Personalized Approach to Revascularization of Critical Limb Ischemia

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Critical limb ischemia (CLI) is a complex disease process that often occurs alongside numerous comorbidities, and as such requires a personalized, multidisciplinary treatment approach in every patient. Patient outcomes are generally poor and there remains a lack of consensus on the optimal revascularization strategy in individuals with CLI. In recent years, the angiosome (or direct) revascularization concept has gained wider acceptance because it guides reperfusion to the artery supplying the vascular territory containing the ischemic lesion on the foot (Figure). However, it stands in contrast to the one straight-line inflow (or indirect) approach classically advocated, in which the largest vessel available for revascularization is targeted regardless of the vascular territory it supplies. Comparisons between both strategies have emerged, with few studies demonstrating equivalent outcomes and many others demonstrating improved wound healing and reduced amputation rates with the angiosome approach.

The current study by Kawarada et al in this issue of *Circulation: Cardiovascular Interventions* is important, as it is one of the first analyses to address the impact of the angiosome concept on microcirculation in patients with CLI. However, there are a few limitations of the current study that should be considered and discussed. The authors concluded that both direct and indirect single tibial artery revascularization of either the anterior tibial artery or posterior tibial artery (PTA) led to comparable changes in skin perfusion pressure (SPP) on both the dorsal and plantar sides of the foot. Although the study design was strong, its sample size was small, which raises concerns about its validity. First, of the 40 patients that had anterior tibial artery revascularization, 8 patients (20%) also had peroneal artery recanalization, which could provide collateral circulation to the PTA territory. Thus, these patients by definition are not true single tibial artery revascularizations, and this could have confounded SPP measurement.

Although such perfusion assessment is important, clinical outcomes such as amputation and limb salvage trump any surrogate end point, and thus should carry more weight. A recent meta-analysis of 15 cohort studies found that angiosome-directed revascularization improved wound healing rates compared with indirect revascularization (odds ratio, 0.40; 95% confidence interval, 0.29–0.54), and also improved limb salvage rates at 1 year (odds ratio, 0.24; 95% confidence interval, 0.13–0.45). Similarly, a second meta-analysis of 9 studies in which the vast majority of patients were diabetic found that angiosome-directed revascularization was associated with a lower risk of unhealed wound (hazard ratio, 0.64; 95% confidence interval, 0.52–0.80), and a lower risk of major amputation at 1 year (hazard ratio, 0.44; 95% confidence interval, 0.26–0.75). The results of the current study, therefore, should be viewed in the context of these studies. Nevertheless, despite the current evidence, there are no randomized clinical trials comparing the angiosome-directed and indirect revascularization strategies. Hence, although the angiosome concept makes intuitive sense, enthusiasm of 1 approach over another should be tempered until more definitive trials are conducted.

The current focus in the vascular field is on major adverse limb events and amputation-free survival. Indeed, most published studies on CLI outcomes have used major adverse limb events, amputation-free survival, or repeat revascularization as their primary end point(s), yet few have evaluated metrics...
of wound healing, or more importantly, time to wound healing. This is possibly because these outcomes are more difficult to measure and standardize. However, a focus on time to wound healing would be particularly relevant in the CLI population, as even if amputation is eventually performed, a treatment may be considered a success if it delays amputation for as long as possible. Furthermore, unhealed ulcers limit weight-bearing status, mobility, and predispose to limb and life-threatening infections. From a societal perspective, prolonged time to healing leads to increased healthcare expenditures and the use of resources for wound care, and loss of work productivity, as well. Thus, although amputation-free survival and major adverse limb events are important outcomes, a changed focus on time to wound healing would move the field of CLI forward dramatically. The angiosome concept may be the bridge to this approach.

Although we think revascularization based on the angiosome is important, it is likely not necessary for all patients. Even in the current article, 64% of the anterior tibial artery and 47% of the PTA groups had higher SPP on the angiosome-directed side. Although reasons for this are unclear, proper patient selection is likely the key to optimizing outcomes, and not every patient will benefit equally from the angiosome-based approach. In the presence of collaterals, branch vessels, and an adequate plantar arch, one straight-line inflow may be enough, whereas in the absence of these, the angiosome approach may be preferred. Most studies have been heterogeneous in correcting their results for the presence of these factors, and thus it is not surprising that some studies have suggested a benefit for the angiosome approach, whereas others have not.

Furthermore, the angiosome-directed approach is just 1 aspect of caring for patients with CLI, whom are often complicated and require multidisciplinary care. Therefore, the angiosome concept should only be considered in the context of a whole patient. Factors such as degree of distal run-off beyond the lesion, partial stenosis versus complete occlusion, presence of comorbidities (such as diabetes mellitus or chronic kidney disease), technical difficulty of intervention, and expertise of the provider treating the lesion should always be taken into consideration when deciding on the best approach.

The debate between the proponents of the angiosome-directed and indirect revascularization strategies is healthy, as it may drive research and accelerate progress toward improved patient outcomes in this area. The current study adds to this dialogue; however, does not settle the issue of which approach is best. Rather, it raises further questions and emphasizes the need for an adequately powered study correlating measures of microcirculation with hard clinical outcomes in patients treated with either an angiosome or indirect approach. Such studies should correct for the presence or absence of collaterals, branch vessels, and plantar arch anatomy to be considered valid. Furthermore, a focus on time to wound healing would be valuable, and in the bigger picture, there is a need to assess the impact of time to wound healing on amputation rates, quality of life, and overall cost to society. In the absence of randomized controlled trials in this area (which are unlikely), studies of hard clinical outcomes should guide patient care, and at the moment, these tend to favor the angiosome concept. Regardless of the strategy used, successful treatment of CLI relies on a multidisciplinary approach tailored to each unique patient, and future research should emphasize this personalized strategy rather than a one-size-fits-all approach. With this renewed emphasis, and a tireless commitment to improving the lives of patients with peripheral artery disease, outcomes of patients with CLI will likely continue to improve.

Disclosures
Dr Shishehbor has disclosed education and consulting without compensation for Abbott Vascular, Medtronic, Covidien, Spectranetics, Cook, Terumo, and Boston Scientific. The other author reports no conflicts.
References


Key Words: Editorials ■ peripheral arterial disease ■ wound healing
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Circ Cardiovasc Interv. 2014;7:642-644
doi: 10.1161/CIRCINTERVENTIONS.114.001923
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/7/5/642

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