The Evolving Role of 2D Perfusion Angiography for CLI

How this technology can assist in the evaluation and treatment of CLI patients.

BY JOS C. VAN DEN BERG, MD, PhD

Endovascular treatment of critical limb ischemia (CLI) has been shown to be effective in preventing amputation. The primary goal of revascularization is to improve wound perfusion and, thus, better healing and a higher rate of limb salvage. The level of revascularization that is needed to achieve sufficient limb perfusion is difficult to define before and during the endovascular procedure. Currently, it is impossible to determine which patients will benefit from the interventional procedure because a technically successful revascularization does not always translate into a clinical benefit.[1]

THE ANGIOSOME CONCEPT

The angiosome concept is regularly used, but variations in infrapopliteal vessel anatomy, the presence of collateral connections, and changes in microcirculation that are not related to angiosomes still exist. Two recent meta-analyses addressed the angiosome concept, and the conclusions were not equivocal. The first analysis evaluated a total of 715 patients' legs treated by direct revascularization (according to the angiosome concept) and 575 patients' legs that were treated by indirect revascularization[2]; no randomized studies were available to include in the review. The risk of an unhealed wound and major amputation was significantly lower after direct revascularization when compared to indirect revascularization. Pooled limb salvage rates after direct and indirect revascularization were 86.2% versus 77.8% at 1 year and 84.9% versus 70.1% at 2 years, respectively. The authors concluded that, when feasible, direct revascularization of the angiosome of the foot affected by ischemic tissue lesions may improve wound healing and limb salvage rates compared to indirect revascularization; however, they emphasized that higher-quality studies are needed.

The second meta-analysis came to a different conclusion, indicating that there is insufficient evidence in the form of prospective trials and large patient populations to recommend the conceptual model of angiosome-directed revascularization.[3] A comment on the first meta-analysis, which also took into account the meta-analysis by Sumpio et al, stated:

> The angiosome concept was developed in healthy patients. Very little consideration has been given to the distribution of angiosomes in patients with CLI or diabetes. Recent evidence suggests that the traditional angiosome model may not accurately predict the distribution of blood flow in an unselected group of patients with CLI, whose pattern of perfusion is distorted by abnormalities of the vascular bed, development of collaterals (especially in patients with diabetes), and atrophy of existing microvasculature.[4]

Other authors have pointed out that in addition to macrovascular obstructions (leading to decreased inflow), microcirculatory problems that involve mismanagement of blood flow in the limb play a significant role, especially in patients with diabetes.[1,5]

For this reason, there is a place for indirect revascularization from a theoretical perspective, as well as from a practical point of view, as it is not always possible to achieve direct revascularization. It is likely that the more vessels that can be opened, the better the outcome will be; however, extensive three-vessel revascularization may be very time consuming and incur a higher cost.

An improvement or reappearance of "wound blush" after endovascular therapy is associated with higher skin perfusion pressure and can predict the possibility of limb salvage in patients with CLI.[6] This wound blush concept is independent from the angiosome concept, but it is only a qualitative parameter, and a method to quantify the "blush" is not yet available. Other methods such as indocyanine green fluorescence imaging and tissue oxygen saturation foot mapping are currently available and can reliably evaluate local perfusion.[7-9] The drawback to these techniques is that they cannot be easily implemented in the interventional suite while the patient is completely draped and on the angiographic table.

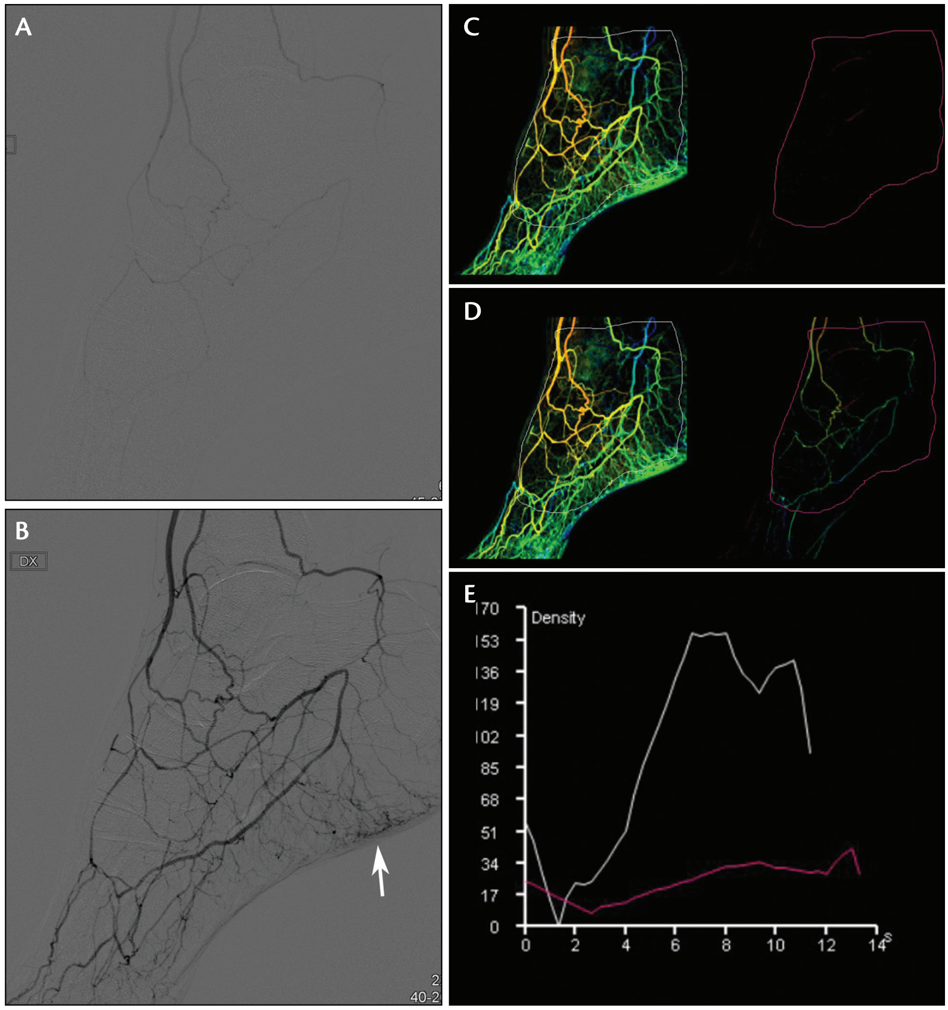

Figure 1. Digital subtraction angiography of a 65-year-old woman's right foot with a plantar lesion, occlusion of the superficial femoral (not shown) and posterior tibial artery, very faint filling of the dorsalis pedis, medial, and lateral plantar artery through collaterals from the anterior tibial and peroneal artery (A). Digital subtraction angiography after recanalization of the superficial femoral artery demonstrating increased arterial filling (B). Two-dimensional perfusion angiography at the early (C) and later (D) phases before (right-hand side, purple region of interest [ROI]) and after (left-hand side, white ROI) revascularization, which demonstrates a significant increase of perfusion despite only undergoing indirect vascularization. A diagram indicating peak density in relation to time, showing a significant increase of density after recanalization of the superficial femoral artery (white line) as compared to the baseline (purple line) (E). Based on 2D perfusion angiography, it was decided not to recanalize the posterior tibial artery.

TWO-DIMENSIONAL PERFUSION ANGIOGRAPHY

Two-dimensional (2D) perfusion angiography using flat detector technology has been successfully applied in neurointerventional procedures related to acute stroke treatment.[10] The application allows assessment of cerebral blood volume in acute stroke patients and can predict final infarct volume, improving the management of these patients.

The technique of 2D perfusion angiography in the peripheral field is based on standard digital subtraction angiography with a frame rate of three images per second. Two-dimensional perfusion images are obtained by automatic reconstruction with postprocessing software on a dedicated workstation (Philips Allura Xper FD20 and Interventional Workspot, Philips Medical Systems). The technique requires additional software acquisition but does not induce additional radiation exposure or an increase in contrast dose. The software for analyzing the perfusion is based on a calculation of the change in density per pixel over time with images obtained before and after the revascularization procedure. Care should be taken to fully immobilize the foot. The reconstructed images can be evaluated for arrival time, time to peak, wash-in rate, width, area under the curve, and mean transit time. The operator can choose an area (freehand) of interest to determine a time-density curve (this is typically done at the level of the ulcer/wound). Comparison of the density before and after the interventional procedure is subsequently performed. The difference in preprocedural and postprocedural perfusion is best demonstrated by the change in the area under the curve and the change in maximal peak density. A typical case is demonstrated in Figure 1.

The initial experience with 2D perfusion angiography in the endovascular treatment of patients with CLI is promising, and its feasibility has been demonstrated in two studies.[1,11] Two-dimensional perfusion angiography can be used in two different ways during the evaluation and treatment of patients with CLI: (1) to select patients who may benefit from intervention (by testing the functionality of the microcirculation) and (2) to determine the endpoint of revascularization by measuring the increase in volume flow (judgment of treatment result).

Judgment of the treatment result is done using the relative increase of area under the curve and the maximal peak density. In a group of 68 patients, 59 showed an average maximal peak density increase of 21% and an average increase in the area under the curve of 48% after successful percutaneous transluminal angioplasty.[1] In the remaining nine patients, no increase was seen, despite successful angioplasty. In this study, no correlation to the clinical outcome was made. Quantification of flow (in volume over time) is not yet feasible, but future studies will focus on both of these issues. The technique should be able to create the opportunity, being instantly available during the endovascular treatment, to decide whether it is necessary to open more vessels or outflow prior to ending a procedure to achieve optimal inflow.[1] This has potential benefits in regard to reducing the length of the procedure, the amount of radiation exposure, and the amount of contrast medium used.

Functionality testing can be done by inducing vasodilation using tolazoline.[1] Contrary to nitrates, which mainly act on the macrocirculation, tolazoline is a nonselective α-adrenergic receptor antagonist that causes an increase in arteriovenous shunting at the level of the capillaries. In patients with diabetic microcirculatory problems, arteriovenous shunting is typically reduced.

Based on their initial experience, Reekers et al proposed the so-called capillary resistance index (CRI).[1] The CRI is calculated by dividing the maximal peak density after stimulation with tolazoline by the maximal peak density at baseline. Preliminary results, as presented by Jim Reekers during the Roesch lecture at CIRSE 2015, included the evaluation of 21 patients (10 patients with revascularization, 11 patients without revascularization). The CRI was > 0.9 in six patients and < 0.9 in 15 patients. In the group with a CRI > 0.9 (meaning no functional response to vasodilation), six early amputations were seen, whereas in those with a CRI of < 0.9, only one early amputation was seen. Therefore, patients with a CRI of < 0.9 may have a better outcome. This index could have implications in the future that are, in a way, comparable to the use of fractional flow reserve in coronary revascularization,[12] by allowing one to select patients who will have the best outcomes, which also has implications regarding the costs of treatment.

CONCLUSION

Two-dimensional perfusion angiography is feasible and can help to determine an endpoint for revascularization. It also has the capacity to allow functional imaging that may help select patients who will optimally benefit from revascularization. ■

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