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Revascularisation of Chronic Limb Threatening Ischaemia in Patients with no Pedal Arteries Leads to Lower Midterm Limb Salvage☆

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WHAT THIS PAPER ADDS

The impact of chronic occlusion of pedal arteries (no patent pedal arteries, N-PPAs) in patients with chronic limb threating ischaemia (CLTI) is not well established in the literature. In this analysis, N-PPA was present in almost one third of patients ($n = 218$) revascularised for CLTI. Although survival, technical success, and primary patency of a proximal revascularisation was not hampered by N-PPA, this condition led to significantly lower midterm limb salvage compared with patients with at least one patent pedal artery. These results should be considered when defining the indications for revascularisation in patients with N-PPA in the clinical practice.

Objective: Chronic limb threatening ischaemia (CLTI) involving the infragenicular arteries is treated by distal angioplasty or pedal bypass; however, this is not always possible, due to chronically occluded pedal arteries (no patent pedal artery, N-PPA). This pattern represents a hurdle to successful revascularisation, which must be limited to the proximal arteries. The aim of the study was to analyse the outcome of patients with CLTI and N-PPA after a proximal revascularisation.

Methods: All patients with CLTI submitted to revascularisation in a single centre (2019 − 2020) were analysed. All angiograms were reviewed to identify N-PPA, defined as total obstruction of all pedal arteries. Revascularisation was performed with proximal surgical, endovascular, and hybrid procedures. Early and midterm survival, wound healing, limb salvage, and patency rates were compared between N-PPA and patients with one or more patent pedal artery (PPA).

Results: Two hundred and eighteen procedures were performed. One hundred and forty of 218 (64.2%) patients were male, mean age 73.2 ± 10.6 years. The procedure was surgical in 64/218 (29.4%) cases, endovascular in 138/218 (63.3%), and hybrid in 16/218 (7.3%). N-PPA was present in 60/218 (27.5%) cases. Eleven of 60 (18.3%) cases were treated surgically, 43/60 (71.7%) by endovascular and 6/60 (10%) by hybrid procedures. Technical success was similar in the two groups (N-PPA 85% *vs.* PPA 82.3%, $p = .42$). At a mean follow up of 24.5 ± 10.2 months, survival (N-PPA 93.7 ± 3.5% *vs.* PPA 95.3 ± 2.1%, $p = .22$) and primary patency (N-PPA 53.1 ± 8.1% *vs.* PPA 55.2 ± 5%, $p = .56$) were similar. Limb salvage was significantly lower in N-PPA patients (N-PPA 71.4 ± 6.6% *vs.* PPA 81.5 ± 3.4%, $p = .042$); N-PPA was an independent predictor of major amputation (hazard ratio [HR] 2.02, 1.07 − 3.82, $p = .038$) together with age > 73 years (HR 2.32, 1.17 − 4.57, $p = .012$) and haemodialysis (2.84, 1.48 − 5.43, $p = .002$).

Conclusion: N-PPA is not uncommon in patients with CLTI. This condition does not hamper technical success, primary patency, and midterm survival; however, midterm limb salvage is significantly lower than in patients with PPA. This should be considered in the decision making process.

Keywords: Chronic limb threatening ischaemia, Endovascular treatment/therapy, Pedal arteries, Percutaneous transluminal angioplasty, Peripheral artery disease, Peripheral bypass

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INTRODUCTION

Chronic limb threatening ischaemia (CLTI) is the end stage of peripheral artery disease (PAD) and is associated with a significant mortality rate, pain, reduced quality of life,[1] and also a high long term amputation rate,[2] which can be as high as 67%.[3] The anatomical distribution of arterial disease is crucial to define the revascularisation technique and

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establishing a direct line flow to the foot is an important technical aim.[1]

For involvement of the infragenicular arteries, treatment options include distal endovascular angioplasty or surgical bypass to the foot; as a matter of fact, the majority of pedal arch anatomies are suitable for revascularisation, but some patients present challenging patterns. The occlusion of all named arteries of the foot such as the dorsalis pedis, dorsal metatarsal, common medial, and lateral plantar arteries (Fig. 1) is considered a high risk CLTI subgroup.[4] In fact, this pattern is often a no option disease and represents a serious hurdle to the success of the revascularisation, which has to be limited to more proximal arteries. The impact of total occlusion of the pedal arteries (no patent pedal arteries, N-PPAs), on the success of more proximal revascularisation is not well established in the literature.

The aim of this study was to analyse a series of patients with CLI and N-PPA, submitted to proximal revascularisation in order to determine rate and predictors of success.

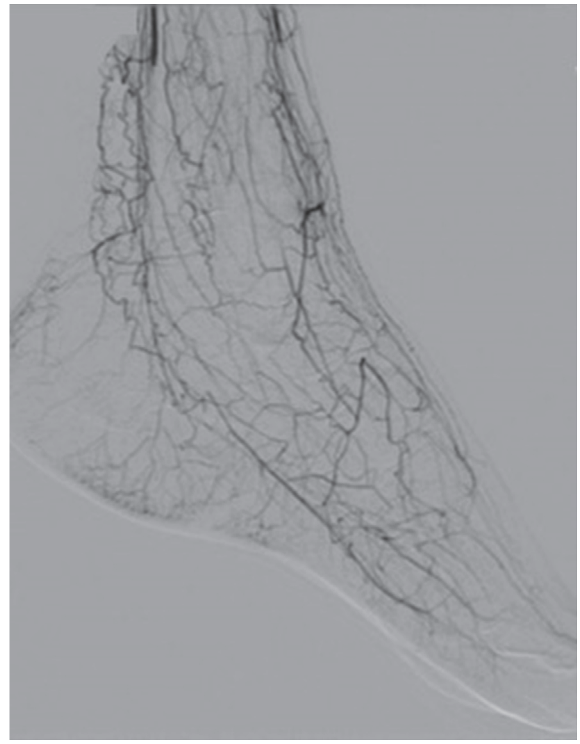


Figure 1. One case of no patent pedal arteries at pre-operative lower limb angiography.

MATERIALS AND METHODS

Patient selection

All patients with CLTI submitted to peripheral revascularisation between January 2019 and December 2020 were analysed retrospectively.

CLTI, $\geq$ grade 4 in the Rutherford classification, was defined as peripheral artery disease (PAD) associated with rest pain and gangrene or lower limb ulceration present for more than two weeks.[1]

All lower limb pre-operative angiograms were examined retrospectively, and patients were divided into two groups: patients with at least one patent pedal artery (PPA) and patients with no patent pedal arteries (N-PPAs). According to the Global Limb Staging System (GLASS), the pedal modifier system (P0, P1, and P2) was used to describe inframalleolar and pedal disease status; all patients with a P2 status (no target artery crossing ankle into foot) were selected for the N-PPA group.

A comparison between N-PPA and PPA in terms of pre-operative characteristics, procedural and post-operative outcome, as well as midterm results was performed.

All patients signed informed consent before treatment as usual practice. All data used in the retrospective analysis were anonymous and processed according to the institute's guidelines and conformed to the ethical guidelines of the 1975 Declaration of Helsinki (and following modifications).

Pre-operative characteristics

An accurate medical history was obtained, inclusive of patient demographics (sex, age), comorbidities and hypertension (defined as presence of systolic blood pressure $>$ 140 mmHg or diastolic blood pressure $>$ 90 mmHg), dyslipidaemia (defined as total cholesterol level $>$ 200 mg/dL or low density lipoprotein level $>$120 mg/dl or specific therapy), diabetes mellitus (pre-diagnosed on therapy with oral hypoglycaemic drugs or insulin), coronary artery disease (defined as a history of angina pectoris, myocardial infarction or coronary revascularisation), chronic obstructive pulmonary disease (defined as chronic bronchitis or emphysema), active smoker, chronic kidney disease (defined as glomerular filtration rate $<$ 60 mL/min), dialysis (defined as the need for renal replacement therapy), obesity (defined as a body mass index $>$ 30), and atrial fibrillation (paroxysmal or permanent). The severity of limb threatening ischaemia was stratified using the Wound, Ischaemia and Foot Infection (WIFi grading) system according to the most recent European Society for Vascular Surgery (ESVS) CLTI guidelines.[1]

Diagnosis

All patients with infra-inguinal peripheral arterial disease underwent a pre-operative arterial duplex ultrasound (DUS) performed by a vascular surgeon. DUS examination was performed from groin to foot evaluating the extent of disease. If a surgical treatment with bypass was planned, during the DUS evaluation the diameter and the quality of the wall of the proximal and distal target vessels were analysed; the run off resistances were also evaluated in the tibial arteries in order to identify the best target vessels for distal anastomosis.[5] The examination was extended to the iliac arteries if the flow detected at the level of the common femoral artery was abnormal. All patients underwent pre-operative selective arterial angiography performed from the ipsilateral common femoral artery; for severe kidney disease pre-operative angiography was performed with carbon dioxide. Computed tomography angiography was performed in selected cases of iliac and femoropopliteal lesions.

The Global Limb Anatomic Staging System (GLASS)[1] was used to define the complexity of the preferred target arterial path.

Procedural outcome

The revascularisation technique (surgical, endovascular, or hybrid) was chosen considering the arterial disease extent, the patient surgical risk, the availability of autologous veins, and the severity of the lesions in terms of tissue loss and infection.

Revascularisation types were stratified into surgical (femoral endarterectomy, femoropopliteal or femoro—infrapopliteal bypass), endovascular (plain or drug eluting balloon [DEB] angioplasty), and hybrid (femoral endarterectomy combined with percutaneous transluminal angioplasty (PTA) or femoropopliteal bypass combined with tibial PTA) procedures. All procedures were performed by a minimum of two qualified vascular surgeons in a dedicated Philips hybrid room (Philips Healthcare, Best, The Netherlands) for endovascular manoeuvres with general, spinal, or locoregional anaesthesia according to the clinical characteristics of the patient. All patients underwent a preventive broad spectrum antibiotic infusion and intraoperative systemic heparinisation (60 — 80 UI/kg)

Percutaneous transluminal angioplasty

Percutaneous ipsilateral femoral access was obtained under DUS guidance; surgical access or percutaneous contralateral access was performed for common femoral artery disease. Visipaque iodinate contrast (General Electric Health Care Inc.) was generally used; for moderate to severe kidney disease pre- and post-operative hydration with bicarbonate was administrated and the amount of Visipaque administration during the procedure was reduced. According to the experience at the centre, some procedures were performed using carbon dioxide angiography with a CO_2 automated injector (Angiodroid, San Lazzaro, Bologna srl), for moderate or severe chronic kidney disease (estimated glomerular filtration rate < 60 mL/min) and the patient not on chronic haemodialysis.[6] An 11 cm long 6F sheath was placed; arterial lesions were crossed with an angled 5F catheter Vert and 0.014 guidewire. The lesions were treated with increasing diameter balloons up to the normal diameter of the healthy vessel; in selected patients with diabetes or restenosis, DEBs were used in femoropopliteal lesions. The procedure was completed with stent placement in rare cases of endovascular treatment of long femoropopliteal occlusions according to surgeon preference; no tibial stents were used. A final angiogram was performed routinely to document the effectiveness of the procedure. Haemostasis of percutaneous access was obtained with manual compression and subsequent DUS to evaluate the presence of groin haematomas. The location of treated lesions, whether femoropopliteal and or tibial, was reported.

Femoral Endarterectomy

All patients underwent broad spectrum antibiotic infusion and systemic heparinisation (60 — 80 UI/kg). Common femoral artery or femoral bifurcation endarterectomies were performed using a standard technique and were usually closed with a bovine pericardial or Dacron patch.

Surgical bypass

The ipsilateral great saphenous vein was the first choice material; alternatively, the contralateral saphenous vein and composite saphenous and arm veins. Synthetic polytetrafluoroethylene (PTFE) grafts were used for femoropopliteal bypass above the knee. A completion angiogram was always performed. The type of conduit used, and the sites of proximal and distal anastomosis were collected.

Hybrid procedures

These treatments included femoral endarterectomy combined with PTA or femoropopliteal bypass combined with tibial PTA as described above.

Digital or forefoot amputation

At the end of the revascularisation procedure debridement of necrotic tissue or minor amputations (digital or forefoot) were performed depending on the extent of the gangrene. For suspected tissue infection, amputation margins were not sutured as a first step; deep tissue biopsies were performed for microbiological analysis to achieve a complete healing from the infective process and allow final closure of the wound.

Technical success

Technical success (TS) was defined as patency of the treated arteries — those above the ankle in case of N-PPA — on final angiogram ($>$ 50% of the lumen) for endovascular treatment and patent bypass with in line flow to the distal arteries on the final angiogram and without anastomotic haemodynamic defects on post-operative DUS for surgical treatment.

Post-operative outcomes (30 day)

Post-operative death was defined as the death of the patient within 30 days from the intervention. Post-operative primary patency was defined as post-operative patent graft or treated vessels without morphological stenosis $>$ 50% of the lumen and without peak systolic velocity ratio $>$ 2.0. Post-operative major amputation was defined as the need for transfemoral (above the knee) or transtibial amputation at 30 days.

Midterm outcome

Late survival was defined as the survival rate at the end of the study period. Primary patency was defined as a patent graft or treated vessels without morphological stenosis $>$ 50% of the lumen and without peak systolic velocity ratio

Table 1. Pre-operative characteristics of all patients with peripheral artery disease and chronic limb threatening ischaemia (n= 218)

	Total (n = 218)	N-PPA (n= 60)	PPA (n= 158)	p value
Age – y	73.2 ± 10.6	75.4 ± 10.3	72.4 ± 10.6	.61
Male sex	140 (64.2)	34 (56.7)	106 (67.1)	.15
Right leg	114 (52.3)	30 (50)	84 (53.2)	.47
Cigarette smoking	34 (15.6)	5 (8.3)	29 (18.4)	.093
Hypertension	201 (92.2)	57 (95)	144 (91.1)	.52
Hypercholesterolaemia	159 (72.9)	40 (66.7)	119 (75.3)	.23
Diabetes mellitus	125 (57.3)	29 (48.3)	88 (55.7)	.10
Coronary artery disease	91 (41.7)	19 (31.7)	72 (45.6)	.062
Chronic obstructive pulmonary disease	68 (31.2)	19 (31.7)	49 (31)	1.0
Atrial fibrillation	49 (22.4)	14 (23.3)	35 (22.2)	.25
Obesity – BMI ≥ 30	42 (19.2)	10 (16.9)	32 (20.3)	.70
Chronic kidney disease – stages 1–4	123 (56.4)	27 (45)	88 (55.7)	.29
Haemodialysis	50 (22.9)	10 (16.7)	40 (25.5)	.20
ASA				.43
2	6 (2.8)	3 (5)	3 (1.9)	
3	108 (49.5)	28 (46.6)	80 (50.6)	
4	104 (47.7)	29 (48.3)	75 (47.4)	
Rutherford classification category				.87
4	15 (6.9)	5 (8.3)	10 (6.3)	
5	128 (58.7)	37 (61.6)	91 (57.5)	
6	75 (34.4)	19 (31.6)	56 (35.4)	
WIfI classification grade				.76
1	5 (2.3)	1 (1.7)	4 (2.5)	
2	33 (15.1)	9 (15)	24 (15.2)	
3	68 (31.2)	16 (26.7)	52 (32.9)	
4	112 (51.4)	34 (56.7)	78 (49.4)	
GLASS stage				.48
I	49 (22.5)	13 (21.7)	36 (22.8)	
II	88 (40.4)	21 (35)	67 (42.4)	
III	81 (37.2)	26 (43.3)	55 (34.8)	

Data are presented as n (%) or mean ± standard deviation. N-PPA= no patent pedal artery; PPA = patent pedal artery; BMI = body mass index; ASA = American Society of Anesthesiologists; WIfI = Wound, Ischemia and Foot Infection; GLASS = Global Limb Anatomic Staging System.

> 2.0. Limb salvage was defined as no need for major amputation during the follow up.

A Cox model was used to identify possible predictors of major amputation. Wound healing was defined as the complete resolution of trophic lesions or the complete healing of the surgical incision for minor amputations.

All patients underwent clinical and DUS examination before discharge to verify bypass patency, the quality of the runoff or the absence of re-stenosis for endovascular treatment. The follow up program included DUS examinations at one, three, six, 12 months, and yearly thereafter. Wound healing and absence of rest pain were also considered.

Statistical analysis

All categorical variables were expressed as frequencies and compared using Fisher's exact test; continuous variables were expressed with mean ± standard error and compared using Student t test. Late survival, wound healing, and limb salvage rate were evaluated using Kaplan–Maier curves and compared using the log rank test. Cox's proportional hazards model, expressed with hazard ratio (HR) and 95% confidence interval (CI), was used to identify predictors of major amputation. A Cox regression model was used to identify the independent risk factors for multivariable analysis. A p value < .10 on univariable analysis was considered the criterion for inclusion in the model. In all the statistical tests $p \leq .05$ was considered statistically significant. Statistical analysis was performed using SPSS 23.0 for Apple (SPSS Inc, Chicago, IL, USA).

RESULTS

In the study period, 218 patients with PAD and CLTI were revascularised in a single tertiary centre with a mean age of 73.2 ± 10.6 years; 140/218 (64.2%) patients were male and 125/218 (57.3%) were diabetic. Two hundred and three of 218 (93.1%) were classified as Rutherford category 5 – 6 at their admission.

Analysis of pre-operative angiograms returned 60/218 (27.5%) cases of N-PPA and 158/218 (72.5%) cases of PPA patterns in pedal vascularisation. Fifty-six of 60 (93.3%) patients with N-PPA presented with Rutherford category 5 – 6. One of 60 (1.7%) patients presented with WIfI stage 1, 9/60 (15%) patients with stage 2, 16/60 (26.7%) with stage 3, and 34/60 (56.7%) with stage 4. Thirteen of 60 (21.7%)

Table 2. Details of all procedures in patients (n = 218) with peripheral artery disease and chronic limb threatening ischaemia

	Total (n= 218)	N-PPA (n= 60)	PPA (n= 158)	p value
Angioplasty (PTA) only	138 (63.3)	43 (71.7)	95 (6.1)	.086
Femoropopliteal PTA	95 (43.6)	30 (50)	65 (41.2)	1.0
Tibial PTA	130 (59.6)	42 (70)	88 (55.7)	.82
Drug eluting balloon PTA	20 (9.1)	2 (3.3)	18 (11.3)	.030*
PTA stenting	4 (1.8)	0	4 (2.5)	.30
Surgical bypass only	64 (29.4)	11 (18.3)	53 (33.5)	.083
Femoropopliteal bypass	45 (2.6)	8 (13.3)	37 (23.4)	1.0
Femorotibial bypass	15 (6.8)	4 (6.6)	11 (6.9)	.44
Popliteotibial bypass	8 (3.6)	0	8 (5)	.33
Hybrid procedure	16 (7.3)	6 (10)	10 (6.3)	.085
Femoral endarterectomy + PTA	12 (5.5)	5 (8.3)	7 (4.4)	1.0
Bypass + PTA	4 (1.8)	1 (1.6)	3 (1.9)	1.0
Venous graft bypass	34 (15.6)	5 (8.3)	29 (18.3)	.75
PTFE graft bypass	34 (15.6)	7 (11.6)	27 (17)	.75
Minor amputations	117 (53.6)	33 (55)	84 (53.1)	.95
Digital amputations	103 (47.2)	29 (48.3)	74 (46.8)	
Forefoot amputations	14 (6.4)	4 (6.6)	10 (6.3)	

Data are presented as n (%). N-PPA = no patent pedal artery; PPA = patent pedal artery; PTA = percutaneous transluminal angioplasty; PTFE = polytetrafluoroethylene.
* $p < .05$ considered statistically significant.

patients presented with GLASS stage I, 21/60 (35%) with stage II, and 26/60 (43.3%) with stage III.

The pre-operative characteristics of all patients are reported in Table 1.

Procedural outcome and technical success

The patients underwent revascularisation with a surgical procedure in 64/218 (29.4%) cases, an endovascular procedure in 138/218 (63.3%) cases, and a hybrid procedure in 16/218 (7.3%) cases. All procedural details are reported in Table 2. There were no differences in terms of surgical approach between the two populations except from the PTA with DEB, which was significantly less frequent in N-PPA population (2/60, 3.3%, N-PPA *vs.* 18/158, 11.3%, PPA, p = .030).

In the N-PPA subgroup, 11/60 (18.3%) cases were treated surgically, 43 (71.7%) by endovascular techniques and six (10%) with hybrid procedures. Toe and forefoot amputations were performed intra-operatively in 29 (48.3%) and four (6.6%) cases respectively.

Technical success was achieved overall in 181/218 (83%) patients, with no significant differences between N-PPA and PPA groups (TS 51/60, 85%, N-PPA *vs.* 130/158, 82.3%, PPA, p = .42).

Post-operative outcome

Thirteen of 218 (6%) patients had died by 30 days, with no significant differences between the N-PPA and PPA groups in terms of post-operative mortality rate (1/60, 1.7%, N-PPA *vs.* 12/158, 7.6%, PPA, p = .11). Post-operative primary patency was 100% (181/181) in all cases in which technical success was reached. Moreover, the post-operative amputation rate was similar between the N-PPA and PPA populations (3/60, 5%, N-PPA *vs.* 11/158, 7%, p= .76).

Midterm outcome

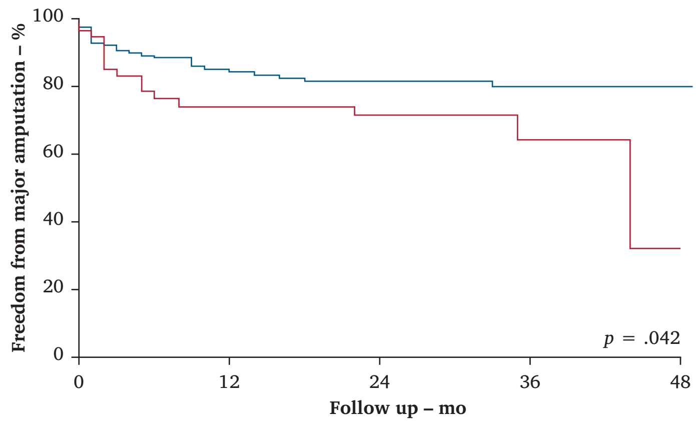
At a mean follow up of 24.5 ± 10.2 months, the overall survival was 94.9± 1.8%. The overall primary patency in those patients in whom technical success was reached was 54.8± 4.3%. Overall wound healing was 39.6± 4.5% and mean wound healing time was 10.2± 7.5 months. The overall limb salvage was 78.8± 3.1% at the same mean follow up time.

At log rank evaluation, there were no significant differences between N-PPA and PPA groups in terms of midterm survival (N-PPA 93.7 ± 3.5% *vs.* PPA 95.3 ± 2.1%, p = .22), primary patency (N-PPA 53.1 ± 8.1% *vs.* PPA 55.2 ± 5%, p = .56) in patients in whom technical success was achieved, and wound healing (N-PPA 40.4 ± 8.9% *vs.* PPA 40.2 ± 5.1%, p = .67). Furthermore, the mean time to wound healing was similar between the two populations (N-PPA 9.8 ± 3 *vs.* PPA 10.8 ± 4.2 months, p = .52). The limb salvage rate was significantly lower in the N-PPA than PPA group (N-PPA 71.4 ± 6.6% *vs.* PPA 81.5 ± 3.4%, p = .042), as reported in Figure 2.

Table 3 shows the major amputation risk factors on univariable analysis; patient age > 73 years (HR 2.12, 95% CI 1.08 − 4.18, p = .032), chronic haemodialysis treatment (HR 2.33, 95% CI 1.23 − 4.40, p = .009), and the presence of N-PPA (HR 1.85, 95% CI 0.99 − 3.46, p = .040) were all significant. On multivariable analysis, patient age > 73 years (HR 2.32, 95% CI 1.17 − 4.57, p = .012), haemodialysis treatment (HR 2.84, 95% CI 1.48 − 5.43, p = .002) and N-PPA (HR 2.02, 95% CI 1.07 − 3.82, p = .038) were independent risk factors for major amputation (Table 4).

DISCUSSION

This single centre analysis showed the clinical outcomes of revascularisation in patients with total occlusion of the pedal arteries (N-PPA). According to this analysis,



No. at risk					
PPA	158	100	78	39	2
Estimates ± SE – %	100	84.2 ± 3.1	81.5 ± 3.4	79.9 ± 3.7	79.9 ± 3.7
N-PPA	60	31	26	8	1
Estimates ± SE – %	100	74 ± 6.3	71.4 ± 6.6	64.3 ± 9	32.1 ± 23.2

Figure 2. Cumulative Kaplan–Meier estimate of mid-term limb salvage rate in patent pedal artery (PPA) and no patent pedal artery (N-PPA) groups. SE = standard error.

approximately one quarter of the population undergoing lower limb revascularisation had N-PPA. Other studies in the literature showed a comparable rate of N-PPA in patients with CLTI, ranging from 18% to 28 %.[7–10]

In patients with N-PPA, PTA with a DEB was used less frequently compared with PPA (2/60, 3.3%, N-PPA *vs.* 18/158, 11.3%, PPA, $p = .030$). This aspect has not been reported in the literature before. The main reason for this result can be found in the pre-operative characteristics of the two subgroups. The use of DEBs in patients with diabetes with infrapopliteal PAD is recommended due to the higher primary patency, as reported in the literature.[11,12] In this case series there were fewer patients with diabetes in the N-PPA (48.3% *vs.* 55.7% PPA) subgroup and this probably explains why a DEB was used less frequently.

According to experience, technical success of the revascularisation procedure is not affected by inframalleolar artery patency (TS 85% N-PPA *vs.* 82.3% PPA, $p = .42$); however, the quality of the pedal arch may impact the clinical outcomes, such as wound healing and limb salvage. In contrast, some studies reported a successful endovascular recanalisation of the pedal arch even for total occlusion with satisfactory immediate technical success; however, long term patency or outcome data are lacking in these case series.[13,14]

In this analysis, post-operative primary patency was 100% (181/181) in patients in whom technical success was achieved, but it was 181/218 (83%) in the overall population. Moreover, the midterm primary patency rate (in case of TS) was very similar in the N-PPA and PPA groups (N-PPA 53.1 ± 8.1% *vs.* PPA 55.2 ± 5%, $p = .56$). Similar results were reported by Rashid *et al.*,[8] who evaluated pedal arch quality in relation to limb salvage and surgical revascularisation patency rates. One hundred and fifty-four patients with CLTI underwent infrapopliteal bypass and were classified according to pedal arch quality (complete pedal arch, incomplete pedal arch, and no pedal arch; 19%, 62%, and 19% respectively); analysing the primary and assisted patency rates at 12 months, no differences between the three groups were found ($p = .51$ and $p = .80$ respectively).

Available primary patency data after endovascular recanalisation related to pedal arch patency condition are scarce. Recent studies have focused on the clinical outcomes related to complete, incomplete, or absent pedal arch patency; however, treated vessels were not followed with proper imaging to directly assess the durability of the achieved patency.[7,9,15]

Several authors have reported percutaneous deep venous arterialisation as an alternative to arterial revascularisation in patients with no patent pedal arteries.[16,17] The results in this field are promising (97% technical success among 32 patients) but should be validated in case series of larger populations with extensive short and long term outcomes.[17] Schmidt *et al.*[17] reported a 71% of freedom from amputation rate at two years after deep venous arterialisation in patients with no option CLTI, and this rate is the same as the 71% limb salvage in patients with N-PPA who underwent conventional revascularisation in the case series. This result reinforces the concept that conventional proximal revascularisation in patients with no patent pedal arteries remains effective and should be attempted before resorting to deep venous arterialisation.

In this case series, the wound healing rate was similar between the N-PPA and PPA groups (N-PPA 40.4 ± 8.9% *vs.* PPA 40.2 ± 5.1%, $p = .67$) as well as the mean time to wound healing (N-PPA 9.8 ± 3 *vs.* PPA 10.8 ± 4.2 months, $p = .52$). Several authors have found that pedal artery disease is a predictor of delayed wound healing.[7,9,18,19] A recent series by Jung *et al.*[9] analysed the impact of endovascular pedal artery revascularisation (PAR) on wound healing. This study demonstrated that successful PAR may

Table 3. Risk factors for major amputation on univariable analysis

	HR (95% CI)	*p value*
Age >73 years	2.12 (1.08–4.18)	.032*,†
Male gender	0.93 (0.67–1.30)	.69
Right leg	1.55 (0.78 – 3.82)	.99
Cigarette smoking	1.18 (0.54–2.55)	.67
Hypertension	0.81 (0.29–2.22)	.68
Hypercholesterolaemia	1.34 (0.65–2.73)	.41
Diabetes mellitus	0.76 (0.49–1.16)	.20
Coronary artery disease	0.96 (0.59–1.56)	.88
Chronic obstructive pulmonary disease	1.36 (0.73–2.53)	.32
Atrial fibrillation	1.63 (0.83–3.20)	.15
Obesity (BMI ≥30)	1.27 (0.62–2.60)	.49
Chronic kidney disease (Stage 1–4)	1.13 (0.90–1.42)	.28
Haemodialysis	2.33 (1.23–4.40)	.009*,†
ASA classification	1.31 (0.74–2.31)	.34
Rutherford classification category	1.08 (0.65–1.79)	.76
WIfI classification grade 4	1.4 (0.77–2.63)	.25
GLASS stage	1.22 (0.81–1.84)	.33
Type of treatment (endovascular, open, hybrid)	0.92 (0.56–1.50)	.74
N-PPA	1.85 (0.99–3.46)	.040*,†

73 years was used as threshold since it was the mean age of the overall population. HR = hazard ratio; CI = confidence interval; BMI = body mass index; ASA = American Society of Anesthesiologists; WIfI = Wound, Ischemia and Foot Infection; GLASS = Global Limb Staging System; N-PPA = no patent pedal artery.
* $p < .05$ considered statistically significant.
† Risk factors included in the multivariable analysis, since p value <0.10.

achieve higher rates of wound healing than infrapopliteal revascularisation alone. According to Nakama *et al.*,[7] not only is the global rate of wound healing significantly higher, but also the time to achieve complete wound healing is significantly shorter in patients submitted to pedal arch angioplasty (PAA) compared with non-PAA patients. A recent analysis[20] based on the GLASS Inframalleolar Modifier analysed the outcome of inframalleolar bypass, finding a wound healing rate of 79% in patients with P2 status; the overall wound healing rate was significantly lower than that obtained in patients with P0 and P1 status (97% and 93%, respectively), but still satisfactory. However, considering the technical difficulty and the reduced haemodynamic impact and midterm patency, as reported in the results, the role of endovascular revascularisation in the inframalleolar area remains uncertain.[1] Moreover, the inframalleolar disease modifier, according to the ESVS CLTI guidelines, is not considered within the primary assignment of limb GLASS stages, due to the absence of strong outcome evidence.

Table 4. Risk factors for major amputation on multivariable analysis

	HR (95% CI)	*p* value
Age >73 years	2.32 (1.17-4.57)	.012*
Haemodialysis	2.84 (1.48-5.43)	.002*
N-PPA	2.02 (1.07-3.82)	.038*

73 years was used as threshold since it was the mean age of the overall population. HR = hazard ratio; CI = confidence interval; N-PPA = no patent pedal artery.
* $p < .05$ considered statistically significant.

In the analysis, the limb salvage rate was significantly lower in N-PPA than in PPA groups (N-PPA 71.4 ± 6.6% *vs.* PPA 81.5 ± 3.4%, $p = .042$) at two years and N-PPA was also an independent risk factor for major amputation on multivariable analysis (HR 2.02, 95% 1.07 – 3.82, $p = .038$), confirming the trend reported by other studies that a patent pedal arch has a significant impact on limb salvage.[21] In fact, according to Ricco *et al.*,[22] freedom from amputation at three years in patients with CLTI undergoing revascularisation was 73% in patients with a patent pedal arch and 46% in patients with incomplete pedal arch. A similar trend was afterwards reported by Jung *et al.*,[9] with freedom from major amputation at a mean follow up of 644 days in 96% of patients with PPA and 84% of patients with N-PPA ($p = .009$). In contrast, Kobayashi *et al.*[20] found that pedal arch status was not related to limb salvage: analysing 204 patients submitted to inframalleolar bypass considering pedal arch status (P0 32%, P1 50%, P2 18%) the limb salvage rates were comparable (94%, 89%, 93%, respectively).

On multivariable analysis, patient age > 73 years was an independent risk factor for major amputation (HR 2.32, 95% CI 1.17 – 4.57, $p = .012$) as well as chronic haemodialysis [HR 2.84, 95% CI 1.48 – 5.43, $p = .002$). Similar results in patients with CLTI are reported in many studies in the literature. End stage renal disease requiring haemodialysis has been reported recently as an independent risk factor for major adverse limb events (odds ratio 7.43, 95%. CI 1.12 – 49.17, $p = .038$) by Zhang *et al.*[23] and for major amputation by Miyata *et al.*[24] among a large population of 2 906 patients with CLTI. Patient age is slightly more controversial in the literature; some authors, such as Kim *et al.*[25] and Weissler *et al.*,[26] found that younger patients face more frequent amputation than older patients, whereas Houghton *et al.*[27] and Abualhin *et al.*[28] reported age as a risk factor for amputation in patients with CLTI. Indeed, both age and haemodialysis are strong indicators of a patient's frailty, especially in those with CLTI and should be always considered in the revascularisation decision making process.

Due to the higher rate of major amputation, the results suggest avoiding revascularisation in patients with CLTI with N-PPA; however, the two year freedom from amputation remains acceptable (71%) in patients with N-PPA who underwent proximal revascularisation. Revascularisation is probably not worthwhile in those patients when old age and chronic haemodialysis treatment is associated with N-PPA; at that point the risk of clinical failure in terms of limb salvage is too high.

This study has several limitations. It reports a retrospective analysis of a prospectively maintained database: the retrospective nature of this study might hinder the risk of bias in collection of data on severity of lower limb ischaemia and extent of foot lesions. The revascularisation strategy was decided case by case using pre-operative imaging and after team discussion, but not using a standardised method for all patients. Moreover, revascularisation outcomes in the N-PPA and PPA groups could not be compared with controls treated with medical therapy alone. Considering the small sample, further studies are required to validate these findings: a prospective multicentre investigation with a well defined enrolment protocol should be considered in future investigations.

Conclusions

Patients with CLTI can frequently present with total occlusion of the pedal arteries in the foot that are not suitable for revascularisation.

Although the presence of this condition does not hamper the technical success and primary patency of a proximal revascularisation, midterm limb salvage in these patients is significantly lower than in patients with patent pedal arteries; these data should be considered when determining the indication for revascularisation.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

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COUP D'OEIL

Floating Thrombus after Endovascular Aneurysm Repair with a Bifurcated Stent Graft

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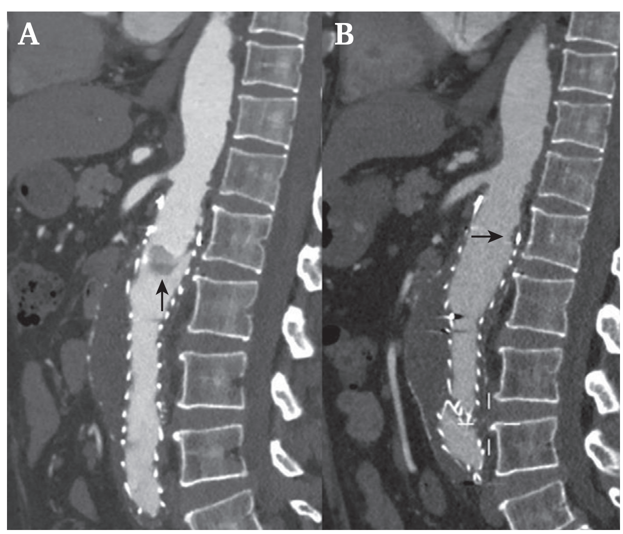

A 66-year-old male with an infrarenal abdominal aortic aneurysm confirmed by computed tomography angiography (CTA) underwent elective endovascular aortic aneurysm repair with an Aegis bifurcated stent graft (MicroPort, Shanghai, China) with 10% oversizing. He was put on dual antiplatelet therapy (aspirin 75 mg and clopidogrel 75 mg) post-operatively. At three months follow up, CTA revealed a newly pedunculated mass at the origin of the aortic stent graft (A, arrow). Dual antiplatelet therapy was continued for another six months. No symptoms of embolization occurred. Subsequent CTA examination performed six months later showed that the lesion had disappeared (B, arrow).

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