Chapter 8

Percutaneous deep venous arterialization in patients with critical limb ischemia

Steven Kum, Eline Huizing, Michiel A. Schreve, Çağdaş Ünlü, Roberto Ferraresi, Lasitha B. Samarakoon, Daniel A. van den Heuvel

ABSTRACT

Background
Critical limb ischemia (CLI) is the presentation of end stage peripheral arterial disease and typically presents with rest pain, ulceration, and gangrene. The outcome of conservative treatment is poor and often leads to amputations. Arterial revascularization plays an important role in amputation prevention. Unfortunately, a significant percentage of CLI patients cannot be revascularized and subsequently end up with a palliative amputation. This has led to the need and exploration of new treatment options in this no option subgroup of CLI. Deep venous arterialization (DVA) is one of them and has been reported as a safe and feasible novel and promising alternative to amputation. The goal of DVA is to provide arterialized blood in significant volumes and pressure to the plantar venous arch and ischemic tissue to enable wound healing. Selecting the right patients is critical for successful DVA and requires that extra attention is paid to the wounds as well as arterial and venous vascular status.

Methods
The procedure was previously described in our initial experience in the first-in-man study performed on 7 patients with NOP-CLI. The angiographic goal of the procedure is to deliver arterialized blood to the plantar venous arch in significant volumes and pressure, circumventing the numerous valves in the process. The clinical goal is to achieve wound healing.

Results
Technical success was achieved in all patients. Flow in the plantar arch was achieved in 5 of the 7 patients. One patient with chronic rest pain became pain free within 48 hours after the procedure. Complete wound healing was achieved at 12 months in 5 of the 7 patients. Reinterventions were performed in 5 of 7 patients to maintain patency. Of the 7 study patients, five underwent minor amputation of one or more toes, and two underwent major amputations within 12 months (limb salvage, 71%).

Conclusions
The LimFlow system is currently the only registered device a total percutaneous DVA can be performed with. In addition to the percutaneous creation of an arteriovenous fistula (AVF), it also allows disruption of the veins with a dedicated valvulotome.
INTRODUCTION

Arterial revascularization is widely considered to be an important mainstay for the management of critical limb ischemia (CLI). Advances in techniques and modern devices have enabled interventionalists to perform adequate infrainguinal revascularization for wound healing and resolution of rest pain. More distal angioplasty and retrograde approaches have revolutionized and improved technical success rates. However, a significant number of patients are not candidates for conventional angioplasty or bypass. These patients have no options for revascularization and are termed “no-option CLI” (NOP-CLI).

Despite a potentially salvageable foot that can still be functional if revascularization is achieved, these NOP-CLI patients represent a therapeutic dilemma that often ends with a palliative amputation. Surgical and hybrid approaches to deep venous arterialization (DVA) have been reported and are increasingly popular alternatives to amputation, with admirable rates of limb salvage in the NOP-CLI patients. This report describes the indications for DVA, the technical considerations, and the post-procedural issues for this procedure.

PATIENTS AND METHODS

The procedure was previously described in our initial experience in the first-in-man study performed on 7 patients with NOP-CLI. The angiographic goal of the procedure is to deliver arterialized blood to the plantar venous arch in significant volumes and pressure, circumventing the numerous valves in the process. The clinical goal is to achieve wound healing.

Patient selection
Selection criteria for percutaneous DVA should be focused on 3 main areas: general factors, angiographic factors, and wound-related factors.

With regards to general factors, patients should generally not have an impaired heart function of less than 40%. Although current experience does not seem to suggest any clear sequelae of increased shunting, we adopt this precautionary approach based on the theoretical risk. On the same note, caution should also be applied to patients with a pre-existing high-output fistula for dialysis access. Patients with pre-existing coronary lesions should probably also be optimized.

Angiographic factors are also important when selecting these patients. Inflow should be optimized. Crossing from a proximal tibial artery into a vein enables sufficient inflow to drive flow and pressure to the foot. In our opinion, this is essential for wound healing and moreover carries a lower risk of occlusion compared to a distal crossing site. Formation of a distal arteriovenous fistula (AVF) can be plagued by the high (re)stenosis rate in a diseased proximal tibial vessel, which will compromise patency. Effort should also be made to avoid coverage of significant tibial vessels (e.g., peroneal artery) when the crossing covered stent is deployed.
Our experience has almost been exclusively based on crossing into the posterior tibial vein (PTV), which we think has the best chance to deliver a sufficient volume of blood to the foot. It has been shown that the lateral plantar veins are larger, can accommodate more blood and are therefore ideal to direct blood to the plantar venous arch. In evaluating the anterior tibial vein, one should consider the anatomical presence of the angulation as well as the numerous fascia overlying the distal anterior and dorsalis pedis veins (superior and inferior extensor retinaculum), which may lead to kinking of the stent graft and kinking of the outflow veins, respectively.

Lastly, wound-related factors must be considered. Patients with extended and irrecoverable foot gangrene must be excluded. Because covered stents are used, patients with systemic sepsis from the foot are not suitable. Wounds around the distal retrograde access site (medial malleolus) are also no suitable candidates. In these cases guillotine amputation, necrectomy and antibiotics to drain and treat infection should be performed before performing pDVA. Only after the most severe infection has been dealt with a pDVA can be considered after which more definite trans metatarsal amputation can be planned.

**Procedure**

Before the procedure, the physician should be prepared to deal with venous anatomy of the lower leg and the foot that can be variable. The procedure can last 90 minutes to 4 hours. The operator is required to perform retrograde access and crossing of valves, which can be technically demanding.

For the patient, we recommend anesthetic support with intravenous sedation. We routinely supplement this with a regional anesthetic (popliteal block) to make the patient more comfortable during and after the procedure. Before the procedure, the patient is pre-treated with aspirin and clopidogrel and is hydrated according to standard institutional protocol. Carbon dioxide angiography has been used to perform this procedure when there was a high risk of contrast nephropathy.

**DVA technique**

The following describes percutaneous DVA done with the LimFlow system (LimFlow SA, Paris, France), the only dedicated device used to perform DVA. After systemic heparinization, the target inflow vessel is accessed via an antegrade 7F femoral sheath. An ultrasound-emitting arterial catheter with an embedded hollow crossing needle is placed over a standard 0.014-inch guidewire using a monorail system.

Venous access is achieved by percutaneous ultrasound-guided puncture of the posterior tibial vein near the ankle. The venous catheter is placed over a standard 0.014-inch guidewire via a 5F sheath in an over-the-wire system. The venous catheter is advanced proximally to the intended point of crossing, which is selected after simultaneous digital subtraction arteriography and venography (i.e., double injection) of both vessels.

The tips of both arterial and venous catheters have an ultrasound emitting and receiving probe, respectively. The venous “receive” catheter is initially placed at
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The selected crossing point. The arterial “send” catheter is then adjusted to achieve optimal alignment between the two as confirmed by maximum peak ultrasound signals. This allows both catheters to be aligned at the same transverse level with both probes rotated toward each other (Figure 1A). The crossing needle is driven across the artery and into the vein (Figure 1B) using the pusher ring at the handle of the arterial catheter. This is followed by advancing a 0.014-inch Spartacore guidewire (Abbott Vascular, Santa Clara, CA, USA) through the needle into the vein. 

Figure 1. Illustration of percutaneous deep vein arterialization. A. The venous “receive” catheter is initially placed at the selected crossing point. The arterial “send” catheter is adjusted to achieve optimal alignment. B. The crossing needle is driven across the artery and into the vein using the pusher ring at the handle of the arterial catheter. C, D. The AVF is matured with a proprietary self-expanding tapered covered stent with a diameter of 3.5 mm at the proximal aspect and 5.5 mm at the distal aspect (courtesy of LimFlow SA).

With the help of a support catheter the wire is advanced distally passing the venous puncture site into the foot. This requires patient crossing of the valves in the foot. In the posterior tibial system of veins, there are valves around the ankle and also in the middle portion of the lateral plantar vein. The wire and support catheter are sent across the un-diseased plantar venous arch into the dorsalis pedis vein. This is subsequently exchanged for the more supportive V18 wire (Boston Scientific, Marlborough, MA, USA).

Successful arterialisation of the foot veins relies heavily on breaking the valves. To this end the percutaneous valvulotome (a proprietary, 4F, braided, over-the-wire, forward-cutting) that lyses the valves, some as far distal as the midfoot is introduced over the V18 wire.

After pre-dilatation across the vein and artery to create an AVF, multiple 5.5-mm extension stents (proprietary to LimFlow) are placed from the ankle and stacked upward. The extension stents then serve as an “endoconduit” to bring blood to the foot. Apart from destroying the valves in the tibial vein by stenting, the reasonably large caliber ensures adequate flow down to the foot. These covered stents also cover multiple venous collaterals that “bleed off” the flow to the foot.

The AVF is matured with a proprietary self-expanding tapered covered stent with a diameter of 3.5 mm at the proximal aspect and 5.5 mm at the distal aspect (Figure 1C). The crossover stent is sized to accommodate the size discrepancy between the artery and the vein. The use of a covered stent is critical because it prevents leakage at the crossover point and redirects blood distally, preventing it from immediately
following the flow of the normal venous return to the heart. A completion angiogram should show rapid flow into the deep venous arch (Figure 2).

**Postoperative care**

After the procedure, the patient is monitored for standard postprocedural issues such as contrast nephropathy and access-related issues. In our practice, we tend to keep the patients on oral clopidogrel and therapeutic anticoagulation with warfarin or direct oral anticoagulants (DOAC) for 3 months, followed by lifelong aspirin and clopidogrel. The patient is kept on antibiotics as per institutional practice. We tend to be more liberal with the use of prolonged antibiotics due to the extensive use of covered stents.

Surveillance of the DVA is done with duplex ultrasound. Because it is essentially an AVF, flow volumes (mL/min) are surveyed within the stent grafts as well as below and above the stent grafts. This is in addition to standard duplex ultrasound regimens. The detailed description of the surveillance protocol is beyond the scope of this report.

Wound physiology after DVA is different than after standard revascularization. In addition to the need for a dedicated and integrated wound clinic, we refrain from definitive foot surgery or flaps for 6 to 8 weeks. We believe it takes time to develop retrograde tissue nutrition by veins and venules and stimulation of the angiogenesis process that leads to a remodelling of the vascular distribution system of the foot.

**Figure 2.** Angiogram after the procedure showing blood flow into the plantar venous arch.
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RESULTS

The results of this approach have been described in our previous study. In this first-in-man study, 7 NOP-CLI patients underwent percutaneous DVA, performed as described above. The procedure in 2 initial patients was performed with off-the-shelf devices. Technical success was achieved in all patients. The immediate angiogram showed a striking increase in blood flow to the foot (Figure 3). Flow in the plantar arch was achieved in 5 of the 7 patients. One patient with chronic rest pain became pain free within 48 hours after the procedure. Negative pressure therapy was used in 5 of 7 patients to achieve wound healing, and a split skin graft was used in 3 of 7 patients. Complete wound healing was achieved at 12 months in 5 of the 7 patients.

Reinterventions were performed in 5 of 7 patients to maintain patency. Of the 7 study patients, 5 underwent minor amputation of 1 or more toes, and 2 underwent major amputations within 12 months (limb salvage, 71%). Amputation was because of DVA thrombosis in 1 patient and because of infection in the other patient.

DISCUSSION

NOP-CLI is a loosely defined description of a limb in extremis. Typical patients have a long exposure to diabetes, are dialysis dependent, and are frequently elderly and have undergone multiple previous attempts at surgical or endovascular revascularization. Angiographically, they have extensive small distal artery disease (below the ankle disease), are heavily calcified, and may or may not have a discernible target vessel for bypass or a reasonable target for wiring. This is commonly termed the “desert foot” to illustrate the absence of flow on angiogram and the severity of ischemia. However, the definition of NOP-CLI may differ from physician to physician and may be contentious. What one surgeon or interventionalist defines
as “no option” could be an option to a surgeon or interventionalist in another center.

The failure of prior interventions, the absence of a reasonable surgical target for a high-risk bypass, and the lack of a good-quality saphenous vein are all contributory factors that need to be considered. The consensus that a major amputation is the only option left is also essential.

One of the most difficult parts of the procedure is to reliably cross from the target artery into the vein. Although the artery and vein are commonly thought to be encased in a sheath, achieving crossing was challenging before the use of the LimFlow system. We have found that the artery and vein can sometimes “spiral” around each other and may not be parallel, as commonly expected. The use of the ultrasound alignment system allows a reliable means of aligning the crossing needle in a longitudinal and radial fashion. Combined with visual cues, this greatly aids the procedure.

The last hurdle is to navigate past the valves in the foot. This is essential to bring pressurized blood to the foot, which is the ultimate goal of the procedure. The forward-cutting over-the-wire push valvulotome achieves this. In contrast to a conventional surgical valvulotome the LimFlow valvulotome is pushed rather than pulled. The authors prefer the valvulotome over high pressure balloon angioplasty or cutting balloon angioplasty because of the less traumatic destruction of the valves. This will result in a more sustainable result with less trauma induced stenosis in the outflow veins. We postulate that the percutaneous approach allows us to routinely address valves that are not addressed with traditional open surgical bypass.

**CONCLUSION**

Percutaneous DVA of a patient with NOP-CLI represents an emerging alternative to revascularize limbs in extremis. The key to success is the ability to deliver pressurized arterial blood to the venous arch of the foot and an adjusted follow-up and wound care. Multicenter trials in Europe and the United States are currently evaluating this technology.
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REFERENCES


