



Go With the Flow?

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J CRIT LIMB ISCHEM 2023;3(2):E54-E55

Key words: amputation, angiography, critical limb ischemia, lower extremity, microcirculation,

Endovascular treatment of critical limb ischemia has been shown to be effective in preventing amputation and is oftentimes the treatment modality of first choice. The primary goal of any revascularization is to achieve a better wound perfusion, and this will lead to better healing and higher limb salvage rates. When treating patients with CLI it is important to determine which patients will benefit most (or not at all) from a revascularization procedure, and to know when revascularization can be considered adequate. Especially when dealing with complex multilevel disease it is very difficult to define the extent of revascularization that is needed to obtain sufficient limb perfusion both before and during the endovascular procedure. The first is important because a technically successful revascularization procedure not always translates into a clinical benefit.¹ The latter is important to reduce the duration and cost of the procedure as well as the risk of complications, radiation exposure and the amount of contrast medium used. One way to evaluate outcome is by looking at the wound blush. The improvement or re-appearance of 'wound blush' after endovascular therapy has been demonstrated to be associated with a higher skin perfusion pressure and can be a predictor of limb salvage in patients with CLI.² A reliable method to quantify the 'blush' is not available yet. Other methods, like indocyanine green fluorescence imaging and tissue oxygen saturation foot-mapping, are currently available and they can evaluate local perfusion reliably.³⁻⁵ The drawback is that these techniques cannot be implemented easily in the interventional suite, with the patient still on the angiographic table, completely draped.

In this issue of the *Journal of Critical Limb Ischemia*, Prasad et al describe their first experience with the assessment of hemodynamics during peripheral arterial interventions using the Navvus microcatheter in patients with lower extremity PAD.⁶ They did so by evaluating the translesional systolic pressure gradient after each step in the procedure, and for all these steps without and with pharmacologically induced hyperemia. The hyperemia induction simulates walking exercise and provides an insight into the 'functional reserve' of the peripheral vascular bed (which is especially of importance in patients with CLI).

In a hyperemic state a more reliable measurement of the pressure gradient can be obtained, and even more so when a small size catheter or 'pressure-wire' is used: a residual stenosis after angioplasty that does not appear to be hemodynamically significant at baseline ('resting state'), may become hemodynamically significant after vasodilation ('walking state'), and if left untreated could lead to persistence of symptoms. The potential to increase flow during adenosine-induced hyperemia is not only important in the patient with claudication (these constituted 40.9% of the study population), but also in patients with critical limb ischemia (the remaining 59.1%). The idea of a functional evaluation during an endovascular procedure is not entirely new: 2D-perfusion angiography has been used to select patients that may benefit from intervention (by testing the functionality of the microcirculation). This testing of functionality can be done by inducing vasodilation using tolazoline.¹ Contrary to nitrates (that mainly act on the macro-circulation), tolazoline is a non-selective alpha-adrenergic receptor antagonist that causes an increase in A-V shunting at the level of the capillaries. In patients with diabetic micro-circulatory problems A-V shunting is typically reduced. The inability to reduce the peripheral resistance in the foot with a local alpha-blocker is a sign of a dysfunctional sympathetic nervous system of the lower limb. Schreuder et al have proposed the so-called capillary resistance index (CRI),⁷ which is calculated by dividing the maximal peak density after stimulation with tolazoline by the maximal peak density at baseline. In an evaluation of 31 patients that were followed up for 12 months a cut-off point for a non-responsive sympathetic nervous system of ≥ 0.9 was found. All patients ($n=11$) with a $\text{CRI} \geq 0.9$ underwent a major amputation before 12 months. Of all patients with a $\text{CRI} < 0.9$ only 15% underwent major amputation. The positive predictive value for major amputation before 12 months for patients with a $\text{CRI} \geq 0.9$ was 100%. Patients with $\text{CRI} < 0.9$ therefore may have better outcome. This index may have implications in the future in a way comparable to the use of fractional flow reserve in coronary revascularization,⁸ by selecting patients that will have good outcome.

Another way in which the measurement and quantification of flow can be used is in evaluating a treatment result, and to

determine whether additional vessels or vessel segments need to be opened.

Being a feasibility study, Prasad et al did not provide a correlation with clinical outcome, and in the absence of a well-defined threshold could not determine whether a sufficient 'flow endpoint' was reached. This should be the subject of further study. The technique however holds promise, and translesional gradient measurement can be implemented easily as part of the per-procedural monitoring, in an effort to further improve outcomes in patients with CLI.

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Disclosure: The author has completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. No disclosures were reported.
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