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Short Report

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Short Report

Transcatheter arterialization of the deep veins: 1-year outcomes of PROMISE-UK study

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Introduction

Approximately 20% of the general population over the age of 55 years have peripheral arterial disease (PAD), which is the main cause of leg amputations in the UK National Health Service (NHS) and other healthcare systems[1,2]. An estimated 20% of those with symptomatic PAD progress to develop chronic limb-threatening ischaemia (CLTI), the most advanced form of PAD[3]. A subgroup of patients with CLTI not suitable for conventional endovascular or open revascularization owing to lack of an arterial target for bypass or endovascular intervention, or multiple failed open and endovascular revascularization attempts, are referred to as 'no-option' patients. These patients represent up to 20% of all those presenting with CLTI[4–6], and historically have been offered major amputation of the affected limb which has an associated 1-year mortality rate of over 30%[7]. A novel endovascular procedure called transcatheter arterialization of the deep veins (TADV), which uses the only CE mark-approved system has been reported as a potential treatment for selected no-option CLTI patients and is currently available in the UK under special arrangements[8–15].

The PROMISE-UK study was conducted with the objective of establishing real-world outcomes among patients with CLTI treated with TADV using the commercially available LimFlow® system (Inari Medical, Irvine, CA, USA) across multiple centres in the UK NHS.

Methods

PROMISE-UK was a single-arm, multicentre, open-label, prospective, postmarket follow-up study of the LimFlow® system used for TADV (*Fig. 1*). PROMISE-UK was approved by the London Westminster Research Ethics Committee (19/LO/0408) and registered at ClinicalTrials.gov (NCT03807661). Study details are available in the *supplementary material*.

Patients were recruited and screened for eligibility by an independent medical advisory committee. Key inclusion criteria included diagnosis of CLTI with Rutherford class 5 (tissue loss or focal gangrene) or 6 (extensive gangrene), and site-level vascular multidisciplinary team agreement on unsuitability for either open or endovascular revascularization options.

The primary endpoint was 1-year amputation-free survival (AFS), defined as both freedom from above-ankle amputation and all-cause mortality. Secondary endpoints included technical success, limb salvage, and wound healing at 1 year.

Results

Between December 2019 and October 2022, 28 patients were enrolled across 6 sites in the UK (*Fig. S1*). Patient characteristics are summarized in *Table S1*.

Study endpoints and outcomes

The LimFlow® TADV procedure achieved technical success in 27 of 28 patients, with no unanticipated adverse device-related events. All patients completed protocol-required follow-up. The AFS rate at 1 year was 67% and the limb salvage rate was 81% (*Fig. 2*). Nine of the 28 patients experienced either major amputation (5) or death (4). Three of the five major amputations were undertaken after acute early/in-hospital occlusions of the arterialized venous network. All five major amputations occurred within 60 days of the index procedure, and all five patients were alive at 1 year. Study deaths were adjudicated as

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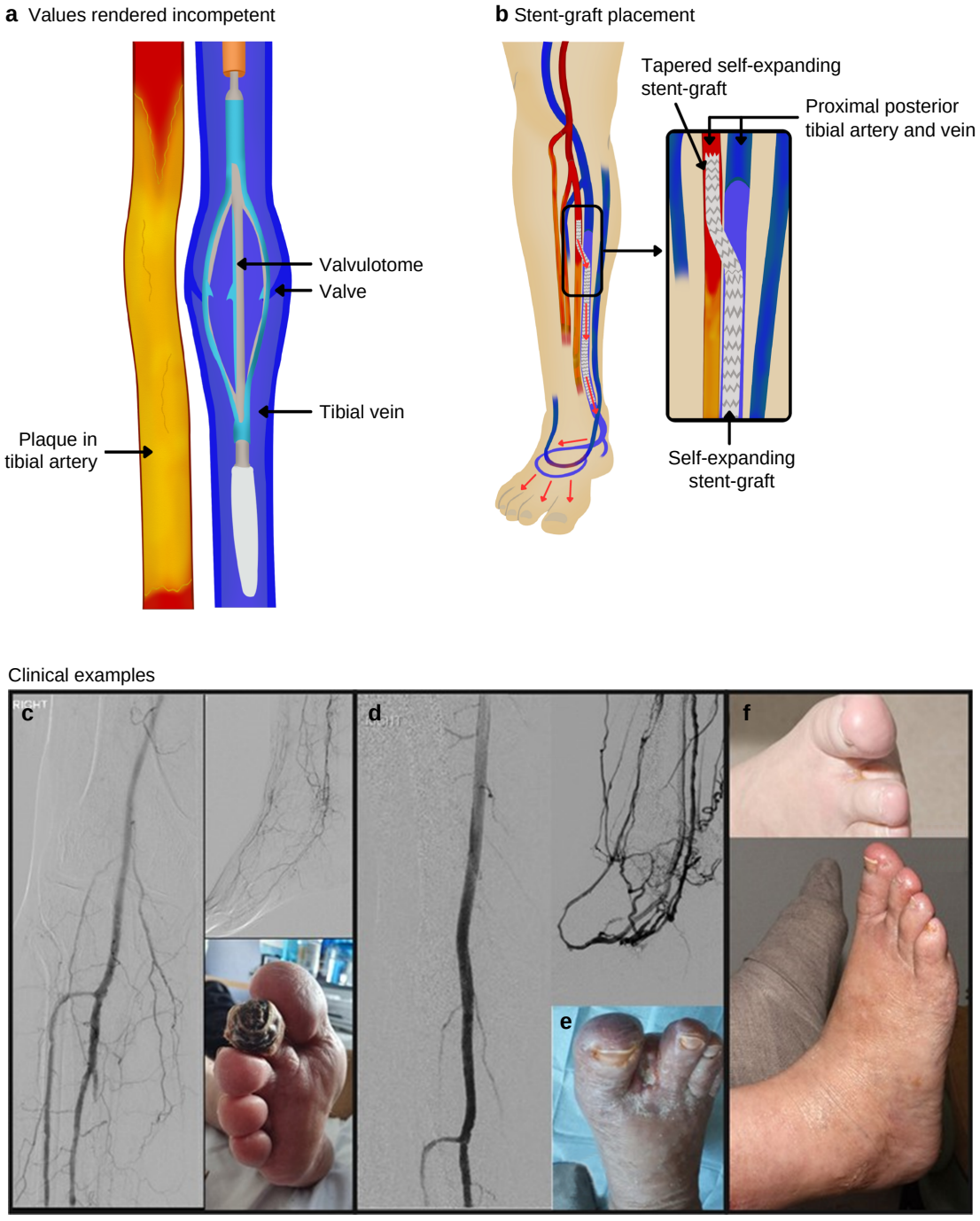


Fig. 1 LimFlow® system, procedure, and wound healing

Important steps for performing transcatheter arterialization of the deep veins using the LimFlow® system. **a** Valves in the tibial vein are rendered incompetent with a push valvulotome. **b** A LimFlow® stent-graft is placed in the vein and a tapered, self-expanding, covered stent-graft is inserted at the arteriovenous junction to direct arterial blood flow within the venous system. **c–d** Images from an example patient course during the PROMISE-UK study. **c** Screening angiography and wound of a 63-year-old man with type II diabetes and hypertension. At baseline, he was classified as having Rutherford stage 5 disease with a gangrenous wound and had greater than moderate pain. **d** Index LimFlow® procedure and inflow treatment outcome angiography showing the newly established transcatheter arterialization venous network. **e** The patient had a planned minor toe amputation between 30 and 60 days after the LimFlow® procedure. **f** At 6-month follow-up, the wound was fully healed; the disease was classified as Rutherford stage 0, and the patient had no pain.

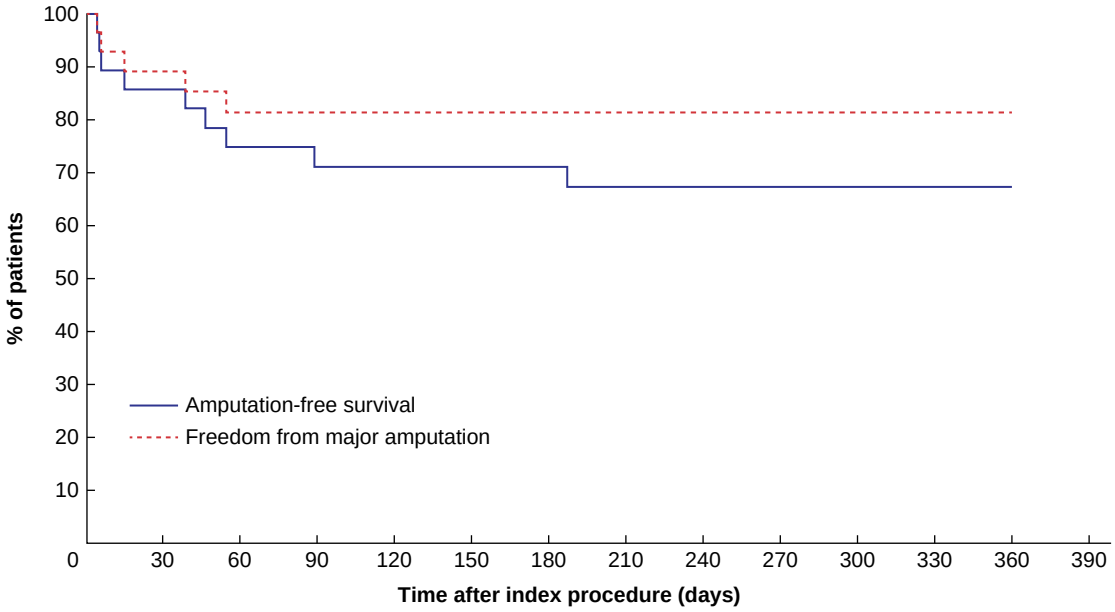
unrelated to the study device and procedure. Additional results are reported in *Tables S2 and S3* (*supplementary material*).

At 1 year, 17 of 17 patients had fully healed or almost-healed wounds with an accompanying median 1-year wound area of 0 (i.q.r. 0–0.50) cm^2.

During the 1-year follow-up, 12 of 28 patients underwent 17 clinically driven reinterventions to restore patency of the arterialized pedal vein circuit or to address worsening ischaemia (*supplementary material*).

Discussion

The PROMISE-UK study was a national prospective cohort study undertaken among established vascular centres in the UK NHS,



No. at risk													
Amputation-free survival	28	24	20	20	19	19	19	18	18	18	18	18	6
Freedom from major amputation	28	24	20	20	19	19	19	18	18	18	18	18	6

Fig. 2 One-year amputation-free survival and freedom from amputation

Kaplan–Meier estimates of amputation-free survival and freedom from major amputation during 1-year follow-up.

assessing the safety and effectiveness of the TADV procedure using the LimFlow® system. PROMISE-UK demonstrated an AFS rate of 67% and limb salvage rate of 81% at 1 year in a group of patients presenting with Rutherford 5 and 6 symptomatology, and who were deemed not to be candidates for conventional endovascular or surgical approaches. The results confirm the feasibility of delivering this treatment in the NHS in a pragmatic environment, with acceptable safety and high rates of limb salvage in no-option CLTI patients who would likely have required a major limb amputation.

The PROMISE-UK outcomes demonstrate consistency with a growing body of global evidence on the safety and efficacy of TADV with the LimFlow® system[12–14]. Previous pilot studies[12,13] evaluating the use of LimFlow® in Europe, Asia, and the USA reported a 70–71% AFS limb salvage rate at 1 year, and 2-year limb salvage rate of 80%. Additionally, the PROMISE II pivotal study (in the USA) reported a 66% AFS rate at 6 months with no unanticipated safety concerns[14], and sustained outcomes with a 69% limb salvage rate at 12 months[16].

Overall, the PROMISE-UK results compare favourably with the amputation and mortality outcomes for this population of no-option patients when no intervention is offered. The CLariTI Study[17], a prospective natural history of no-option CLTI patients, assessed outcomes of patients who did not receive treatment using the LimFlow® TADV system and reported much lower 1-year rates of AFS (32.6%) and limb salvage (48.4%). In light of the CLariTI outcomes, conducting an RCT of TADV *versus* no intervention would constitute a significant ethical dilemma given the available data demonstrating higher AFS and limb salvage rates with the LimFlow® system. The PROMISE studies provide evidence to support the use of LimFlow® TADV in achieving limb salvage in this group of no-option CLTI patients[13,14].

PROMISE-UK emphasizes the importance of strict and frequent patient follow-up (particularly in the early stages) to achieve optimal outcomes. Early and frequent imaging with duplex ultrasonography paired with close clinical monitoring allows assessment of the maturation of the TADV arterialized deep venous network, and guides the staging of any optimization procedures, such as embolization of proximal venous branches stealing blood flow away from the distal tissue or management of inflow/outflow stenoses. This approach may have been a major contributing factor to achieving a limb salvage rate of 81% at 1 year with a notably high wound healing rate.

The findings of this study are of particular interest and applicability to the NHS and UK healthcare, as well as similar systems. Despite advances in healthcare, the number of amputations owing to PAD is rising in certain patient groups within the NHS, such as those with diabetes or people with multiple long-term conditions[1,18,19]. Of note, the National Institute for Health and Care Excellence (NICE)[15] has recently recommended TADV for CLTI in people with limited treatment options, to be used with special arrangements for clinical governance, consent, and audit or research. The PROMISE-UK study provides important data on the use of the procedure within the NHS and a template for adherence to NICE guidance, including close monitoring and follow-up of patients, and early interventions to achieve satisfactory outcomes.

TADV with the LimFlow® system appears to represent a safe and effective limb salvage technique in selected no-option CLTI patients. This multicentre prospective study demonstrated a limb salvage rate of 81% with complete or near-complete wound healing at 1 year in a high-risk group of patients who were at high risk of major amputation.

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Disclosure

H.Z. is a speaker/proctor/trainer for Abbott Medical, Boston Scientific, Shockwave, Bentley, Inari Medical, Gore, Cook, and Cordis. A.S. has received honoraria and lecture fees/consulting fees from Shockwave, Abbott, and Cook; educational grant support from Cook; and research funding from Shockwave, Abbott, Boston Scientific, and Angiodroid. A.D. has received lecture fees and consulting fees from Abbott Medical, Boston Scientific, and Cordis. S.L. is a proctor/trainer for LimFlow® and has received speaking fees from Shockwave Medical. N.T. has received speaking and consulting fees from Shockwave and Philips. K.S. has received consultancy and speaking fees from Shockwave Medical and Abbott Medical. The authors declare no other conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Data from this study are not openly available but are available on reasonable request with the permission of all authors and the PROMISE-UK study group.

Author contributions

Hany Zayed (Investigation, Supervision, Writing—original draft, Writing—review & editing), Athanasios Saratzis (Investigation, Writing—original draft, Writing—review & editing), Paul Moxey (Investigation, Writing—review & editing), S. Tawqeer Rashid (Investigation, Writing—review & editing), Peter Mezes (Investigation, Writing—review & editing), Athanasios Diamantopoulos (Investigation, Writing—review & editing), Symeon Lechareas (Investigation, Writing—review & editing), Joo-Young Chun (Investigation, Writing—review & editing), Michael Twigg (Investigation, Writing—review & editing), Narayanan Thulasidasan (Investigation, Writing—review & editing), and Kaji Sritharan (Investigation, Writing—original draft, Writing—review & editing).

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