CHAPTER

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Angiosome concept for vascular interventions

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Introduction

General considerations of the angiosome concept

After the initial work of Taylor and Palmer published in 1987, the angiosome concept (AC) in the field of plastic and reconstructive surgery was increasingly developed.[1] In these previous studies, the anatomy of the structures responsible for blood supply to the different regions of the human body, from the skin to the deeper layers, was assessed.[1,2] Results showed the reproducible patterns of arterial and venous allotments with distinct topographic orientation in the human body.[1,2]

Studies published in the last decade in vascular pathology revealed the potential benefit of the AC in the management of chronic limb-threatening ischemia (CLTI) and in topographic inferior limb revascularization.[3–5]

The AC appears increasingly cited in the current treatment of CLTI and limb salvage. However, its current utilization by bypass or transcatheter techniques only began in recent years.[6–8] Angiosome-guided direct revascularization has been increasingly utilized with particular soar in the field of endovascular interventional techniques.[3,5–8]

However, there are still some unanswered questions about the current technical feasibility of this strategy in the actual management of CLTI, definitions for direct (DR) versus indirect revascularization (IR), and indications for the use of bypass versus endovascular techniques (EVTs) in specific high-risk groups of patients.[3–5]

In this chapter, we performed a succinct review of the main benefits of angiosome-guided direct revascularization and the unanswered questions focusing on this continually evolving concept in the current vascular practice guidelines.

Angiosome concept: anatomical and pathophysiological data

In the initial work of Taylor et al., 44 angiosomes and appended source arteries (SA) in the human body were described. Of them, 6 maintain the normal vascularization in the lower leg and foot.[1] Adjacent angiosomes are linked by a vast collateral web containing numerous small-to-large collaterals,[1,2,9] arterial–arterial communicants, and thousands of millimetric choke vessels (CV)[1,2,9] with important compensatory roles.[1,6,7] In cases in which the main angiosomal arteries are interrupted or occluded, this rescue system redirects the blood flow via available collaterals toward the neighboring angiosomes.[1,2,6,7,9] The diameter and topography of the compensatory collaterals vary based on anatomic location, patient's age, and type of CLTI aggression.[6,10–14]

Anatomy of the distal leg angiosomes

Based on the initial description of Taylor, SAs have related collaterals and CVs present with their own specific and reproducible regional distribution to tissues.[1,9,10]

Angiosomal SA and their collateral system

The angiosomal topographic partition was initially pictured as a continuous three-dimensional (3D) network that is harmoniously dispensed to tissue,[1,2,9] and that holds several levels of dichotomy[13] toward specific parts of the skin and deep tissue region.[1,10] Each

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angiosome has correspondent « arteriosomes » and « venosomes »,[1,2] which share harmonious patterns of vascular architecture.[1,2] This flow arrangement indicates a fractal distribution of flow to specific limb regions.[6,13]

Angiosomes were initially described as distinct *anatomical* entities, named from the Greek term *angeion* (meaning vessel) and *somite*, or *soma* (indicating the section of the body).[10] However, their *clinical* significance conveys concomitant functional features that are dependent on each angiosome's *perimeter of anastomotic vessels*.[10,15]

Primary *SA* of the distal leg and foot

Based on the characteristics of the six-foot angiosomes,[1] the SA and underlying tissue territories are depicted as follows (Fig. 33.1):

The posterior tibial artery provides flow to its *medial calcaneal* branch and appended angiosome, adjoining the *medial* and *lateral plantar* arteries and subsequent angiosomes, the plantar heel territory, and the entire medial and lateral plantar regions of the foot and toes.

The anterior tibial artery transitions into the *dorsalis pedis* artery below the ankle level and supplies its appended dorsalis pedis angiosome that covers the dorsum of the foot down to the dorsal toe territories.

The peroneal artery provides flow to its *lateral calcaneal* artery and angiosome to a more restricted zone in the posterolateral heel and to its *anterior perforating branch*. Moreover, it irrigates the lateral and anterior upper ankle and appended angiosome.[1,2,9]

From a practical perspective, the anterior tibial artery nourishes the anterior ankle and the dorsal aspect of the foot and toes. Meanwhile, the posterior tibial artery provides flow to the medial, posteromedial ankle, and heel territories and equally to the entire sole and the plantar side of the toes. The peroneal artery irrigates the anterolateral upper ankle zone and the lateral and plantar heel regions.[1,9,15]

Collateral network surrounding the foot angiosomes

Before reaching the capillary system, the interangiosomal collaterals can be differentiated in *large-* (approximately 1 mm in diameter), *medium-* (<1 mm), and *small*-sized caliber (<0.5 mm).[13,15,16] Taylor et al. additionally described the *cutaneous perforator* branches that provide flow to each 3D tissue block, specifically supplying the skin.[15] These *cutaneous arteries* (CAs) emerge directly from the main SA and provide direct flow to the skin.[15] Other indirect or spent terminal ramifications were referred to as *cutaneous perforators* (CPs),[10,15] and they are derived from the deep tissue layers in continuity with the artery that is the initial source of perfusion.[10,15] CVs, CAs, and CPs include tiny vessels (approximately 0.5 mm in diameter) that often can be detected on routine

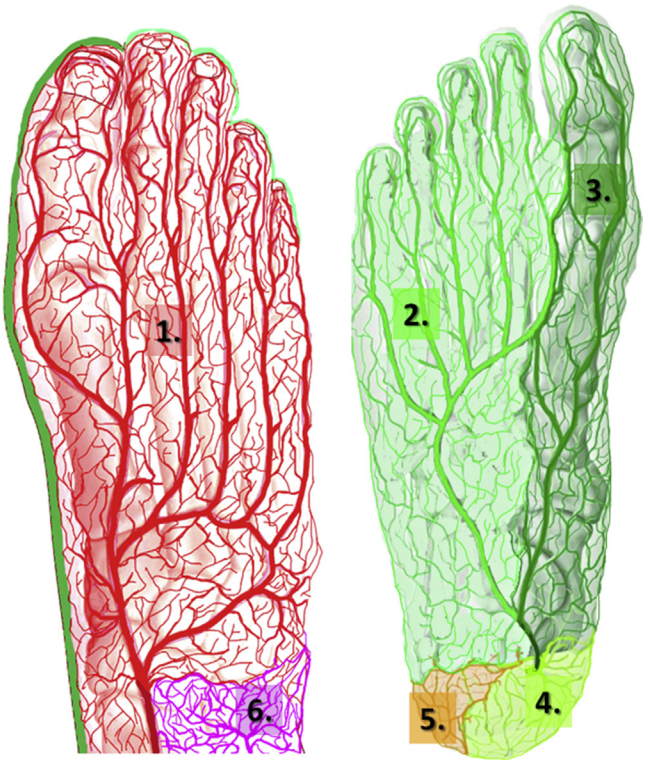

FIGURE 33.1 Schematic dorsal (left side), and plantar (right side) distribution of the foot angiosomes: 1. Dorsalis Pedis angiosome (Anterior Tibial territory), 2. Lateral Plantar angiosome (Posterior Tibial territory), 3. Medial Plantar angiosome (Posterior Tibial territory), 4. Medial calcaneal angiosome (Posterior Tibial territory), 5. Lateral calcaneal angiosome (Peroneal territory), 6. Anterior perforator branch angiosome (Peroneal territory).

angiography.[12,13,16] However, the visual accuracy is limited for vascular structures <500 μm.[17]

Specific CLTI pathologies such as diabetes mellitus or renal insufficiency inflict foot collateral destruction (from CAs and CPs, down to the small CVs and capillaries) and enhance a notable risk for tissue loss and major amputation.[6,18–21]

Main connections between the foot angiosomes

Apart from the accepted anatomical variations (9%),[22–24] specific groups of collaterals, which provide prompt flow compensation, were identified at the foot level.[1,9,13] Numerous *large* collaterals retain a specific weight in supplying neighboring foot angiosomes in CLTI.[6,9,12,13] Moreover, they play a pivotal role in topographic *wound-targeted* revascularization.[5–7] These vital branches comprise the *foot arches*,[6,16,25] forefoot *metatarsal perforators*,[6,9,16] and anterior or posterior arcuate artery *interconnections*.[6,9,16] Other sizable *arterial–arterial* branches, such as the dorsal foot-to-plantar, or the peroneal perforators to the posterior, or the anterior tibial arteries were evoked, such as "*rescue*" midfoot, or heel collaterals.[6,9,13]

From a topographic perspective, the communicants between the posterior tibial and peroneal artery via their lateral and medial calcaneal branches, along with the posterior peroneal branch, play a major compensatory role in providing blood supply in *ischemic heel ulcers*. If available, these collaterals yield equal valuable flow shifts when intentional hindfoot or heel DR is performed.[3–7]

The interconnections relying on the dorsalis pedis (the anterior tibial artery flow) to the plantar arteries (the posterior tibial artery circulation) comprise the medial or lateral tarsal branches, metatarsal perforators, or paired metatarsal anterior and posterior interdigital collaterals.[9,15,16] They also significantly contribute in maintaining viable forefoot and toe perfusion during ischemic threat.[9,15,16]

Lastly, the lateral and medial communicants in both plantar arteries (the posterior tibial circulation) link the lateral and medial tarsal arteries (the anterior tibial flow). Moreover, they provide support between the dorsal and plantar foot perfusion in patients exempted from wide CLTI collateral extinction.[9,10,15,16]

Foot angiosomes as fractal levels of perfusion in the inferior limb

All individuals possess a specific inherited collateral reserve that compensates blood flow between bordering angiosomes. This remarkable self-regulating vascular web continuously undergoes dynamic adaptations to various endogenous and exogenous stimuli.

In a larger picture, the entire inferior limb vasculature can be described as balanced and reproducible patterns of peripheral tissue irrigation.[11,16] In this harmonious scaffolding, each arterial trunk gradually divides into inferior levels of segmentation to generate a wider cross-sectional area of flow toward the peripheral tissues.[16] Each staged dichotomy constantly creates branches smaller than its parent trunk.[10,16] For every arterial bifurcation, the assembled sectional area of the derived branches is greater than that of the primary vessel.[1,10,16]

From the iliac inflow down to the myriad of distal foot ramifications, a remarkable sequential distribution of blood supply was observed.[13,16] These characteristic levels of dichotomic flow dispensation (Table 33.1) can be stratified as per rank of tissue perfusion and can be summarized as follows:[13,16]

Level I gathers the primary inferior limb arterial bundles of irrigation (i.e., iliac and common femoral vessels). *Level II* assembles the following branches in the thigh and calf (i.e., the superficial and profunda femoris and the tibial arteries), and *Level III* joins specific ramifications for precise cutaneous and deep tissue territories in the leg and foot.[13] This third level holds a peculiar interest in CLTI revascularization. It contains the angiosomal SA, large (1 mm) collaterals, foot arches, and correspondent metatarsal communicants.[13] It also provides specific clinical applications for angiosome-targeted or wound-directed revascularization (WDR).[6,13,16] The next level, *level IV*, assembles the *medium* and *small* collaterals ($\leq$0.5 mm in diameter), including the CAs, CPs, and CVs.[13,16] The subsequent division ranks further assemble the microcirculatory network containing *level V* (the arterioles) and *level VI* (the capillary system) that hold countless micrometer–diameter vessels.[13,16]

Main arterial anatomical variants of the lower leg

Specific lower limb arterial variants, most of which concerning *Level III* of flow segmentation, were

TABLE 33.1 The inferior limb specific levels for dichotomic blood irrigation.

Inferior limb levels of perfusion	Type of inferior limb arteries	Arterial segmentation
Level I.	The original arterial and venous bundles of the inferior limb	The iliac and common femoral vessels
Level II.	The first rank of arterial division: Main branches in the thigh and calf	The superficial and profunda femoris, The three tibial trunks
Level III.	The second rank of arterial division: specific tissue sectors large branches	The pedal and angiosomal branches, The foot arches, The large collaterals (around 1 mm).
Level IV.	The third rank of arterial division: Smaller interconnections between different inferior limb regions	The medium-sized collaterals (0.5–1 mm), The small collaterals (<0.5 mm), The "choke-vessels", The skin and muscular perforators.
Level V.	The microcirculatory arteriolar ramifications	The arterioles
Level VI.	The capillary tier	The capillaries

identified.[13,16] Native variations of the leg arteries were observed in approximatively 7.9%–10% in individuals in the general population.[22,23] Among these atypical presentations, hypoplastic or aplastic posterior tibial arteries were described in 3.3% cases, whereas the anterior tibial artery anomalies were reported in 1.5% of subjects.[23] The high (popliteal) emergence of the anterior tibial artery (5.6%)[23] associated or not with abnormal dorsalis pedis paths was observed in about 6% of individuals.[23,24] The presence of one popliteal artery variation on the targeted leg for revascularization may predict about 21% of other possible ipsilateral vascular abnormalities and up to 48% of eventual contralateral arterial variants.[22–24] The precise identification of these variations may help interventionists establish a diligent flow reconstruction in planning WDR.[6,12,16,22]

Pathophysiological data of angiosomal flow

The basic pathophysiological mechanisms of limb ischemia may be associated to *acute* (brisk presentations) or *chronic* (slow unfolding) tissue ischemia.[11,26] These two clinical entities are dependent on three major factors: *time* of ischemic threat, number and size of available *compensatory collaterals*, and individual *cardiac output*.[25,26]

The amount of collateral network is not uniformly allocated in the whole angiosomes of the human body.[9,15] For example, compared with forefoot, thigh, myocardial, or pulmonary angiosomes, the hindfoot and heel angiosomes have fewer compensatory native collaterals, CVs, and CPs.[9,13,16] In hemodynamic terms, about 16 collaterals with a diameter of 0.25 cm may match the flow of 625 collaterals with a diameter of 0.1 cm to provide peripheral resistance as low as that of an unobstructed artery with a diameter of 0.5 cm.[25] A few large collaterals played a more efficient role in flow compensation than hundreds of small collaterals, arterioles, and capillaries.[25]

Two major processes trigger collateral development during ischemic threat. These processes include *angiogenesis* (sprouting capillary development enhanced by hypoxia and macrophages) and *arteriogenesis* (remodeling and enlargement of preexisting collaterals enhanced by the vessel's shear stress and by reactionary inflammatory cells).[11,26] Arteriogenesis is essentially stimulated by pulsatile pressure flow in the collateral bed, and it can determine an increase in the diameter and length of the appended arterioles.[11,25,27,28] Moreover, it is influenced by the release of specific endothelial factors and by the local migration of macrophages.[26,29–31]

In the treatment of CLTI, compared to angioplasty, bypass facilitates a higher volume of blood flow in the peripheral collateral system and pulsatile pressure flow.[32] This phenomenon may be extremely beneficial for surgical treatment, regardless of whether revascularization has an angiosome-oriented topography.[13,32]

Angiogenesis and arteriogenesis processes can be significantly inhibited by the CLTI condition itself[29] and by associated pathologies, such as metabolic syndrome[30,31] and renal insufficiency.[31–34] Normal inferior limb perfusion does not express enlarged collaterals, unless a reactional response to ischemic conditions is requested.[26]

In addition to the well-known devastating features of acute ischemia–reperfusion syndrome after acute hypoxic tissue damage,[26,35] countless intermediate functional patterns of chronic tissue reperfusion were observed.[26,34]

In accordance with previous studies on plastic reconstructive surgery,[9,15] interventional cardiology,[36] vascular surgery,[25] and neurosurgery,[37] several phases of flow redistribution were noted before and after the retrieval of chronic ischemic conditions.[11,25,26] These functional stages are based on specific time intervals, and they expand according to the intensity and duration of CLTI aggression.[11,25–28]

Flow compensation during preischemic conditions

An impressive flow compensation system was recognized in ischemic conditions according to adjacent angiosomes and appended collaterals and CVs.[9,10,15]

Since flow pressure in specific SA significantly decreases, the CVs between adjacent angiosomes progressively open and convey maximal compensatory capacity. In CLTI circumstances, advancing alteration in SAs and parallel collateral decay lead to the gradual activation of the remaining branches and CVs.[13,19–21]

Postischemic reperfusion stages

CLTI injury inhibits large BTK arterial trunks and various amounts of collaterals.[12,13,25] When hypoxic burden is relieved after revascularization, a cascade of pathophysiological changes is enhanced, and it can be schematized as the reperfusion stages (subject to changes upon each individual lasting collateral network), which are as follows:[11,27–29]

The initiatory flow redistribution stage involves large and medium collaterals around the ischemic angiosome. This starting phase operates via the lasting permeable branches (of all sizes), scattered around the ischemic zone, and allows rapid rescue flow toward low-resistances territories.[11,30] This stage lasts for hours. Flow mainly follows the surviving channels with low resistances and native angiosome partition.[34]

The *average* flow dispensation phase, which is the next stage, can be further observed over the medium-

to-small collaterals (including the CVs, CPs, and arterioles).[34,38–40] Some of these connections are open and visible on perioperative angiographic examinations. Meanwhile, others express higher flow resistances and only progressively become functional during these two periods (the « dormant collaterals »).[34,39,40]

Both initial phases can persist for several days and may be juxtaposed to the delay phenomenon, as described in previous publications about skin flap surgery.[9,15,41] Both starting flow redistribution phases are conditioned by changing flow resistances; thus, they may have a minimal topographic correlation with standardized anatomical angiosome orientation.[34,39,40]

The *retarded* postischemic phase, which is the third step, can last for several weeks.

It is essentially characterized by consolidation of flow, via available collaterals and arterial–arterial interconnections, which are reorganized throughout the whole process of arteriogenesis and angiogenesis.[11,26,38,40] Flow still dwells partially characteristic to the basic marks of anatomic angiosomes (which vary based on the amount of preserved collaterals). The true connections between neighboring angiosomes now have a new physiological entity, which is referred to as *the functional angiosome*.[42]

Functional angiosome

In 2017, 30 years after the first anatomical angiosomal description, Taylor et al.[1,42] completed their pioneering work by defining the *physiological*, or the functional angiosome (FA).[42] This novel hemodynamic entity completed previous anatomical studies[15] and identified the volume of tissue that can be clinically isolated on a specific source vessel.[42] Moreover, it represents the area of perfusion that one particular SA can afford throughout the true collaterals beyond its anatomical territory.[15,42] This functional area stretches upon a wider clinical region of the foot by capturing adjacent angiosome territories, owing to *efficient* connections via CVs or, more likely, via true anastomoses.[42]

True connections assist the broader FA to operate and remodel CVs throughout the angiogenesis and arteriogenesis processes,[27] starting with *the second phase* of flow reperfusion.

Collateral flow reserve and microvascular resistances between angiosomes

CLTI encompasses a multilevel arterial disease associated with variable collateral loss that invariably increases distal limb flow resistances.[30,38,39] Remote foot collateral resistances steadily and proportionally increase to the degree of lumen narrowing, systemic changes in heart rate, and collateral destruction rate.[25,27–30]

These significant hemodynamic interactions between flow and hindered collateral network are not new. A previous research by Macci et al. has reported these discrepancies in 1996 using the Windsor perfusion index,[43] which was recently updated by parallel studies conducted by Mangi et al.[44] or Ikeoda et al.[45] These studies focus on peripheral vascular flow reserve (VFR) and peripheral fractional flow resistances (PFFRs).[44,45] These latest indicators have been assessed recently also in CLTI. However, in the current literature, data on these indicators are still limited. Clinical correlations between PFFR and routine noninvasive examinations including the ankle–brachial index (ABI) and duplex imaging were already established.[44] PFFRs and VFR are also correlated with microvascular $TcPO_2$ or Laser Doppler skin perfusion pressure (SPP).[45] Both methods can equally merge to describe a derived collateral index for specific tissue perfusion (initially evoked in interventional cardiology).[46]

These studies provide a better understanding of regional collateral reserve in ischemic foot syndrome and adding parallel useful associations with evoked phases of reperfusion.

Clinical implementation of the angiosome model in the current treatment of CLTI

Defining angiosome-directed revascularization

Each CLTI presentation is unique due to its specific anatomical patterns, countless collateral pathophysiological changes, and distinct individual risk factors for tissue healing.[6,29–31] The implementation of the true AC in current vascular practice undoubtedly implies detailed macro- and microvascular individual evaluation (Fig. 33.2).

Although initial CLTI studies defined DR mainly as intentional reperfusion in SA,[3–6] surgical and endovascular studies in recent years broadened the purpose of DR by including other Level III and IV arterial ramifications. The foot arches, large- and medium-sized collaterals, and CVs completed DR purposes in topographically oriented foot reperfusion.[6–9,12,47] However, in contemporary literature, there is no clear consensus regarding the definition of DR versus IR or WDR.[48–55]

Some authors have observed improvement in clinical results via direct angiosome SA revascularization.[3–9] Meanwhile, others have described similar results using available collateral-enhanced reperfusion (with or without wound orientation), which is referred to as *indirect* revascularization.[9,47] More refined clinical data have shown improvement in healing and limb preservation in

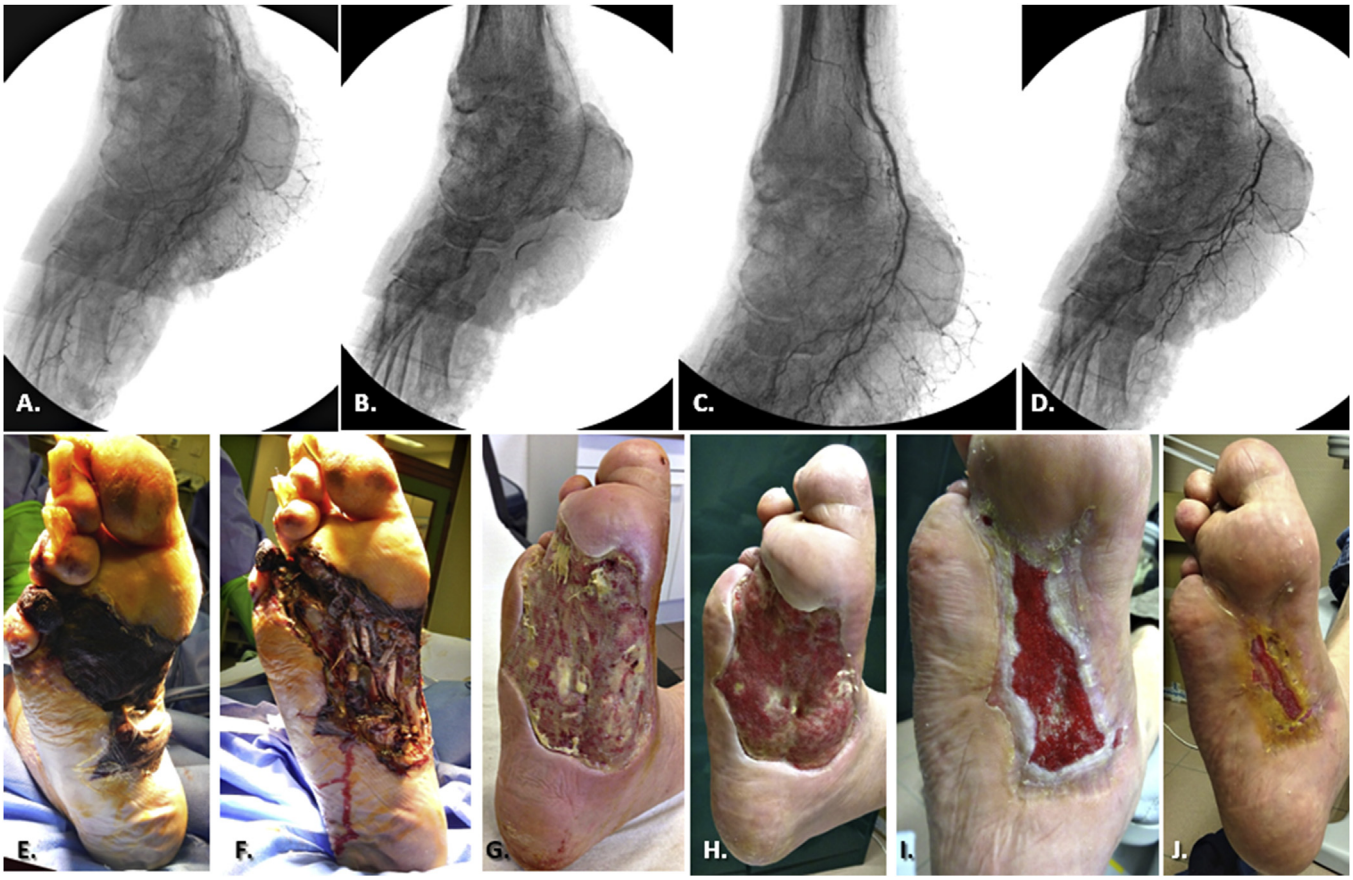

FIGURE 33.2 Clinical application of the angiosme strategy in CLTI and diabetic neuro-ischemic foot treatment: (A and E) initial angiographic and clinical presentation of a Rutherford 5, CLTI - GLASS stage 3, Wagner 4, diabetic neuro-ischemic foot wound, (B) Intraoperative aspect of related endovascular approach. According to the ulcer's location, a targeted recanalization of the posterior tibial artery adding the angiosomal lateral and medial plantar branches was planned. A 0.014 in. guidewire (Terumo Japan) was placed at the posterior tibial artery bifurcation and the initial part of the plantar arteries, as to allow subsequent angioplasties in these specific plantar regions. (C) Angiographic result after intentional angioplasty at the posterior tibial and plantar arteries junction, (D) The procedure completion angiography, demonstrating a correct flow throughout the plantar arteries and their appended angiosomes (including the wound's sole territory). (F) Intraprocedural aspect of tissue debridement for extended plantar ulcer and deep tissue necrosis, performed during the same initial interventional stage. (G–J) Sequential clinical aspects of wound healing and plantar tissue regeneration after targeted "direct plantar revascularization." Wound cicatrization features at 8, 14, 21, and 26 weeks postoperatively, owning regular multidisciplinary team follow-up.

individuals with CLTI on DR angioplasty,[3,5–8] DR bypasses,[4,9] or both.[47,56] However, parallel studies did not show statistical differences between DR and IR in terms of clinical success and limb preservation rates.[57–60] Analogous revascularization series highlight the key role played by permeable pedal arteries,[12,32,50] foot arches,[6,9,32,50–52] or available large foot collaterals[6,9,12,13,32,47] in tissue healing regardless if the angiosome location is targeted.[61] The accuracy in using limb salvage as an indicator for DR/IR clinical success remains controversial.[19,31,48,53] The limb salvage refers to a heterogeneous group of limb-threatening factors and issues, in addition to vascular DR/IR anatomic and hemodynamic effects.[19,31,32,53]

Špillerová et al.[62] showed that the clinical results and the prognosis of DR versus IR primarily depend on the protocol for the type of revascularization in each study.[62] Due to the limited prospective data in the literature,[6,56] several recent metaanalyses have provided a better understanding of these current concepts.[8,63,64]

Biancari et al.[63] conducted a systematic review of 1290 limbs. Results showed that since DR is feasible, it was found to enhance better wound recovery and had a higher limb salvage rates than IR for both EVT and bypass techniques.[63] In two analogous analyses of 1868 and 779 cases, Bosanquet et al.[8] and Huang et al.[65] revealed that DR can improve tissue healing and limb salvage compared with IR.[8,65] However, in all studies, compared to IR, DR was not considered superior in terms of survival and reintervention rates in these patients. Based on the same type of analysis, Jongsma et al.[66] found that the angiosome model may be less

applicable for bypass surgery due to distal leg anastomosis that is generally performed on the less affected pedal artery.[32,66] Thus, limb preservation in CLTI may be less affected by DR or IR for bypass compared with EVTs.[66,67] These results were in accordance with those of Dilaver et al.[64] and with other analogous studies in this field.[32,67]

Stimson et al. conducted another remarkable updated metaanalysis.[68] Results showed that the AC may be useful for both EVT and bypass in CLTI revascularization. In particular, endovascular DR (Fig. 33.1) is considered superior to IR.[68] Alternatively, open surgery appears less dependent on anatomical angiosome partition since adequate foot arches and large collaterals are still patent. Similar publications showed that lasting foot collaterals may not follow the classical angiosome sectorization in the diabetic foot syndrome.[6,8,19,68]

The importance of uniform standardization of DR/IR in surgical and endovascular practice is again emphasized.[53,64,66–70]

Technical feasibility of intentional direct revascularization

Most angiosome-targeted arteries (SA) for revascularization are described to harbor severe atherosclerotic and calcific occlusive lesions,[6,16,40] equivalent to GLASS stage III degree of anatomical severity.[32] Endovascular DR is often associated with long chronic total occlusions (CTO) and dense calcifications recanalizations.[6,40,49] Alternatively, comparable challenges in bypass DR in terms of selecting permeable runoff branches in extensively diseased pedal SA were described.[4,16,47,49]

Based on modern interventional standards, the feasibility of endovascular DR can vary from 61% to 88% in different studies.[3,5–8,12,49] The technical success of EVT may be also correlated with the number of treated angiosomes.[49] In a recent study, the technical feasibility rate in one specific angiosome revascularization was 69%.[49] However, DR could be performed in 86% of cases with two targeted foot angiosomes, in 85% for three, and only in 25% of limbs requiring four angiosome EVT reperfusion.[49]

The feasibility of bypass or endovascular DR indicates that the diligent use of all available foot collaterals, arterial–arterial communicants, and, eventually, permeable foot arches remains essential.[6,12,51,53,62–66]

Chronic limb-threatening ischemia and chronic angiosome-threatening ischemia: two competitive or rather complementary notions

In 1982, the term of critical limb ischemia (CLI) was first introduced,[54] and it referred to a heterogeneous population with ischemic inferior limb presentations, including diabetic and renal patients.[32,55,71]

Recent publications show that at the collateral and arteriolar levels[13] (levels III–V), not all foot territories may have shear equivalent ischemic burden.[19,30,31,40] The predominant infragenicular and inframalleolar forms of CLTI were particularly observed in diabetic and renal patients.[30,39] These distal limb anatomical patterns of CLTI are not new,[72] and difficulties in achieving an accurate clinical[73] and hemodynamic diagnosis[40,71] were already described.[40,71–73] These specific CLTI patterns are commonly associated with extensive tibio-pedal CTOs (Fig. 33.2) and calcifications and often indicate severe concomitant neuropathic autonomic denervation in diabetic patients.[31,74,75]

In these particular cases, sole macrocirculatory assessment based on ABI,[76] TBI,[77] Computed Tomography angiography, or Magnetic Resonance angiography[19,40] can be only partially helpful, combined to digital subtraction angiography.[17,19,71,76] Meticulous microcirculatory assessment[40,71] can add complementary information about the precise dispensation of the ischemic load throughout each region of the CLTI foot.[40,53,71] Particularly in diabetic patients, the concomitant location of dominant neuropathic and true neuroischemic ulcers may not always be easy to ascertain in each region of the threatened limb.[18,40,53,73]

In these patients, a more precise microvascular CLTI diagnostic as topographic angiosome-threatening ischemia assignment may be useful in current practice.[40,53] As pointed in recent publications, this simultaneous microcirculatory evaluation could associate methods like Indocyanine green dye-based fluorescent angiography imaging,[34,40] to parallel microcirculatory exams[18,32] that more specifically explore Levels III-V angiosomal and intraangiosomal ramifications. Levels III–V although represent the anatomical ground of derived "chronic angiosomal threatening ischemia" (CATI) notion.[34,40,53] Among focused diagnostic methods, $TcPO_2$, transcutaneous laser Doppler (SPP), hyperspectral imaging, or PET/SPECT scan nuclear imaging can all afford useful information in microcirculatory assessment of specific ischemic foot regions.[40]

The CATI concept showing that a more detailed quantification of the ischemic burden in each foot region influences CLTI perception is not new.[34,40,68–71]

A more refined CATI assessment that includes the features of each diabetic foot's *end-artery occlusive disease*,[31] every disrupted *arterio-* and *angiogenesis* processes,[19,30,31,39] in addition to standard CLI[54] or CLTI[32] characteristics (Fig. 33.2), proved to be particularly useful in diabetic patients.[19,34,53,69–71]

Current investigation and perspectives for angiosome-targeted revascularization in the treatment of CLTI

Similar to new strategies of multidisciplinary interest, the AC should be validated in larger prospective and multicentric clinical studies for current vascular applications.

However, unlike other new medical theories, the accuracy of angiosome-guided revascularization is dependent on the rigorous control of *several risk factors* among participants associated with clinical failure. These factors include individual anatomic and hemodynamic SA condition,[32,53] local wound characteristics,[32,40] specific anatomical[15,16] and pathophysiological features of the local collaterals,[34,42] and individual patient's specificities, that embodies all CLTI presentations.

Since there is no current consensus about foot collateral evaluation and utilization, the best diagnostic method for assessing CATI and CLTI features[34,53] was not yet standardized. Although balanced comparison between DR/IR owing multidisciplinary team approaches is observed in only 20% of contemporary studies,[53,64] a centralized perception of the angiosome strategy based on unitary recommendations in daily practice is still expected nowadays.

Finally, equivalent research criteria for tissue recovery, time for healing, and complete rehabilitation[34,53] indicators, all with undeniable clinical utility, should be more clearly categorized by future publications.[34,53]

The recent Global Vascular Guidelines document and recommendations[32] states that angiosome-guided revascularization may be of real importance "in the setting of endovascular intervention for midfoot and hindfoot lesions but is likely to be irrelevant for ischemic rest pain and of marginal value for most forefoot lesions and minor ulcers."[32] However, the precise role of topographic foot bypass,[64,67,68,78] or multivessel (tibial) revascularization, remains equally unknown in current CLTI practice.[32,68–70]

It appears reasonable that for selected high-risk patients with specific high-risk tissue regions (i.e., WIfI stages 3 and 4)[32] to benefit from first endovascular DR,[32] if this technique can be safely performed (concerning GLASS stages I–II), without compromising runoff to the foot for eventual bypass target.[32,79]

Summary

Despite lack of pertinent data in current CLTI treatment, angiosome-guided revascularization appears preferable for inducing better wound cicatrization and limb salvage, whenever technically achievable. Higher levels of evidence for the use of direct revascularization in the daily management of CLTI based on standardized definitions, anatomic and functional diagnostics, and uniform indications for each type of treatment are required. Larger multicentric and prospective studies are therefore expected before routine application of this strategy in current clinical practice. Since direct revascularization proves difficult to achieve, alternative indirect reperfusion via available foot collaterals is recommended.

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