperfusion, only 73% of the ulcerations had healed after 12 months, while the healing rate for direct reperfusion did not change.

In contrast, in a retrospective Japanese study of 228 patients, of whom 81% were diabetics, no difference was observed in the healing of ulcers after direct or indirect reperfusion.[18] Two other studies, one by Deguchi et al,[19] involving vascular surgery, and one by Blanes et al,[20] using an intravascular approach, demonstrated no difference in healing and limb salvage between the two techniques. However, as these studies included only a small number of patients they had limited statistical power.

On the other hand, it is well known that the diabetic leg represents a large target group for the application of these reperfusion techniques. Accordingly, Alexandrescu et al[21] focused specifically on direct reperfusion by angioplasty of lesions in the diabetic leg, and found a better rate of healing and limb salvage using the angiosome model. Thus, in a group of 124 patients who underwent direct reperfusion, limb salvage was achieved in 91% at one and 84% at three years. In addition, a multivariate analysis found that elevated levels of C-reactive protein were an independent prognostic factor for major amputation in the indirect, but not the direct (angiosome model) perfusion group.[15] The investigators hypothesized that indirect reperfusion was ineffective for the treatment of ulcerations with inflammation.

Clinical implications and future prospects

Peripheral vascular disease, and in particular critical limb ischemia, is on the increase as our average lifespans become longer. In response to this disease, which affects the patient's quality of life and autonomy, advances in intravascular reperfusion, with new techniques and new materials, are coming to replace the classical surgical bypass interventions, given their equivalent results, lower cost,[8] and shorter hospitalization time.[22]

The concept of direct angiosome reperfusion is quite attractive and is consistent with our pathophysiological knowledge. Healing of possible trophic lesions of the foot may be achieved by restoring arterial flow at the level of the ankle, and it is logical that the result will be better when the flow reaches the lesion site. As demonstrated by the above studies, direct reperfusion is especially useful in the context of end-stage renal failure,[16] ulcerations with inflammation, and in the absence of collateral circulation.[17] It is particularly important to detect the presence or absence of collateral circulation.

Even though the positive evidence for the use of the angiosome model is increasing rapidly, there are several limitations. All the studies that compared direct and indirect reperfusion were retrospective and suffered from heterogeneity in patient selection (given the varying clinical manifestations of the disease).

The boundaries of the angiosomes vary, and patients usually need to undergo diagnostic arteriography in order to determine the anatomical arterial distribution in each region.[23] However, at least so far, the use of stents in very distal lesions of the leg, especially the ankle region, is extremely difficult with the materials that are available on the market, especially taking into account the diameter of the vessels in question and the high restenosis rate. In addition, not all lesions can be treated based on the angiosome model, because of technical limitations (such as anatomical anomalies, difficult access to the vessel, or retrograde access via collateral circulation) or severe stenosis of the vessel. Thus, the indirect technique is also used should direct reperfusion fail. There is also the possibility of hybrid treatment of multifocal LLAD, with satisfactory results, as was described in a recent study.[24]

Overall, there are only a few studies that recommend targeted reperfusion of the artery supplying the angiosome where the trophic lesions are located.[25] Nevertheless, there is a clear need for further investigation of the angiosome model through randomized studies of large numbers of patients, including groups with greater homogeneity in their distribution, so as to determine the possible advantages or disadvantages of this strategy for reperfusion of significant ischemia of the affected limb.

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