Interventional procedure overview of percutaneous deep venous arterialisation for chronic limb-threatening ischaemia

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Table 1 Abbreviations

Abbreviation	Definition
AFS	Amputation-free survival
ATA	Anterior tibial artery
ATV	anterior tibial vein
AVF	Arteriovenous fistula
CI	Confidence interval
CLI	Critical limb ischaemia
CLTI	Chronic limb-threatening ischaemia
COPD	Chronic obstructive pulmonary disease
DVA	Deep venous arterialisation
IQR	Interquartile range
MACE	Major adverse coronary event
MALE	Major adverse limb event
PDVA	Percutaneous deep venous arterialisation
PopA	Popliteal artery
PopV	Popliteal vein
PTA	Posterior tibial artery
PTV	Posterior tibial vein
PA	Peroneal artery
PV	Peroneal vein
SAE	Severe adverse events
SD	Standard deviation
$TcPO_2$	Transcutaneous oxygen pressure
TPT	Tibioperoneal trunk
TPV	Tarsal pedal vein
VAST	Venous arterialisation simplified technique
WIfI	Wound, Ischemia, and foot Infection

Indications and current treatment

CLTI of the lower extremities is caused by severely narrowed or blocked arteries. It is an advanced stage of peripheral arterial disease. The severely diminished blood supply causes ischaemic pain, ulceration, tissue loss or gangrene. It is associated with high amputation and mortality rates, and poor quality of life.

CLTI usually needs treatment to re-establish blood flow to the affected area and to prevent major amputation. Treatment options include medications, endovascular interventions (such as angioplasty, stents and directional atherectomy), surgical treatments (such as bypass) or a combination of the two. Management of CLTI is described in NICE's clinical guideline on peripheral arterial disease.

What the procedure involves

This procedure uses an endovascular, minimally invasive approach. An arterio-venous fistula is created to allow venous arterialisation in the below-the-knee vasculature. The aim is to restore blood flow to the ischaemic foot.

Preoperative investigation is needed to confirm adequate pedal venous anatomy and identify a proper crossover point between the vessels.

This procedure is usually done using general anaesthesia, and with ultrasound guidance. Antegrade arterial access via in the common femoral artery and retrograde venous access via the tibial vein are established. The arterial and venous catheters are inserted and advanced to the target artery and vein (most frequently the posterior tibial artery and vein). Once both catheters are positioned at the crossover point, a needle is deployed to create an arteriovenous fistula. After balloon dilatation valvulotomy of the vein is performed, usually from the crossing point to the midfoot. Multiple stents are placed from the level of the

calcaneus to the arteriovenous crossover point, and a crossing stent is then inserted to maintain the arteriovenous fistula. This establishes retrograde blood flow down the veins which become arterialised.

Arteriography is done at the end of the procedure to visualise blood flow into the deep venous arch.

Outcome measures

Outcomes measures included technical or procedural success, clinical improvement (including wound healing), tissue oxygenation ($TcPO_2$), survival, amputation-free survival, limb salvage/amputation, patency and associated reintervention. Mortality and adverse events were also reported. The main measures used are detailed in the following paragraphs.

Technical success was defined as successful creation of AVF with PDVA and direct blood flow to the deep venous arch.

Procedural success was defined as the combination of technical success and absence of all-cause death, above-ankle amputation, or clinically driven major reintervention of the stent graft at 30 days.

Clinical improvement was defined as resolution of rest pain, tissue formation of granulation tissue/complete wound healing, or both. It also referred to a decrease in at least 1 point from baseline of the Rutherford category:

- 0: asymptomatic
- 1: mild claudication
- 2: moderate claudication
- 3: severe claudication
- 4: ischaemic rest pain
- 5: minor tissue loss
- 6: ulceration or gangrene

Wound healing: fully healed was defined as all surfaces of the wound fully epithelialised, and healing was defined as evidence of granulation tissue formation, apparent wound edge epithelialisation, and evident contraction of wound edges.

WIfI classification system was used, based on the 3 main factors (wound, ischaemia and foot infection) that have an impact on limb amputation risk. The ischaemia category focused on measuring the hemodynamic or perfusion of the patient using several different diagnostic measurements. Grades for each factor are shown below:

Wound:

- 0: no ulcer and no gangrene
- Small ulcer and no gangrene
- Deep ulcer and gangrene limited to toes
- Extensive ulcer or extensive gangrene

Ischaemia: toe pressure/$TcPO_2$:

- 0: more than 60 mmHg
- 1: 40 to 59 mmHg
- 2: 30 to 39 mmHg
- 3: less than 30 mmHg

A $TcPO_2$ value of 40 mmHg is the critical value below which wound healing is impaired and ischaemia develops. $TcPO_2$ values of 40 mmHg or above are predictive of wound healing.

Infection:

- 0: noninfected
- 1: mild (less than 2 cm cellulitis)
- 2: moderate (more than 2 cm cellulitis/purulence)
- 3: severe (systematic response/sepsis)

AFS was defined as freedom from above-ankle amputation of the index limb and freedom from all-cause mortality.

Limb salvage was referred to freedom from major amputation.

MACE included cardiac-related death, cardiac events and stroke.

MALE was defined as major amputation (transtibial or above) or major vascular reintervention (bypass graft, thrombectomy, or thrombolysis) in the index limb but not including percutaneous reinterventions.

SAE were defined as events that resulted in death, a life-threatening condition, cause either an inpatient hospitalisation or a prolonged existing hospitalisation, result in persistent or significant disability or incapacity, or require intervention to prevent permanent impairment or damage.

Evidence summary

Population and studies description

This interventional procedure overview is based on 213 patients with CLTI who had the procedure and were reported in 7 studies including 1 single-arm pivotal study, 2 single-arm pilot studies, and 4 case series. The flow chart of the literature selection process for this rapid review of the literature is shown in figure 1. The key evidence is presented in table 2 and table 3, and another 16 relevant studies are listed in table 5. Additional documentation in confidence (evidence from a single-arm, UK-based study, and evidence comparing this procedure to standard of care) provided by a company was also considered by the committee.

Studies were carried out in US, Japan, Singapore, and European countries (France, German, Italy and Netherlands). Of the 7 studies included in the main evidence, 2 studies were retrospective in nature. The recruitment period ranged from 2013 to 2022. Of the 213 patients, 141 patients were male and 72 patients were female. Their age ranged from mean 58 to 82 years in 6 studies and had a median age of 85 years in 1 study (Kum 2017). The longest follow up was

median 34 months (Schmidt 2020), followed by median 20 months (Kum 2017). In other studies follow up was limited to 6 to 12 months.

All patients had CLTI with no other options for arterial revascularisation techniques (so called ‘no-option CLTI’) because of the absence of a viable distal target vessel, viable conduit, or other comorbidities. Most studies included patients with Rutherford category 5 or 6 CLTI, and 1 study selected patients with Rutherford category 4 to 6 CLTI, with Rutherford category 4 in 1 patient (Del Giudice 2018). Notable comorbidities were, but not limited to, diabetes, hypertension and renal insufficiency. Table 2 presents study details.

Figure 1 Flow chart of study selection

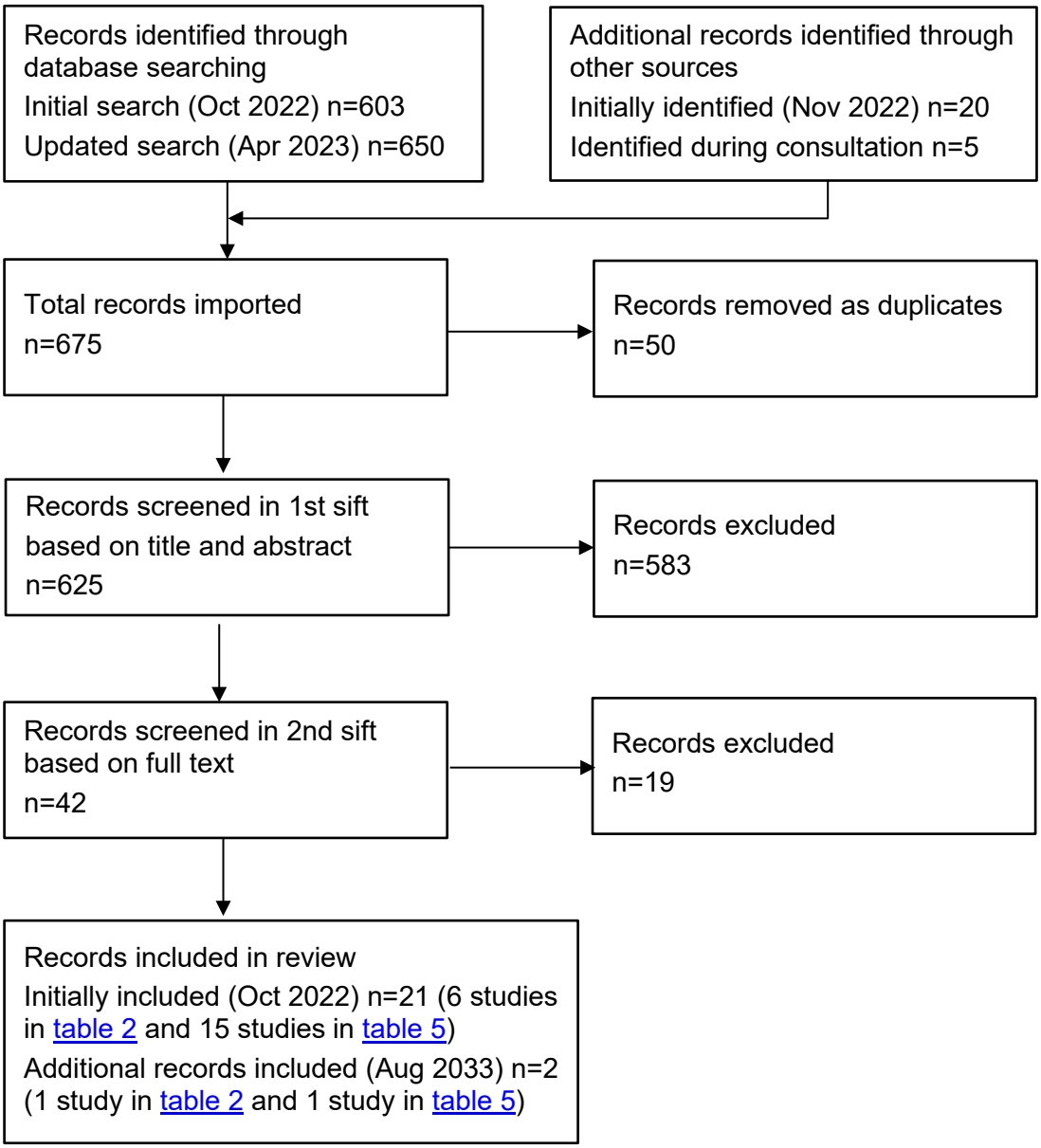

Table 2 Study details

Study no.	First author, date, country	Patients (male: female)	Age, (years)	Study design	Inclusion criteria	Intervention	Follow up
1	Shishehbor (2023) US (20 sites)	105 (72:33)	Median 70 (range 38 to 89)	Single-arm, pivotal study (PROMISE 2; NCT03970538)	Adult patients with Rutherford class 5 or 6 no-option CLTI (defined as either the absence of a pedal artery target for endovascular or surgical therapy, or the absence of a viable single segment of an autogenous vein conduit despite the presence of a pedal artery target that could receive a graft).	PDVA using the LimFlow system	12 months, with 6-month outcomes being reported
2	Clair (2021) US (7 centres)	n=32 (32 limbs) 21:11	Mean 71	Single-arm, feasibility study (PROMISE I; NCT03124875)	Adult patients with no-option CLTI (beyond medical management)	PDVA using the LimFlow system	12 months
3	Schmidt (2020) Netherlands, Germany, France and Singapore (4 centres)	n=32 (32 limbs) 20:12	Mean 67	Case series (retrospective; ALPS)	Rutherford category 5 or 6 CLTI, no angiographically evident distal target artery for endovascular therapy or a distal bypass, and at least 1 patent tibial artery in the proximal segment.	PDVA using the LimFlow system	Median 34 months (range 16 to 63)
4	Nakama (2022)	n=18 (18 limbs) 14:4	Mean 75.5	Case series (retrospective; DEPARTURE Japan)	Patients with CLTI who underwent PDVA during the study period and with tissue loss (Rutherford 5 or 6).	PDVA using ordinary devices	12 months

Study no.	First author, date, country	Patients (male: female)	Age, (years)	Study design	Inclusion criteria	Intervention	Follow up
	Japan (multiple centres)						
5	Cangiano (2021) Italy (single centre)	n=14 8:6	Mean 82	Case series	Patients with CLTI (Rutherford category 5 or 6; TASC II C-D infrapopliteal disease) who were at risk of major amputation without revascularisation; the presence of a patent posterior tibial artery vessel proximally as an inflow vessel for AVF; at least 1 prior endovascular or surgical failed attempt for revascularisation due to lesion recoil despite optimal balloon angioplasty and/or absence of a reasonable target foot vessel for bypass or angioplasty.	PDVA using Pioneer Plus for AVF creation	Mean 12 months
6	Del Giudice (2018) 2 European centres	n=5 4:1	Mean 58	Case series	CTLI Rutherford 4 to 6; severe disease associated to lack of vessel outflow; no-options patients; proximal patency of at least 1 BTK vessel	PDVA using the LimFlow system	Mean 10 months (range 1 to 21)
7	Kum (2017) Singapore (single centre)	n=7 2:5	Median 85	Open-label, single-arm pilot study	Adult patients aged 21 to 100 years with CLTI (Rutherford category 5 or 6) who were at risk of major amputation without revascularisation, had at least 1 patent tibial vessel as an inflow	PDVA using the LimFlow system or ordinary devices	Median 20 months (IQR 6 to 32)

Study no.	First author, date, country	Patients (male: female)	Age, (years)	Study design	Inclusion criteria	Intervention	Follow up
					vessel for PDVA, and had no conventional endovascular or surgical options for revascularisation due to lesion recoil despite optimal balloon angioplasty and/or absence of a reasonable target foot vessel for bypass or angioplasty.		

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Shishehbor (2023)	Technical success: 99% (104/105) Procedural success (technical success with absence of death, major amputation, or reintervention at 1 month): 76% (80/105) 6-month outcomes: • Major amputation: n=23 • AFS: 66.1% (AFS in 19 patients with dialysis-dependent CKD, 36.8%; AFS in 86 patients without dialysis-dependent CKD, 72.7%) • Limb salvage: 76.0% (n=67) • Survival: 87.1% • Primary patency: 25.9% (19/23) • Primary-assisted patency: 45.4% (34/44)	Death at 6 months: n=12 (with 5 deaths considered in relation to COVID-19) No unanticipated adverse device-related events were reported and 93% (98/105) of patients had 1 or more adverse events: • Blood and lymphatic system disorders: n=8 (7.6%) • Cardiac disorders: n=19 (18.1%) • Endocrine disorders: n=2 (1.9%) • Gastrointestinal disorders: n=11 (10.5%) • General disorders and administration site conditions: n=27 (25.7%)

First author, date	Efficacy outcomes	Safety outcomes
	• Secondary patency: 64.2% (50/59) • Reintervention (to address native arterial disease and flow optimisation within the transcatheter arterialization circuit): 36.5% (38/104) • Decrease in Rutherford class (1 class or greater): 42% (27/64) Median primary wound area: baseline, 3.9 cm^2 (IQR 1.7 to 9.3); 6 months, 1.0 cm^2 (IQR 0.0 to 3.6) Wound healing at 6 months: • Target wound complete healing: 25% (16/63) • Target wound in the process of healing: 51% (32/63) All wound complete healing: 28% (24/86)	• Hepatobiliary disorders: n=1 (1.0%) • Immune system disorders: n=1 (1.0%) • Infections and infestations: n=36 (34.3%) • Injury, poisoning and procedural complications: n=20 (19.0%) • Investigations: n=5 (4.8%) • Metabolism and nutrition disorders: n=6 (5.7%) • Musculoskeletal and connective tissue disorders: n=7 (6.7%) • Nervous system disorders: n=4 (3.8%) • Product issues: n=4 (3.8%) • Psychiatric disorders: n=2 (1.9%) • Renal and urinary disorders: n=9 (8.6%) • Respiratory, thoracic and mediastinal disorders: n=9 (8.6%) • Skin and subcutaneous tissue disorders: n=12 (11.4%) • Surgical and medical procedures: n=32 (30.5%) • Vascular disorders: n=42 (40.0%)
Clair (2021)	**Technical success**: 97% (31/32) Technical failure: 4% (1/32) related to an inability to achieve venous access beyond the ankle **Procedural success**: 75% (24/32)	Not reported

First author, date	Efficacy outcomes	Safety outcomes
	AFS rate: • 30 days: 91% • 6 months: 74% • 12 months: 70% **WIfI scoring**: • Mean wound scores: baseline, 1.81; 6 months, 0.81; 12 months, 0.74; 24 months, 0.42 • Mean ischaemia scores: baseline, 2.23; 6 months, 1.35; 12 months, 1.07; 24 months, 0.44 • Mean foot infection scores: baseline, 0.75; 6 months, 0.19; 12 months, 0.11; 24 months, 0.00 Core lab-adjudicated **wound healing** status of 'fully healed' or 'healing': • 6 months: 67% (14/21) • 12 months: 75% (15/20) **Minor amputations**: n=19 in 15 patients • Toe amputations: n=7 • Ray amputations: n=2 • Trans-metatarsal amputations: n=10 **Reintervention** (plain balloon angioplasty, drug-coated balloons, drug-eluting stents, cutting balloon, or atherectomy) rate: 52% (16/31) with 88% (14/16) of the maintenance reinterventions occurring within the first 3 months. Most reinterventions (n=12; 75%) involved the arterial inflow tract proximal to the stented LimFlow circuit, and no in-stent stenoses were determined to have been the cause of reintervention.	

First author, date	Efficacy outcomes	Safety outcomes
Schmidt (2020)	**Technical success**: 97% (31/32) Technical failure: 3% (1/32) because the target vein did not respond to aggressive balloon dilation, which precluded stent-graft implantation. This patient was excluded from further analysis. **AFS estimates**: • 6 months: 83.9% (95% CI 71.9% to 97.9%) • 12 months: 71.0% (95% CI 56.7% to 88.9%) • 24 months: 67.2% (95% CI 52.4% to 86.2%) **Survival estimates**: • 6 months: 93.5% (95% CI 85.3% to 100%) • 12 months: 83.9% (95% CI 71.9% to 97.9%) • 24 months: 80.2% (95% CI 67.2% to 95.8%) **Limb salvage estimates**: • 6 months: 86.8% (95% CI 75.5% to 99.7%) • 12 months: 79.8% (95% CI 66.6% to 95.7%) • 24 months: 79.8% (95% CI 66.6% to 95.7%) All major amputations were done within 9 months of the procedure. **Complete wound healing**: • Estimated rate at 24 months: 72.7% (95% CI 49.6% to 85.3%) • Estimate rates at 6 and 12 months: 36.6% and 68.2% • Median time to complete wound healing: 4.9 months (range 0.5 to15)	Non-fatal myocardial infarction within 30 days: n=2 Death: n=7 due to progression of foot sepsis (n=1), a perforated diverticulum of the bowel despite laparotomy (n=1), myocardial infarction (n=2), pneumonia (n=2), and exacerbation of COPD (n=1) Adverse events: • Bleeding from a superficial vein adjacent to the granulating wound at 6 months: n=1 • Infection of the stent-graft at 10 weeks: n=1 • New wound on the forefoot at 8 months: n=1

First author, date	Efficacy outcomes	Safety outcomes
	Among the 21 patients who remained alive without amputation, the majority (18, 85.7%) had completely healed wounds at 12 months. **$TcPO_2$**: Mean number of TcPO2 measurements per patients: 10.9 • Baseline, 14.5±12.7 mmHg (median 11, range 3 to 37; n=13); after 2 years, 56.1±11.9 mmHg (median 57.5, range 36 to 72; n=6) This became statistically significantly higher after 45 days (increase of 22.1 mmHg, p=0.027) and remained statistically significantly higher during follow up (increase of 41.7 mm Hg, p<0.001) compared with baseline. **DVA circuit occlusion**: n=21 with a median of 2.6 months to occlusion **Reintervention:** • Reintervention for occlusion: n=17 (16 because of unhealed wounds and 1 for a newly developed ulcer) • Reintervention for asymptomatic stenosis: n=2 • Reintervention techniques: thrombolysis (n=6), mechanical thrombectomy (n=9), DCB angioplasty (n=10), and stenting (n=5).	
Nakama (2022)	**Technical success**: 88.9% (16/18) Reason for procedural failure: valvulotomy failure (5.6%; n=1) and AVF creation failure (5.6%; n=1) 30-day **major amputation** rate: 22.2% (n=4) Causes: uncontrollable ischaemia, 16.7% (n=3); uncontrollable infection, 5.6% (n=1); occlusion within 30 days, 22.2% (n=4) **Limb salvage** rates at 6 and 12 months: 72.2% and 72.2%	Major complication (compartment syndrome due to massive haematoma): n=1 fasciotomy and haematoma evacuation was needed for limb salvage.

First author, date	Efficacy outcomes	Safety outcomes
	Overall survival rates at 6 and 12 months: 88.0% and 76.4% **Amputation free survival** rates at 6 and 12 months: 55.6% and 49.4% **Freedom from MALE** rates at 6 and 12 months: 55.6% and 50.0% **Complete wound healing** rates at 6 and 12 months, 23.0% and 53.2%; median time to complete wound healing, 234 days (IQR 127 to 306)	
Cangiano (2021)	**Technical success**: 100% **$TcPO_2$**: median number of measurements per patient, 12 (range 2 to 16) • Baseline, median 8±2 mmHg (range 4 to 32); 6 months, median 56±4 mmHg (range 48 to 75) • $TcPO_2$ value of 40 mmHg or more: 78.6% (11/14) **Clinical improvement**: 100% • Complete wound healing: 6 months, 64.3% (9/14); 12 months: 78.6% (11/14); median healing time, 4.8 months **Primary patency**: median 8 months (range 3 to 12); In one patient, at 3-months follow-up presented occlusion of AVF that was successfully treated with venous thrombectomy. **Minor amputation** of 1 or more toes: 78.6% (11/14) **Major amputations**: n=3; limb salvage, 78.6%	MALE at 30 days: n=0 ST-elevation myocardial infarction (right coronary artery disease) after 2 weeks from PDVA: n=1 Death at 6 months: n=3, each unrelated to the procedure (1 patient died for a neurological complication after a fall in the ward, and 2 patients died for of pneumonia after 5 and 6 months from procedure).
Del Giudice (2018)	**Technical success**: 100% with arterial-venous crossing, AVF creation and direct arterial flow to venous plantar arch. Mean procedure time: 248±45 minutes Mean fluoroscopy time: 76±15 minutes	No major and minor complications or procedure-related death was reported in the periprocedural period. MACE at 6 and 12 months: 20% (n=1)

First author, date	Efficacy outcomes	Safety outcomes
	$TcPO_2$: baseline, 10±2 mmHg; 4 weeks, 35±5 mmHg; 6 months, 43±4 mmHg; 12 months, 54±3 mmHg **Immediate resolution of rest pain**: 100% **Clinical improvement**: 60% (n=3); of whom 2 patients presented complete wound healing at 6 and 7 months, respectively. **Primary patency** at 6 months: 40% (n=2) **Reintervention** at 6 months: 60% (n=3) **Major amputation** at 6 months: 20% (n=1; a Rutherford 6 patient with extensive gangrene had a worsening of the clinical status with osteomyelitis at 6 months, despite the successful creation of the AF and a coiling reintervention of great saphenous collaterals.)	SAE at 6 and 12 months: 80% (n=4) Death: n=1 from multiple organ failure due to a sepsis related to pneumonitis within 1 months after the procedure
Kum (2017)	**Technical success**: 100%, with flow to the plantar venous arch achieved in 5 of 7 patients. **Clinical improvement:** • Formation of granulation: n=7 • Immediate resolution of rest pain: n=2 Complete wound healing: • 6 months: n=4 • 12 months: n=5, with a median healing time of 4.6 months (95% CI 84 to 192). Thermography was improved in all patients. **Median time to loss of primary patency**: 3.3 months (IQR 1.9 to 6.8) **Reintervention** to maintain patency: n=5, occlusions were addressed using percutaneous mechanical thrombectomy and drug-coated balloons to re-establish patency.	MALE within 30 days: n=0, but 2 patients had medical treatment for non-ST-elevation MIs. Perioperative deaths associated with the procedure: n=0 Spontaneous retroperitoneal bleeding: n=1 at 8 weeks, probably from anticoagulation. Death at 12 months: n=3, unrelated to the device or procedure. Swelling: n=7

First author, date	Efficacy outcomes	Safety outcomes
	Minor amputation of 1 or more toes: n=5 **Major amputations** within 12 months: n=2 (limb salvage, 71%) **$TcPO_2$**: Median number of $TcPO_2$ measurements per patients: 13 (IQR 4 to 17) • Baseline: median 8 mmHg (IQR 3 to 27); postprocedure, median 61 mmHg (IQR 50 to 76); p=0.046; in 5 of the 6 patients, the value was >40 mm Hg. • The $TcPO_2$ levels appeared to rise 2 to 4 weeks after treatment and were mostly >40 mm Hg at 6 to 8 weeks after treatment. By the time of wound healing in 5 patients, the median $TcPO_2$ was 59 mmHg (IQR 36 to 67); 4 of these patients had values >40 mmHg.	

Procedure technique

All 7 studies detailed the procedure technique and devices used, although there was variation. In general, this procedure was done with ultrasound and fluoroscopic guidance, and using general anaesthesia, or local anaesthesia and conscious sedation. Once the location for arteriovenous connection was determined, the AVF was created either using a specific device (the LimFlow system) or using alternative techniques (VAST, modified VAST, arteriovenous spear technique, or the use of re-entry devices [such as OUTBACK, Pioneer Plus]). The arteriovenous connection was located at PTA/PA-PTV, ATA-ATV, ATA-TPV, PopA-PopV/PTV, or TPT-PV. Valvulotomy was performed using a dedicated valvulotome (from LimFlow) or a (cutting) balloon, and stents were deployed to reinforce the arteriovenous connection and to increase distal limb perfusion. Different types of stents were used. Angiography was done to visualise blood flow into the ischaemic tissue in the foot at the end of the procedure.

Efficacy

Technical or procedural success

Technical or procedural success was described in all 7 studies. The rate of technical success was 89% (16/18; Nakama 2022), 97% (31/32; Clair 2021; Schmidt 2020), 99% (104/105; Shishehbor 2023) and 100% (Kum 2017; Del Giudice 2018; Cangiano 2021). The rate of procedural success was 75% (24/32; Clair 2021) and 76% (80/105; Shishehbor 2023).

Clinical improvement

Clinical improvement, including wound healing, was reported in all studies. Shishehbor (2023) described that all wounds were completely healed in 28%

(24/86) of patients at 6 months. Target wounds were completely healed in 25% (16/63) of patients and were in the process of healing in 51% (32/63) of patients.

Clair (2021) reported that core lab-adjudicated wound healing status of 'fully healed' or 'healing' was 67% (14/21) at 6 months and 75% (15/20) at 12 months. The authors also found that there was a decreasing mean WIfI score for each of the following 3 factors:

- Mean wound scores:
  - baseline, 1.81
  - 6 months, 0.81
  - 12 months, 0.74
  - 24 months, 0.42.
- Mean ischaemia scores:
  - baseline, 2.23
  - 6 months, 1.35
  - 12 months, 1.07
  - 24 months, 0.44.
- Mean foot infection scores:
  - baseline, 0.75
  - 6 months, 0.19
  - 12 months, 0.11
  - 24 months, 0.00.

Schmidt (2020) described that, of the 32 patients, the estimated rate of complete wound healing was 37% at 6 months, 68% at 12 months and 73% at 24 months. The median time to complete wound healing was 4.9 months (range 0.5 to 15). Nakama (2022) reported that, of the 18 patients, complete wound healing rates were 23% at 6 months and 53% at 12 months, with a median time to complete wound healing of 234 days (IQR 127 to 306).

Cangiano (2021) reported clinical improvement in all 14 patients. The rate of complete wound healing was 64% (9/14) at 6 months and 79% (11/14) at 12 months, with a median healing time of 4.8 months. Del Giudice (2018) observed clinical improvement in 60% (3/5) of patients; of these, 2 patients had complete wound healing at 6 and 7 months, respectively. Kum (2017) described that clinical improvement was observed in all 7 patients with the formation of granulation; 2 of these patients had immediate resolution of rest pain. The authors also reported that the rate of complete wound healing was 57% (4/7) at 6 months and 71% (5/7) at 12 months, with a median healing time of 4.6 months (95% CI 84 to 192).

Tissue oxygenation assessed by $TcPO_2$

$TcPO_2$ values were presented in 4 studies. Schmidt (2020) reported that mean $TcPO_2$ statistically significantly increased from 14.5±12.7 mmHg (n=13) at baseline to 56.1±11.9 mmHg (n=6) after 2 years. The authors stated that this became statistically significantly higher after 45 days (increase of 22.1 mmHg, p=0.027) and remained statistically significantly higher during follow up (increase of 41.7 mmHg, p<0.001) compared with baseline. Kum (2017) described that tissue perfusion was recorded in 6 of the 7 patients. Median $TcPO_2$ values statistically significantly increased from 8 mmHg (IQR 3 to 27) before the procedure to 61 mmHg (IQR 50 to 76) after the procedure (p=0.046); in 5 of the 6 patients, a $TcPO_2$ value of more than 40 mmHg was achieved.

Cangiano (2021) found that median $TcPO_2$ increased from 8±2 mmHg (range 4 to 32 mmHg) at baseline to 56±4 mmHg (range 48 to 75 mmHg) at 6 months, with a $TcPO_2$ value of 40 mmHg or more in 79% of the 14 patients. Del Giudice (2018) described that, of the 5 patients, $TcPO_2$ increased from 10±2 mmHg at baseline to 35±5 mmHg at 4 weeks, 43±4 mmHg at 6 months, and 54±3 mmHg at 12 months.

Survival and AFS rates

Survival and AFS rates were reported in 4 studies. Shishehbor (2023) found that the rates of AFS and survival at 6 months were 66% and 87%, respectively. According to Bayesian analysis, the posterior probability that AFS exceeded a performance goal of 54% was 0.993, which exceeded the prespecified threshold of 0.977.

Clair (2021) reported that the AFS rate was 74% at 6 months and 70% at 12 months. Schmidt (2020) estimated that the AFS rate was 84% at 6 months, 71% at 12 months and 67% at 24 months. In addition, the authors reported that the overall survival rate was 94% at 6 months, 84% at 12 months and 80% at 24 months. Nakama (2022) described AFS rates of 56% at 6 months and 49% at 12 months. The authors also reported the overall survival rate was 88% and 76% at 6 and 12 months, respectively.

Limb salvage and amputations

Limb salvage or amputations were detailed in all 7 studies. Shishehbor (2023) described that the rate of limb salvage was 76% at 6 months, with major amputation in 23 patients. Schmidt (2020) estimated the rate of limb salvage was 87%, 80% and 80% at 6, 12 and 24 months, respectively. Nakama (2022) reported a limb salvage rate of 72% at both 6 and 12 months, and a freedom from MALE rate of 56% at 6 months and 50% at 12 months. Kum (2017) found a limb salvage rate of 71% (5/7), with major amputations in 2 patients within 12 months and minor amputation of 1 or more toes in 5 patients. Cangiano (2021) reported a limb salvage rate of 79% (11/14) within 6 months, with major amputations in 3 patients. Del Giudice (2018) reported that major amputation was needed in 1 patient. Clair (2021) reported 19 minor amputations in 15 of the 32 patients, including 7 toe amputations, 2 ray amputations and 10 trans-metatarsal amputations.

Patency and reintervention

Patency and reintervention were described in 6 studies. Shishehbor (2023) found that, at 6 months, the rates of primary patency, primary-assisted patency, and secondary patency were 26%, 45%, and 64%, respectively. Repeat interventions to address native arterial disease and flow optimisation within the transcatheter arterialisation circuit were done in 37% (38/104) of patients.

Clair (2021) reported that the rate of reintervention was 52% (16/31), with 88% (14/16) of the maintenance reinterventions being done within the first 3 months. Most reinterventions (n=12; 75%) involved the arterial inflow tract proximal to the stented circuit, and no in-stent stenoses were determined to have been the cause of reintervention.

Schmidt (2020) reported DVA circuit occlusion in 21 patients, with a median of 2.6 months to occlusion. The authors also noted that 17 patients had reintervention for occlusion (16 because of unhealed wounds and 1 for a newly developed ulcer) and that 2 patients had reintervention for asymptomatic stenosis.

Cangiano (2021) described a median time of primary patency of about 8 months (range 3 to 12), and 1 patient at 3 months follow up presented with occlusion of the AVF that was successfully treated with venous thrombectomy.

Del Giudice (2018) reported that primary patency remained in 2 patients and reintervention was done in 3 patients at 6 months.

Kum (2017) described that the median time to loss of primary patency was 3.3 months (IQR 1.9 to 6.8). The authors also reported that reintervention to maintain patency was done in 5 patients.

Safety

Mortality

Mortality was described in 5 studies. Shishehbor (2023) reported death in 12 patients at 6 months (with 5 deaths considered to be related to COVID-19). Schmidt (2020) reported death in 7 of the 32 patients because of progression of foot sepsis (n=1), a perforated diverticulum of the bowel despite laparotomy (n=1), myocardial infarction (n=2), pneumonia (n=2), and exacerbation of COPD (n=1). Cangiano (2021) reported death in 3 of the 14 patients at 6 months; these events were unrelated to the procedure. Del Giudice (2018) reported death in 1 of the 5 patients within 1 month after the procedure and this was caused by multiple organ failure because of sepsis related to pneumonitis. Kum (2017) reported death in 3 of the 7 patients at 12 months, but these events were unrelated to the device or procedure.

Myocardial infarction

Schmidt (2020) described that non-fatal myocardial infarction within 30 days was reported in 2 of the 32 patients. Cangiano (2021) reported that ST-elevation myocardial infarction (right coronary artery disease) was experienced in 1 of the 14 patients 'after 2 weeks from the procedure'. Kum (2017) found that 2 of the 7 patients had medical treatment for non-ST-elevation myocardial infarction.

Major and severe adverse events

Nakama (2022) reported a major complication (compartment syndrome because of massive haematoma) in 1 patient who needed fasciotomy and haematoma evaluation for limb salvage. Del Giudice (2018) reported MACEs at 6 and 12 months in 1 patient (1/5) and SAEs at 6 and 12 months in 4 patients (4/5).

Other events

Shishehbor (2023) reported that there were no unanticipated adverse device-related events and that 93% (98/105) of patients had 1 or more adverse events.

Schmidt (2020) reported bleeding from a superficial vein adjacent to the granulating wound at 6 months (n=1), infection of the stent graft at 10 weeks (n=1), and a new wound on the forefoot at 8 months (n=1).

Kum (2017) described spontaneous retroperitoneal bleeding in 1 patient at 8 weeks (probably from anticoagulation) and some degree of swelling in all 7 patients.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following anecdotal and/or theoretical adverse events: pain, venous congestion, arterial injury, stent thrombosis, vessel dissection, distal embolisation, contrast nephropathy, and potential for high-output cardiac failure.

Six professional expert questionnaires for this procedure were received. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

Evidence came from both experimental and observational studies. The total sample size was small. No studies that were carried out in the UK were identified for inclusion in the key evidence. Two studies (Schmidt 2020; Nakama 2022) were retrospective, so recall bias was possible. The follow-up duration was short- to medium-term across studies.

Patients who had no-option CLTI were included. However, the term ‘no-option CLTI’ was not well, consistently defined across studies, resulting in several selection biases. It was suggested that no-option CLTI should be defined by quantitative evaluation (Nakama 2022).

Studies were conducted in difference countries, with some in multiple centres. There might be differences in treatment, such as provision of medical therapy and attentive wound care. It was acknowledged that a comprehensive multi-disciplinary approach to wound care is an essential aspect of the care pathways for this patient population. In addition, post-operational management (including wound care) is important but was only described in 2 studies (Clair 2021; Giudice 2020). Furthermore, there was variation in the procedure technique and devices used. Both the specific endovascular DVA system and ordinary ('off-the-shelf') devices were used for this procedure. It was also noted that this is a technically challenging procedure, particularly relating to AVF creation. This indicates that the experiences of individual operators (interventional cardiologists and vascular surgeons) in performing this procedure play an important role in the success of the treatment. However, operators’ experiences were briefly mentioned in 3 studies only (Shishehbor 2023; Clair 2021; Schmidt 2020). All these factors ultimately affected the efficacy and safety outcomes.

One of the papers included in the key evidence reported that study was funded by a company (Shishehbor 2023). Declarations of interest were reported by 1 or more authors in 5 papers (Shishehbor 2023; Clair 2021; Schmidt 2020; Kum 2017; Nakama 2022).

Overall, evidence on the efficacy showed that the rate technical success ranged from 89% to 100%, the median time to complete wound healing ranged from 4.6 months to 7.8 months, and AFS rates ranged from 56% to 84% at 6 months, 49% to 71% at 12 months, and 67% at 24 months after the procedure. None of the studies reported quality of life outcomes.

The rates of technical success and AFS were lower, and time to wound healing was longer in Nakama (2022) than other studies included in the key evidence. Nakama (2022) argued that PDVA using alternative techniques and non-commercial-based devices (but not the LimFlow system) was performed, and this might have an impact on the key steps of AVF creation and valvulotomy. Also, patients with poorer background might affect the outcomes.

Given the current evidence base, further evaluation of this procedure, and in particular evidence with a longer-term follow up, is warranted. It is worth noting that there are currently several ongoing trials, detailed below:

- PROMISE International; NCT03321552; multiple centres, clinical trial (single group assignment, open-label); actual enrolment, n=35; estimated study completion date, January 2023.
- The PROMISE II Trial, Percutaneous Deep Vein Arterialization for the Treatment of Late-Stage Chronic Limb-Threatening Ischemia (PROMISE); NCT03970538; multi-centre pivotal study (single group assignment, open label); estimated enrolment, n=120; estimated study completion date, February 2025.
- PROMISE III: Percutaneous Deep Vein Arterialization for the Treatment of Late-Stage Chronic Limb-Threatening Ischemia; NCT05313165; clinical trial (single group assignment, open label); estimated enrolment, n=100; estimated study completion date, May 2027.
- Percutaneous Deep Vein Arterialization Post-Market Study (PROMISE UK); NCT03807661; UK, clinical trial (single group assignment, open-label); estimated enrolment, n=25; estimated study complete date, July 2023.
- Natural Progression of High-Risk Chronic Limb-Threatening Ischemia: The CLariTI Study; NCT04304105; US, observational cohort study (patient registry); actual enrolment, n=200; estimated study completion date, October 2023.

Related NICE guidance

Interventional procedures:

Interventional procedures guidance on superficial venous arterialisation for chronic limb threatening ischaemia (published: 24 August 2022).
Recommendation: special arrangements

NICE guidelines

NICE clinical guideline on peripheral arterial disease: diagnosis and management (published: August 2012; Last updated: 11 December 2020)

NICE guideline on diabetic foot problems: prevention and management (2015) (published: August 2015; Last updated: 11 October 2019)

Professional societies

- Vascular Society of Great Britain and Ireland
- European Society for Vascular Surgery
- British Society for Endovascular Therapy
- British Society for Interventional Radiology.

Evidence from patients and patient organisations

NICE did not receive submissions from patient organisations about percutaneous deep venous arterialisation for chronic limb-threatening ischaemia. NICE received 3 questionnaires from patients who had the procedure.

Patients' views on the procedure were consistent with the published evidence and the opinions of the professional experts.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Shishehbor MH, Powell RJ, Montero-Baker MF et al. (2023) Transcatheter arterialisation of deep veins in chronic limb-threatening ischemia. The New England journal of medicine, 388 (13): 1171-80
2. Clair DG, Mustapha JA, Shishehbor M H et al. (2021) PROMISE I: Early feasibility study of the LimFlow System for percutaneous deep vein arterialization in no-option chronic limb-threatening ischemia: 12-month results. Journal of vascular surgery 74(5): 1626-35
3. Schmidt A, Schreve MA, Huizing E et al. (2020) Midterm outcomes of percutaneous deep venous arterialization with a dedicated system for patients with no-option chronic limb-threatening ischemia: The ALPS multicenter study. Journal of endovascular therapy: an official journal of the International Society of Endovascular Specialists 27(4): 658-65
4. Nakama T, Ichihashi S, Ogata K et al. (2022) Twelve-month clinical outcomes of percutaneous deep venous arterialization with alternative techniques and ordinary endovascular therapy devices for patients with chronic limb-threatening ischemia: results of the DEPARTURE Japan study. Cardiovascular and interventional radiology 45(5): 622-32
5. Cangiano G, Corvino F, Giurazza F et al. (2021) Percutaneous deep foot vein arterialization IVUS-guided in no-option critical limb ischemia diabetic patients. Vascular and endovascular surgery 55(1): 58-63
6. Del Giudice C, Van Den Heuvel D, Wille J et al. (2018) Percutaneous deep venous arterialization for severe critical limb ischemia in patients with no option of revascularization: early experience from two European centers. Cardiovascular and interventional radiology 41(10): 1474-80
7. Kum S, Tan YK, Schreve MA et al. (2017) Midterm outcomes from a pilot study of percutaneous deep vein arterialization for the treatment of no-option critical limb ischemia. Journal of endovascular therapy: an official journal of the International Society of Endovascular Specialists 24(5): 619-26

Methods

NICE identified studies and reviews relevant to percutaneous deep venous arterialisation for CLTI from the medical literature. The following databases were searched between the date they started to 12 April 2023: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with CLTI.
- Intervention or test: PDVA.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	12/04/2023	1946 to April 11 2023
MEDLINE In-Process (Ovid)	12/04/2023	1946 to April 11 2023
MEDLINE Epubs ahead of print (Ovid)	12/04/2023	April 11 2023
EMBASE (Ovid)	12/04/2023	1974 to 2023 April 11
EMBASE Conference (Ovid)	12/04/2023	1974 to 2023 April11
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	12/04/2023	4 of 12 2023
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	12/04/2023	4 of 12 2023
International HTA database (INAHTA)	12/04/2023	INAHTA

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

1 Peripheral Arterial Disease/
2 Arteriosclerosis Obliterans/
3 Thromboangiitis Obliterans/
4 ((peripheral adj4 arter* adj4 diseas*) or (arterioscler* adj4 obliterans) or (thromboang* adj4 obliterans) or buerger*).tw.
5 (CLI or CLTI).tw.
6 exp Ischemia/ and Lower Extremity/
7 ((Critical or chronic) adj4 limb* adj4 isch*).tw.
8 (desert adj4 foot).tw.

9 Aneurysm/ and Popliteal Artery/
10 ("Popliteal arter* aneurysm*" and thrombos* and distal).tw.
11 or/1-10
12 ((percutaneous or endovascular*) adj4 deep adj4 (vein* or venous) adj4 (arterialisation or arterialization)).tw.
13 percutaneous DVA.tw.
14 endovascular* DVA.tw.
15 (pDVA or eDVA).tw.
16 Arteriovenous Fistula/
17 (Arterio-venous fistula* or arteriovenous fistula* or A-V fistula* or AVF).tw.
18 (Arterio-venous aneurysm* or arteriovenous aneurysm* or A-V aneurysm*).tw.
19 (Arterio-venous connect* or arteriovenous connect* or A-V connect*).tw.
20 (Limb* adj4 (sparing or spare or save or saving or salvag* or preserv*) adj4 (technique* or method* or procedure*)).tw.1189
21 or/12-20
22 11 and 21
23 LimFlow.tw.
24 22 or 23
25 animals/ not humans/
26 24 not 25

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Clair D and Gibbons M (2021) A review of percutaneous deep vein arterialization for the treatment of nonreconstructable chronic limb threatening ischemia. Seminars in vascular surgery 34(4): 188-94	Review	Patients with no-option CLTI are at an extremely high risk for amputation along with its associated increases in morbidity and mortality. Both the ALPS multicentre study and the PROMISE I multicentre early feasibility study have shown encouraging results for these patients with high rates of limb salvage and wound healing, comparable with previous reports. Further research with larger patient populations is needed to assess the use of percutaneous DVA in patients with no-option CLTI, in order to improve our understanding and management of this disease. The PROMISE II trial is currently enrolling patients to provide information regarding the use of this technology in a larger group of patients and we look forward to the outcomes of this trial.	Review article
Choinski KN, Stafford NJ, Rao AG et al. (2022) The feasibility and applicability of	Review	PDVA is a novel intervention to promise wound healing and amputation-free survival in patients with CLTI. This therapy should be reserved	Review article

percutaneous deep vein arterialization in peripheral artery disease. Surgical technology international 40: 271-279		for patients with end-stage peripheral arterial disease with no alternative endovascular intervention or targets for open bypass. Outcomes from early feasibility trials and authors centre's personal experience with PDVA are encouraging in terms of technical success and limb salvage. However, current data is limited, and patients are still at high risk for complications given their progressive disease, needing close monitoring and coordinated wound care. Further investigation of the technique in multiple centres, with increased number of patients, and long-term follow up is warranted to better understand the feasibility and outcomes for patients undergoing PDVA.	
Gandini R, Merolla S, Scaggiante J et al. (2018) Endovascular distal plantar vein arterialisation in dialysis patients with no-option critical limb ischemia and posterior tibial artery occlusion: a technique for limb salvage in a challenging patient subset. Journal of Endovascular Therapy 25(1) 127–32	Case series n=9 Follow up: mean 6 months	Although further investigations are required, distal plantar venous arterialization may represent a promising technique to improve recanalization rates and limb salvage in diabetic, end-stage renal disease patients with extremely calcified PTA occlusions.	Small sample and short follow up
Ho VT, Gologorsky R, Kibrik P et al. (2020) Open, percutaneous, and	Review	This review provides an up-to-date review of DVA indications, description of various DVA techniques,	Review article

hybrid deep venous arterialization technique for no-option foot salvage. Journal of vascular surgery 71(6): 2152-60		patient selection associated with each approach, and outcomes for each technique.	
Hurwitz M, Bowens N, Miller A et al. (2023) Bilateral percutaneous deep venous arterialisation in an immunosuppressed lung transplant patient with no-option critical limb threatening ischemia. Annals of Vascular Surgery – Brief Reports and Innovations, 3	Case report n=1	PDVA has evolved into a viable therapy for revascularization in select patients with no option CLTI, even in the setting of multiple comorbid conditions and immunosuppression. Patients undergoing PDVA require close monitoring and strict follow-up, often with the need for secondary interventions. Further studies are necessary to identify those who are most likely to benefit from this procedure.	Small sample
Ichihashi S, Shimohara Y, Bolstad F et al. (2020) Simplified endovascular deep venous arterialization for non-option cli patients by percutaneous direct needle puncture of tibial artery and vein under ultrasound guidance (AV spear technique). Cardiovascular and interventional radiology 43(2): 339-43	Case report n=1	the AV spear technique can facilitate the pDVA for non-option CLI patients without the need for a dedicated ultrasonic catheter, re-entry device, or covered stents, making it widely applicable in many countries. However, this is a single case report and larger studies are necessary to evaluate the efficacy of the technique.	Single case report
Karimi A, Lauria AL, Aryavand B et al. (2022) Novel therapies for critical limb-threatening ischemia. Current	Review	Recent advancements in the treatment options of CLTI will likely lead to reducing the rate of major amputations if they are adopted in a collaborative environment in order to apply the most	Review article

cardiology reports 24(5): 513-517		appropriate treatment option to each individual patient based on the anatomy, comorbidities, functional status, and local expertise.	
Kutsenko O, Nasiri A, Maguire MJ et al. (2022) Technical approach to percutaneous femoropopliteal bypass and deep vein arterialization. Techniques in vascular and interventional radiology 25(3): 100843	Review	In the management of patients with CLI, endovascular revascularisation plays a crucial role improving amputation free survival, ischemic rest pain, and wound healing. Although angioplasty and stenting are well established techniques and considered a standard of care, they may fail or achieve suboptimal results in a subset of CLI patients. Alternative techniques such as percutaneous femoropopliteal bypass and deep vein arterialization should be considered by endovascular specialists for long-segment arterial occlusions and patients without distal revascularisation target prior to amputation, respectively.	Review article
Lechareas S, Sritharan K and McWilliams RG (2021) Early and eighteen month clinical outcomes of first UK case of percutaneous deep vein arterialisation (pDVA) to treat “no option” chronic limb-threatening ischemia using the LimFlow system. CVIR Endovascular 4:62	Case report n=1	This case report demonstrates the clinical outcomes of a technically-successful standardised pDVA procedure with the LimFlow system including both limb salvage and wound healing at 18 months. It also highlights the importance of close clinical and radiological surveillance post-index procedure and the requirement for re-interventions to optimise wound healing.	Single case report
Migliara B, Mirandola M, Griso A et al. (2020)	Case report	PDVA can be considered an alternative treatment in patients with “no-option” CLI,	Single case report

Totally percutaneous deep foot vein arterialization in a patient with no-option critical limb ischemia, scheduled for bilateral major amputation. Journal of vascular and interventional radiology: JVIR 31(9): 1505-7	n=1	provided that it is performed in compliance with defined technical key points and associated with specific foot surgery.	
Mustapha JA, Saab FA, Clair D et al. (2019) Interim results of the PROMISE I trial to investigate the LimFlow system of percutaneous deep vein arterialization for the treatment of critical limb ischemia. The Journal of invasive cardiology 31(3): 57-63	PROMISE I (interim results) n=10 Follow up: 6 months	PDVA using the LimFlow system is a novel approach for treating patients with no-option CLI and may reduce amputation in this population for whom it would otherwise be considered inevitable. Initial findings from this early feasibility trial are promising and additional study is warranted.	PROMISE I is included in the key evidence.
N'Dandu Z, Bonilla Jo, Yousef GM et al. (2021) Percutaneous deep vein arterialization: An emerging technique for no-option chronic limb-threatening ischemia patients. Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions 97(4): 685-90	Case report n=1	This study presented a case of a patient with no-option CLTI, at high risk of amputation who failed conventional endovascular revascularisation attempts facing imminent major amputation. The limb was salvaged with a successful PDVA procedure.	Single case report

Pua U and Huang IKH (2019) Percutaneous deep vein arterialization. Journal of vascular and interventional radiology: JVIR 30(4): 610-613	Case report n=1	DVA using off-the-shelf endovascular devices represents a potential last-ditch limb salvage technique in patients with CLI and no other treatment options.	Single case report
Schreve MA, Unlu C, Kum S et al. (2017) Surgical and endovascular venous arterialization: ready to take the "desert" by storm? The Journal of cardiovascular surgery 58(3): 402–8	Review	Venous arterialisation may be a viable alternative to preserving limbs. The percutaneous approach shows promise and is a minimally invasive technique to reduce surgical stress in patients with CLI.	Review article
Yan Q, Prasla S, Carlisle DC et al. (2022) Deep venous arterialization for chronic limb threatening ischemia in atherosclerosis patients – a meta-analysis. Annals of vascular surgery, 1-21	Meta-analysis n=442 (455 limbs; 12 studies)	Venous arterialisation has an acceptable a 1-year limb salvage rate of 79%, however, this is based on low levels of evidence. More randomized controlled trials or high-quality cohort studies are needed to further define the effectiveness of this procedure for CLTI.	6 studies (2 in the key evidence and 4 in the appendix) described PDVA but outcomes for this procedure were not reported separately.
Ysa, August, Lobato, Marta, Mikelarena, Ederi et al. (2019) Homemade device to facilitate percutaneous venous arterialization in patients with no-option critical limb ischemia. Journal of endovascular therapy: an official journal of the	Case series n=5 follow up: 6 months	The described manoeuvres may be a useful option for creating a percutaneous AVF during a venous arterialization procedure in no-option CLI patients. Larger series with follow-up examinations are required to confirm the safety and effectiveness of this technique.	Small sample

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