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SHORT REPORT

Magnetic Resonance Imaging and Histological Insights Into Deep Venous Arterialisation

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Introduction: Percutaneous deep venous arterialisation (DVA) is emerging as a promising alternative for limb salvage in chronic limb threatening ischaemia (CLTI) patients without any reasonable anatomical option for conventional revascularisation techniques. However, its mechanism of action remains incompletely understood. This report aimed to find some of the histological alterations occurring in the limb following DVA.
Report: This short report presents the case of a 53 year old female who underwent DVA for Rutherford 5 CLTI. Although the intervention was successful and showed evidence of improved blood flow to the foot, the post-operative course was notable due to worsening infection leading to a below knee amputation four weeks later. The blood vessels were harvested for histological analysis, which found features of venous arterialisation such as smooth muscle cell proliferation and neointimal hyperplasia, even in the paired posterior tibial vein that did not undergo DVA.
Discussion: This case demonstrated unexpected histological changes occurring in the paired posterior tibial vein that did not undergo DVA. This warrants further investigations to fully understand the mechanisms at play in DVA and to explore the role of the paired vein in sustaining arterialised flow to the foot.

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INTRODUCTION

Chronic limb threatening ischaemia (CLTI) significantly affects the health of approximately two million adults aged ≥40 years within the United States,[1] often leading to major lower extremity amputations in the absence of adequate treatment.[2] The urgent restoration of arterial blood flow through endovascular and or open surgical techniques is the standard approach to prevent limb loss. However, approximately 20% of CLTI patients are classified as no option cases, indicating a lack of reasonable revascularisation options.[3—5] While various factors, such as comorbid conditions precluding revascularisation and limited access to specialised expertise and infrastructure, may contribute to this classification, anatomical limitations are the prevailing factor.[3] In this subset of no option CLTI patients, deep vein arterialisation (DVA) has emerged as a promising alternative for limb salvage and is being performed increasingly in specialised vascular centres.[4] However, the underlying mechanisms and physiological changes that occur to enable sustained arterialised blood flow to the foot remain unclear. In essence, while it is known that DVA works, there remains the lack of a comprehensive understanding of its modus operandi[4] and a lack of studies investigating these physiological mechanisms and histological changes. Therefore, this case report aimed to investigate histological alterations occurring in the limb following deep venous arterialisation. The research subject discussed in this manuscript provided informed consent as part of a prospective study approved by the Institutional Review Board of the Houston Methodist Research Institute.

REPORT

A 53 year old female with a history of type 2 diabetes mellitus presented to the institution with a Rutherford 5 CLTI with wet gangrene of the right forefoot limited to the toes, and a non-healing pressure wound at the heel. She had previously undergone balloon angioplasty of the right anterior tibial and dorsalis pedis arteries, and first and second toe amputations with debridement of infected wounds. On admission, her fasting glucose and HbA1c were 117 mg/dL and 5.2%, respectfully. Pre-operative physiological testing revealed severely diminished pressures in the

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third, fourth, and fifth toes, with absent waveforms. Measurement of the ankle brachial index was limited by the wound dressing at the ankle. Also, her pre-operative duplex ultrasound showed absent doppler signals in the right posterior tibial (PT) and peroneal arteries and monophasic waveforms in the distal right tibial artery. This finding was subsequently confirmed on a distal selective diagnostic angiogram, which showed inline flow into the dorsalis pedis but a desert forefoot and no discernible flow to the heel (Fig. 1). Her non-healing foot wounds were deemed salvageable; however, given the inadequate outflow in the foot, both balloon angioplasty and distal bypass intervention were deemed anatomically non-feasible. Thus, taking the patient's preference into consideration, the decision was made to proceed with percutaneous DVA to attempt limb salvage. To assess the anatomical suitability for DVA, extensive duplex ultrasound vein mapping was performed, which showed a patent posterior tibial vein (PTV) and an adequate plantar venous arch.

Operative details

The procedure was performed in a hybrid suite under general anaesthesia. Ultrasound guided percutaneous access of the proximal superficial femoral artery in the groin and the lateral plantar vein in the foot was achieved in an antegrade fashion using 6F and 4F sheaths, respectively. After visualising the plantar vein loop and confirming adequate vein quality, a guidewire was passed upwards through the plantar vein access into the PTV and a three lobe snare was placed. On the arterial side, a guidewire was advanced through the proximal PTA lesion in an antegrade fashion, aiming towards the arterial wall. A 3 x 100 mm balloon was used to pre-treat the recanalised lesion. A re-entry catheter was then advanced and used to cross from the artery into the adjacent vein to create the arteriovenous fistula. The intravenous end of the wire was then snared from below, establishing through and through access. Subsequently, the anastomosis was dilated with a 3 mm x 10 cm balloon, followed by dilation of the entire length of the PTV using a 4 x 220 mm balloon to disrupt the valves, and a 3 x 15 mm cutting balloon for the anastomosis. A 5 mm x 25 cm Viabahn stent was then implanted across the anastomosis, extending down into the vein up to approximately 5 cm above the medial malleolus. Completion venography displayed brisk retrograde flow through the pedal vein loop with preservation of the inline flow in the distal tibial artery

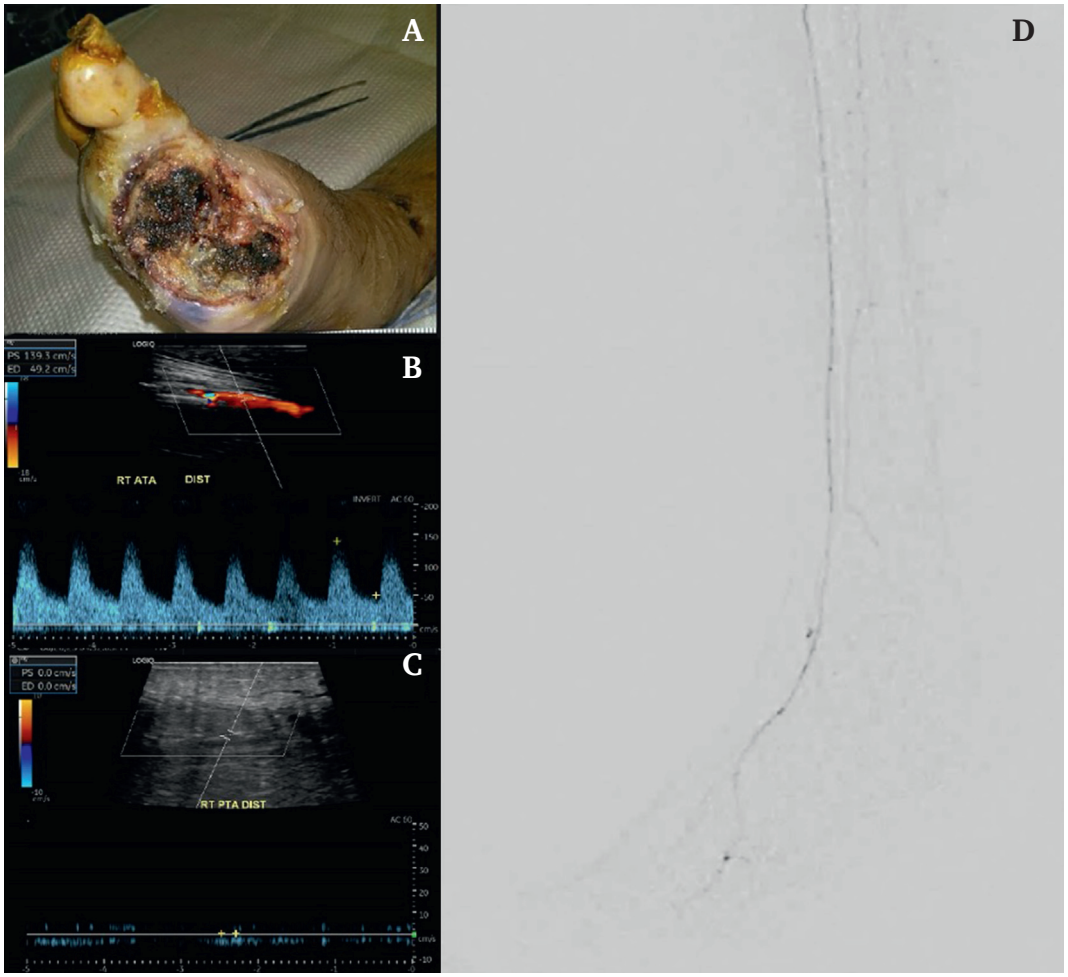

Figure 1. Pre-operative images. (A) Non-healing right foot wound. (B and C) Duplex ultrasound showing monophasic waveform in the anterior tibial artery and absence of signal in the posterior tibial artery. (D) Xray angiography showing inline flow through the anterior tibial artery to the ankle.

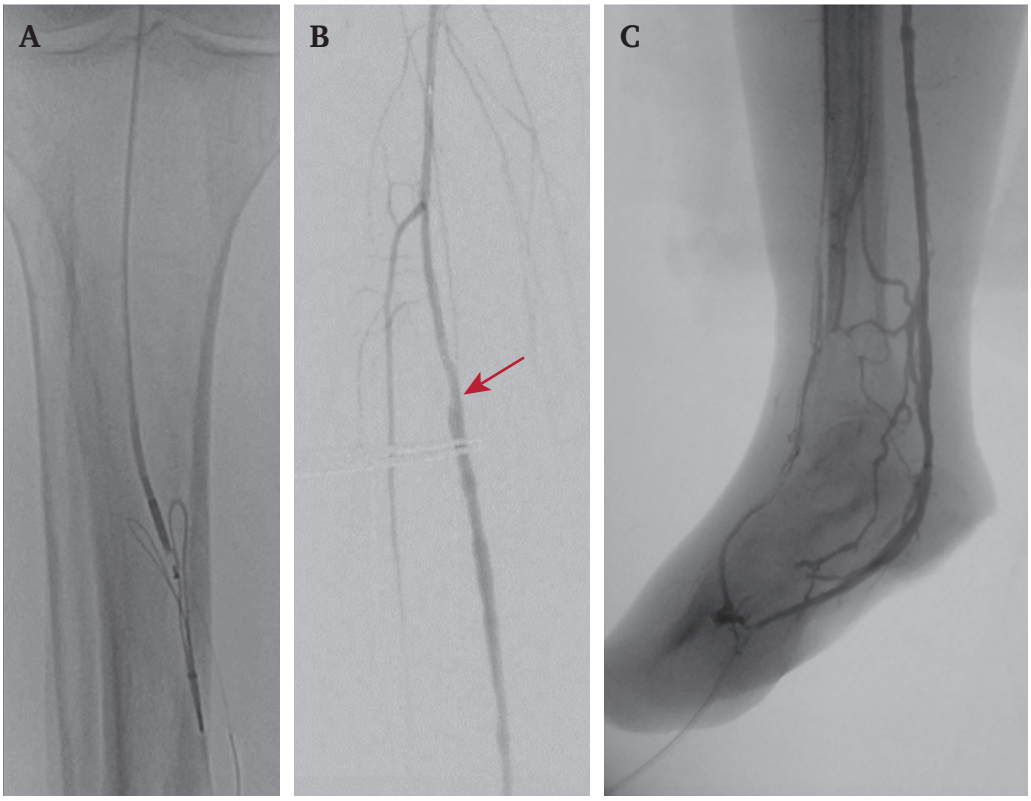

Figure 2. Deep venous arterialisation procedure. (A) After creation of the arteriovenous anastomosis, the arterial guidewire was snared into the vein to achieve through and through access. (B) Angiogram showing the arteriovenous anastomosis (red arrow). (C) Completion venogram showing a brisk retrograde flow through the pedal vein loop.

(Fig. 2). Duplex ultrasound also showed a low resistance biphasic signal in the arterialised vein and a monophasic signal in the dorsalis pedis artery.

Post-operative course

The initial post-operative course showed a notable improvement in blood flow to the foot. However, the patient's foot infection escalated, with worsening inflammatory markers, despite appropriate antibiotic therapy and wound care, leading to a below knee amputation four weeks later due to the sepsis. An angiogram was conducted prior to the amputation, as part of the institutional protocol, to verify the patency of the DVA prior to the post-DVA amputation. This demonstrated sustained retrograde flow into the foot. The amputated limb was scanned with 7T magnetic resonance imaging (MRI) for lesion characterisation. Additionally, samples of the arterialised vein, distal tibial arteries, and the plantar venous loop were harvested for histological analysis.

MRI findings

A 7T MRI of the amputated leg, using a specialised high resolution (0.2 micron isotropic) MRI histology protocol that integrates T2 weighted and ultrashort echo time sequences,[6] confirmed the patency of the Viabahn stent graft (Fig. 3A) and plantar loop.

Histology

Movat's and haematoxylin—eosin staining demonstrated evidence of valvular disruption and eccentric neointimal hyperplasia (NIH) in the PTV that underwent the DVA (Fig. 3B). Most importantly, there was also evidence of NIH in the paired vein that did not undergo DVA (Fig. 3B). Additionally, this vein showed increased smooth muscle cells in the medial layer, resulting in greater thickness compared with the media of the anterior tibial vein at the same level (Fig. 3C). These features were consistent in multiple sections. Additionally, some bridging veins between the pair of PTVs displayed evidence of NIH.

DISCUSSION

This report details the case of a successful DVA procedure that ended in a below knee amputation due to infection. The fundamental principle of DVA is to establish direct communication between the arterial and deep venous systems, enabling tissue oxygenation through retrograde blood flow in the venous capillaries. Initially described over a century ago,[4] this technique has evolved from open and hybrid approaches to more refined percutaneous

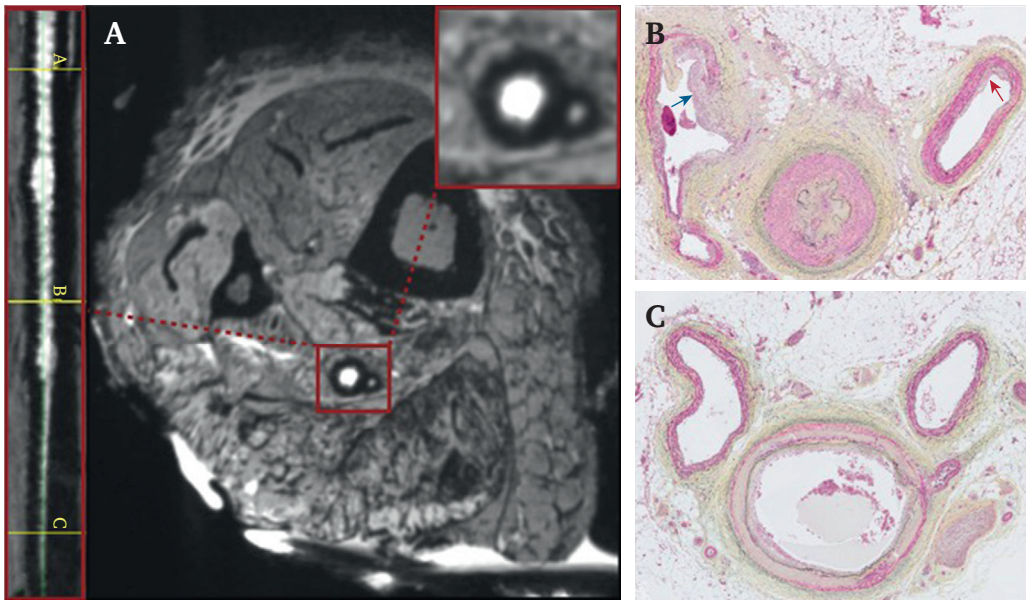

Figure 3. Magnetic resonance imaging and histology. (A) Magnetic resonance imaging showing a patent stent in the posterior tibial vein. (B) Histology revealed intimal thickening (red arrow) and smooth muscle cell proliferation in the paired posterior tibial vein, (C) compared with the anterior tibial vein at the same level.

interventions with the development of dedicated transcatheter arterialisation devices such as LimFlow.[5] The reported technical success rates of percutaneous DVA ranged 97—100%.[5,7] The recent PROMISE II trial,[8] demonstrating a technical success rate of 99%, a six month amputation free survival rate of 66%, and a limb salvage rate of 76%, has highlighted the substantial benefit of percutaneous DVA.

This report sheds light on notable changes, including smooth muscle cell proliferation and NIH, occurring in the tibial and foot veins following DVA. While these changes mirrored alterations observed in superficial veins of the arm after dialysis access creation and was expected in the PTV that was stented during the DVA, it was surprising to find similar and even more pronounced changes in the paired vein that did not undergo DVA. This discovery aligns with previous reports suggesting that some patients continue to progress toward wound healing even when the arterialised vein is thrombosed.[4] Clair et al.[4] have suggested that, similar to the retina, neovascularisation may occur after DVA, potentially explaining the persistent improvement in arterial flow to the foot despite DVA thrombosis. Although the present case did not exhibit evidence of neoangiogenesis, it was speculated that the bridging veins may have played a crucial role in transmitting retrograde arterialised flow from the target vein to the unaltered paired vein. The discovery of NIH in these bridging veins, indicative of turbulence induced by retrograde arterial flow, further supports this hypothesis. Previous studies have indicated a failure rate of 40—50% in DVA[7—10] but the reasons behind these failures are unclear and necessitate further investigation.

This report offers a framework for exploratory studies aimed at understanding the histological changes critical for successful venous arterialisation and tissue oxygenation. Such investigations are currently underway at this institution, involving histological analysis of vascular tissues from amputated specimens obtained from patients undergoing planned transmetatarsal and toe amputations following successful DVA. A comparative analysis will be conducted with specimens from cases where DVA procedures have failed, aiming to further elucidate the distinctive features associated with successful arterialisation. Additionally, this study will potentially help identify radiological markers of successful arterialisation on MRI, validated by histology. It is anticipated that the insight from this research will play a pivotal role in refining patient selection criteria for DVA and optimise the technique, ultimately leading to improved clinical outcomes.

Conclusion

Percutaneous deep venous arterialisation is emerging as a potential game changer for no option CLTI; however, its pathophysiological mechanisms are not yet fully understood. This case demonstrates a possible role of the paired posterior tibial vein that is not directly involved in the arteriovenous fistula in facilitating arterialised flow to the foot. Studies are needed to further investigate these histological changes and identify markers of successful DVA to predict outcomes.

CONFLICTS OF INTEREST

TLR reports a research contract with Boston Scientific and Baylis Medical Technologies Inc. MMB is an educational consultant for Boston Scientific, Cook Medical, Veryan, and LimFlow; and is a stock/owner of HENDOLAT, HENDOSYN,

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