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Successful Revascularization has a Significant Impact on Limb Salvage Rate and Wound Healing for Patients with Diabetic Foot Ulcers: Single-Centre Retrospective Analysis with a Multidisciplinary Approach

António Proença Caetano[1,2,3] · Inês Conde Vasco[1,2] · Filipe Veloso Gomes[2,3] · Nuno Vasco Costa[2,3] · José Hugo Luz[2,3] · Erik Spaepen[4] · Ana Formiga[5] · Élia Coimbra[6] · José Neves[7] · Tiago Bilhim[2,3]

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Abstract

Purpose Analyze the impact of endovascular revascularization on major amputation rates and wound healing for patients with diabetic foot ulcers (DFUs).

Materials and Methods Single-center retrospective study from 2014–2018 including 314 patients with DFUs submitted to endovascular revascularizations. Group A—patients with a successful endovascular revascularization (n = 285; 90.8%); Group B—patients submitted to a failed attempt of endovascular revascularization (n = 29; 9.2%). Baseline data were not significantly different between the 2 groups ($p > 0.05$). Both groups were compared regarding: major amputation rates; wound healing, mortality and adverse events. Survival and regression analyses were used.

Results Mean follow-up time was 734.1 ± 610.2 days. Major amputation rates were 3.9% versus 24.1% ($p < 0.0001$) and complete wound healing was 53.7% versus 20.7% ($p < 0.0001$) for patients from Group A versus Group B, respectively. Major adverse events were

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✉ Tiago Bilhim
tiagobilhim@hotmail.com

António Proença Caetano
aprocaetano@gmail.com

Inês Conde Vasco
inesbcvasco@gmail.com

Filipe Veloso Gomes
fvgomes@gmail.com

Nuno Vasco Costa
nunovpc@gmail.com

José Hugo Luz
jhugoluz@gmail.com

Erik Spaepen
erik.spaepen@sbd-analytics.com

Ana Formiga
formiga.ana@hotmail.com

Élia Coimbra
elia.coimbra@gmail.com

José Neves
jnevesantunes@gmail.com

[1] Centro Hospitalar Universitário de Lisboa Central (CHULC), 1069-166 Lisbon, Portugal

[2] Interventional Radiology Unit, Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central (CHULC), 1069-166 Lisbon, Portugal

[3] Nova Medical School, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal

[4] SBD Analytics, Bekkevoort, Belgium

[5] Diabetic Foot Unit, Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central (CHULC), 1069-166 Lisbon, Portugal

[6] Head Interventional Radiology Unit, Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central (CHULC), 1069-166 Lisbon, Portugal

[7] Head of Diabetic Foot Unit, Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central (CHULC), 1069-166 Lisbon, Portugal

registered in 2 patients (one from each group); minor adverse events included 10 patients from Group A and 2 patients from Group B ($p = 0.3654$). Major amputation rates were: 3.9% versus 27.5% at 1 year; 4.6% versus 27.5% at 2–5 years for Group A versus Group B, respectively ($p < 0.0001$). Survival rates were: 87.8% at 1 year; 84.4% at 2 years; and 77.9% at 5 years with no significant differences between groups. Predictors for major amputation included failed revascularization ($p < 0.0001$), older age ($p = 0.0394$), prior stroke (0.0018), dialysis (0.0476). Predictors for mortality included older age ($p < 0.0001$) and coronary artery disease ($p = 0.0388$).

Conclusion Endovascular revascularization for patients with DFUs is safe and has a significant impact on limb salvage and wound healing.

Keywords Diabetic foot ulcers (DFUs) · Diabetic foot disease · Diabetic foot wounds · Diabetic foot infections · Ulceration of the foot · Percutaneous transluminal angioplasty (PTA) · Critical limb ischemia (CLI) · Infrapopliteal arteries · Infragenicular arteries · Peripheral artery disease · Below-the-knee disease · Major amputation · Limb salvage

Introduction

Diabetic foot ulcers (DFUs) management involves comprehensive multidisciplinary care. Currently, revascularization for improvement in tissue perfusion is an essential part of DFUs care and should be considered in any patient whose ulcer is not healing despite optimal medical management [1]. The safety and effectiveness of endovascular revascularization in patients with diabetes and critical limb ischemia has been well established [2–5]. Revascularization procedures should aim at least at restoration of direct blood flow to one of the foot arteries [5, 6]. Most of these studies are single-arm, without controls to assess the impact of revascularization and focused essentially on patients with CLI. Studies focusing specifically at outcomes in patients with DFUs using control arms are lacking to assess the magnitude of revascularization effect on limb salvage and ulcer healing [2]. The effectiveness of endovascular revascularization in patients with DFU remains difficult to determine as there are limited studies with controls and randomized trials would be impossible to implement [2]. There is the need for more data reporting the impact of revascularization strategies on limb salvage for patients with DFUs [2]. Existing literature indicates that revascularization should always be considered in patients with DFUs and ischemia. However, it still remains unclear if such procedures have any added value for all patients including patients with mild-to-moderate perfusion deficits [2]. The aim of this study was to assess the magnitude of effect that a successful endovascular revascularization had on limb salvage rate and prevention of major amputations in the diabetic population with peripheral artery disease and DFUs, using patients with failed revascularization as a control arm.

Materials and Methods

Participants

Single-center retrospective study from 2014–2018 performed at a diabetic foot unit in collaboration with the interventional radiology unit (Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central, CHULC). All patients provided written informed consent to be treated. Institutional review board approval was waived to perform this retrospective analysis. Inclusion criteria were: patients with DFUs with a diagnosis of peripheral artery disease based on the absence of palpable tibial pulses, confirmed with Doppler ultrasound and/or computed tomography angiography (CTA) that were submitted to endovascular arterial revascularization of the affected limb. After initial clinical assessment, peripheral artery disease was confirmed with dedicated vascular imaging with Doppler ultrasound and/or CTA. Revascularization was attempted for all patients with stenoses (> 50% based on pre-procedural CTA) or occlusions of the lower limb arteries and when there were no patent arteries or only just one patent artery going directly to the foot. Exclusion criteria were: patients with diabetic foot ulcers with an absolute contraindication for revascularization (coagulopathy, non-collaborative patients); patients refusing treatment; bedridden patients without clear benefit from limb salvage; patients submitted to revascularization due to peripheral artery disease but without DFUs; patients with extensive gangrene with indication for immediate major amputation; purely neuropathic DFUs with no evidence of ischemia and patients without available follow-up. The final analysis included 314 patients (Fig. 1). Included patients in the analyses were separated into two groups: Group A consisting of patients who underwent a successful endovascular revascularization of the affected limb ($n = 285$; 90.8%); Group B consisting of patients submitted to an attempt of endovascular revascularization of the affected limb without success ($n = 29$; 9.2%). Successful endovascular revascularization was considered when any artery going to the leg and/or foot that was previously

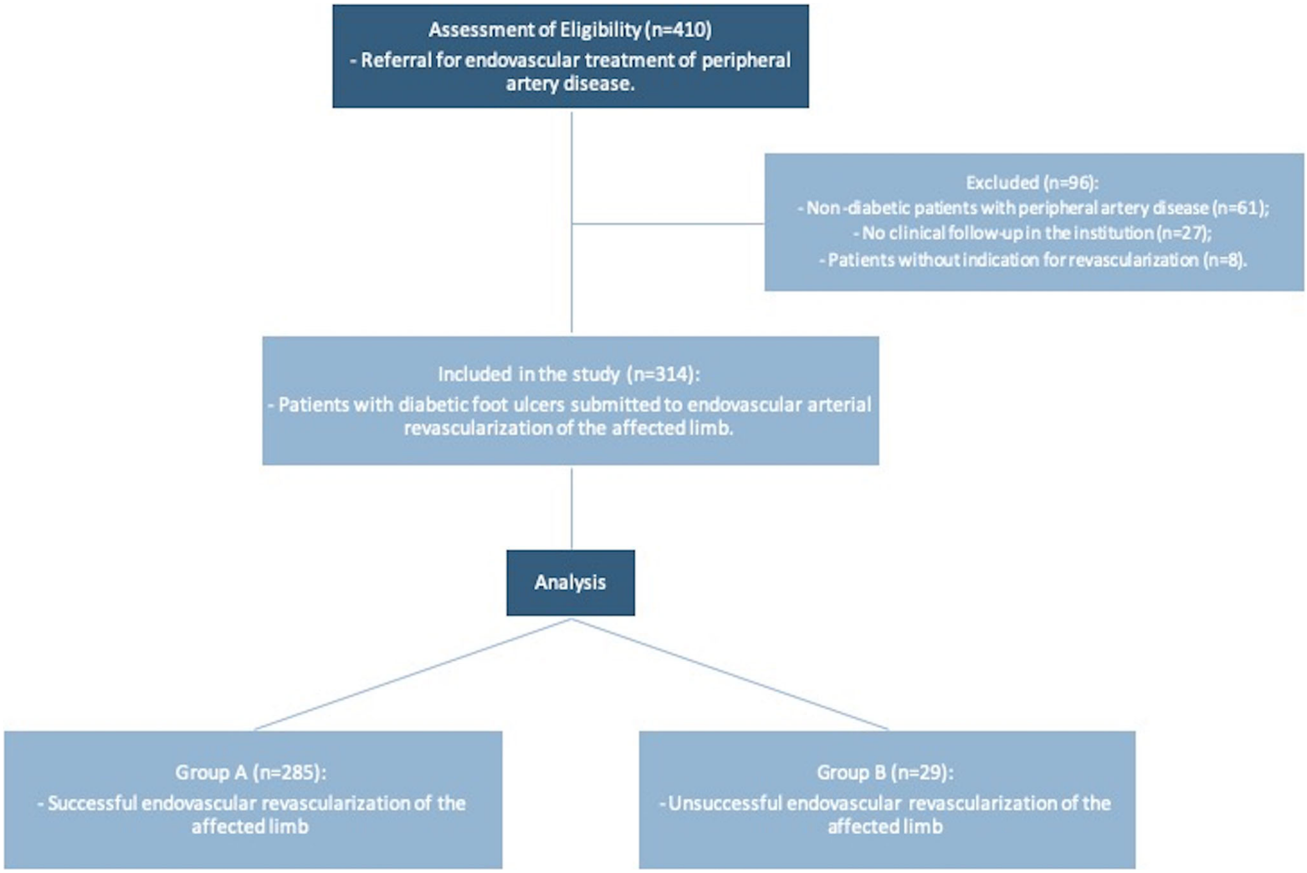

Fig. 1 Flowchart of treated patients and allocation to analyzed groups

stenosed or occluded was revascularized with success without residual stenosis > 30%. Failure of revascularization was considered when stenosed or occluded arteries were identified without revascularization of any artery going to the leg/foot. The Wagner classification scores were used to assess the severity of the DFU [7] and the diabetic foot infection classification scheme of the infectious diseases society of America was used to assess the severity of infection [8]. Baseline data were not significantly different between the 2 groups (Table 1).

Interventions

All admitted patients were first treated surgically by the surgeons of the diabetic foot unit who also performed a vascular assessment to assess peripheral artery disease. Incision and drainage of the foot infections were performed in a longitudinal axis and sufficiently deep to open the plantar aponeurosis in cases of deep infection. Surgical debridement of the infected and necrotic tissues was repeated until the wound bed was clean. In the more complex cases, a damage control surgery was firstly employed to prevent or delay further destruction, repeated as necessary in the subsequent days. If peripheral artery disease was suspected based on physical examination and foot wounds, dedicated vascular imaging with Doppler ultrasound and/or CTA was performed. All patients with identifiable vascular disease were referred for arterial revascularization as soon as possible after multidisciplinary team meeting, to minimize the time of ischemia. All revascularization procedures were performed after the diabetic foot infection was surgically controlled, and all other wound management measures were in place. For patients with severe infections and/or severe DFUs, revascularization was attempted within 24–72 h after surgical debridement. For patients with less severe DFUs and infections, revascularizations were performed within the first week after surgical debridement. In 7 patients, due to the extent of the vascular disease and severity of foot ulcers, surgical bypass revascularization was proposed. All remaining patients were referred for endovascular revascularization. All patients with failed endovascular recanalization were considered poor candidates for bypass surgery and thus excluded from any revascularization.

DFU care was performed by 2 dedicated foot surgeons with 22 and 18 years of experience. Tissue and bone specimens were sent for microbiology evaluation to allow targeted antibiotic therapy. Thin gauzes dressings, wet (or

Table 1 Baseline data comparisons between diabetic foot patients submitted to a successful endovascular revascularization of the affected limb (Group A) versus those submitted to an attempt of endovascular revascularization of the affected limb without success (Group B)

	Group A (*n* = 285)	Group B (*n* = 29)	*p*-values*
Age, mean ± SD	70.17 ± 10.50	73.10 ± 8.42	0.1572
Sex, male, % (*n*)	75.44 (215)	75.86 (22)	0.9598
History of smoking, % (*n*)	29.12 (83)	37.93 (11)	0.3245
Dyslipidemia, % (*n*)	39.44 (112)	55.17 (16)	0.1012
Hypertension, % (*n*)	79.65 (227)	86.21 (25)	0.3988
CAD, % (*n*)	34.40 (97)	28.57 (8)	0.5351
COPD, % (*n*)	7.72 (22)	17.24 (5)	0.0819
Prior stroke, % (*n*)	21.13 (60)	17.86 (5)	0.6849
Obesity, % (*n*)	11.23 (32)	3.45 (1)	0.1938
Hypercholesterolemia, % (*n*)	9.12 (26)	7.14 (2)	0.7265
CRD, % (*n*)	32.98 (94)	17.24 (5)	0.0827
Dialysis, % (*n*)	14.04 (40)	6.90 (2)	0.2827
Prior arterial limb bypass, % (*n*)	5.63 (16)	10.34 (3)	0.3123
Peripheral arterial lesions			0.3322
Iliac, % (*n*)	9.82 (28)	24.14 (7)	–
Femoro-popliteal, % (*n*)	68.42 (195)	62.07 (18)	–
BTK 1 vessel, % (*n*)	17.54 (50)	6.90 (2)	–
BTK 2 vessels, % (*n*)	28.77 (82)	31.03 (9)	–
BTK 3 vessels, % (*n*)	42.46 (121)	37.93 (11)	–
Wound infection (*n*, %)	81.05 (231)	72.41 (21)	0.2663
Wagner classification (0–5) of the DFU, mean ± SD	3.16 ± 0.85	3.38 ± 0.86	0.2123
Severity of foot infection (1–4), mean ± SD	2.77 ± 0.95	2.52 ± 1.02	0.1730

SD standard deviation, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *CRD* chronic renal disease, *BTK* below the knee, *DFU* diabetic foot ulcer

*Statistical test used was the Clopper–Pearson

moist) with octenidine solution were used for foot wound care. In wounds with a high bacterial load and necrotic debris, Dakin's solution at 0.5%, instilled frequently (three times daily) into the wound bed was used in order to maintain a permanent wet environment. All endovascular revascularizations were performed by a group of 5 consultant interventional radiologists with 26, 11, 9, 4 and 2 years of experience. All femoral accesses were obtained with 4–6 French (Fr) introducer sheaths (Terumo, Tokyo, Japan). For retrograde contra-lateral femoral access 6 Fr 55 cm-long hydrophilic sheaths (Destination, Terumo) were used. For distal retrograde tibial-peroneal accesses 4–6 Fr micro-puncture sheaths (Slender, Terumo) were used. Distal retrograde accesses were used when an antegrade approach failed to cross the vascular lesions. Wires used for crossing vascular lesions included 0.035-inch, 0.018-inch and 0.014-inch hydrophilic wires (Glidewire Advantage, Terumo). Angioplasty balloons used were mono-rail 2.0–9.0 mm in diameter (Crosperio, Senri/Crosstella and Metacross, Terumo). After achieving vascular access and crossing the arterial lesions, 5000 Units of Heparin were administered intravenously. Additional 1000 Units of Heparin were administered after 1 h. Routine balloon-inflation times were 2 min and 3 min for residual post-PTA (percutaneous transluminal angioplasty) stenoses. Stent-placement was considered for all patients with significant (> 30%) residual stenosis after prolonged PTA in the iliac and femoral arteries. The use of drug-coated (Paclitaxel) devices was based on operator preference. Thrombectomy was only used when acute thrombosis or in-stent or in-graft occlusions were treated. Dual antiplatelet therapy was used for 2 months after revascularization followed by single antiplatelet therapy ad eternum. Registered technical parameters included the type of arterial access, lesions treated, and type of endovascular revascularization. Repeat revascularization was performed when poor wound healing after revascularization or clinical signs of persistent severe ischemia were present and Doppler ultrasound or CTA-detected re-occlusion of treated arteries.

Outcome Measures

Both groups were compared regarding the following outcome measures: major amputation rates; minor amputation rates, wound healing, length of hospital stay, re-interventions and mortality. Major amputation was defined as any amputation at the level or above the tibio-tarsal joint. Limb salvage rate was defined as the proportion of limbs without major amputations. Minor amputations were all amputations below that level. Adverse events were classified according to the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) criteria [9]. Wound healing was registered based on the subjective foot surgeon's evaluation as complete cure, partial improvement, stable wounds or worsening of DFUs and was documented with serial photography. No imaging screening was performed after revascularization to assess patency. When there was poor wound healing after revascularization or clinical signs of persistent severe ischemia, Doppler ultrasound was used to assess patency. Ankle-arm index was not used during follow-up.

Statistical Analysis Plan

Baseline data from both groups were compared using Clopper-Pearson tests. Univariate and multivariate regression analyses were performed to analyze the correlation of a successful endovascular revascularization on mortality and major amputation rates. A stepwise selection model was created, by iteratively adding the variable with the lowest multivariate p-value, adding variables if the multivariate p-value was lower than 0.40, and retaining variables if the multivariate p-value was lower than 0.15. Survival analyses with Cox-regression analyses were performed comparing Group A and Group B for major amputation and overall survival. Statistical analysis was performed by using STATA (version 13; StataCorp, College Station, Texas) and SAS (version 9.4; SAS, Cary, North Carolina).

Results

Overall, the proportion of patients with DFUs Wagner 2 was 28.0%, Wagner 3 was 25.8%, Wagner 4 was 45.9% and Wagner 5 was 0.3%. Overall, the proportion of patients with mild infection was 2.6%, moderate infection was 61.2% and severe infection was 16.6%. The distribution of arterial disease across the different segments was similar between the 2 groups, with a mean of diseased infragenicular vessels of 2.02 ± 1.03 in Group A and 1.83 ± 1.20 in Group B ($p = 0.4539$). Mean follow-up time was 734.1 ± 610.2 days (median of 597.5 days) for the overall cohort and 759.3 ± 617.0 for Group A and 486.86 ± 480.0 for Group B ($p = 0.0176$). Technical details can be found in Table 2. Failed revascularization was seen in the infragenicular arteries in 17 patients (58.6%), followed by the femoro-popliteal arteries in 10 patients (34.5%) and iliac arteries in 2 patients (6.9%). In the infragenicular arteries, the lesions were not possible to be crossed (16 patients) or did not respond to multiple and prolonged attempts of angioplasty (1 patient). In the femoro-popliteal arteries, a subintimal path was created with failed re-entry in 5 patients, failure to cross heavily calcified lesions was seen in 3 patients and no response to multiple and prolonged attempts of angioplasty and stent placement in 2 patients. For the iliac arteries, in 1 patient it was impossible to cross the lesions and in the other patient it was not possible to re-enter in the true lumen after a subintimal path.

Overall, the major amputation rate was 5.7% ($n = 18$) (limb salvage rate of 94.3%). Unadjusted comparisons regarding outcome measures between both groups can be found in Table 3. Patients from Group A had a major amputation rate of 3.9% (limb salvage rate of 96.1%) whereas patients from Group B had a major amputation rate of 24.1% (limb salvage rate of 75.9%) ($p < 0.0001$). Complete would healing was observed in 53.7% of patients from Group A versus 20.7% from Group B; whereas stable or worsening foot wounds were observed in 22.8% of patients from Group A and 62.1% of patients from Group B ($p < 0.0001$). The revascularization was a re-intervention in 11.9% ($n = 34$) of patients from Group A (due to relapse of the previously treated lesions) and in 27.6% ($n = 8$) of patients from Group B (second attempt to achieve a successful revascularization) ($p = 0.0185$). The mean interval time between interventions was 14.1 ± 11.4 (range 2–36 months) months in Group A and 1.8 ± 0.9 months in Group B (range 1–3 months) ($p < 0.0001$). The length of hospital stay was 81.37 ± 88.41 days in Group A and 60.86 ± 61.40 days in Group B ($p = 0.2834$). The overall mortality rate was 15.9% ($n = 50$). Survival rates were: 87.8% at 1 year; 84.4% at 2 years; 81.2% at 3 years; 80.01% at 4 years; and 77.9% at 5 years. Mortality was due to cardiogenic shock in 19 (38.0%) patients, sepsis in 9 (18.0%) patients, cardiopulmonary disease in 8 (16.0%) patients, septic and cardiogenic shock in 8 (16.0%) patients, stroke in 3 (6.0%) patients, cancer in 3 (6.0%) patients; with 40 (80.0%) of patients being males. No mortality was registered due to the endovascular revascularization.

Survival analyses comparing the two groups regarding major amputation and mortality can be found in Fig. 2, depicting the significant impact of a successful revascularization on major amputation rates ($p < 0.0001$) but not on overall mortality ($p = 0.8466$). Overall, major amputation rates were: 6.0% at 1 year; 6.7% at 2–5 years. When

Table 2 Technical details from the overall cohort

	Technical details (n = 314)
Antegrade femoral access, % (n)	62.42 (196)
Retrograde contralateral femoral access with crossover technique, % (n)	26.43 (83)
Distal retrograde tibial/peroneal access, % (n)	4.78 (15)
Balloon angioplasty, % (n)	71.97 (226)
Drug-coated balloon angioplasty, % (n)	7.32 (23)
Stent placement, % (n)	9.87 (31)
Drug-coated stent placement, % (n)	1.27 (4)
Thrombectomy, % (n)	1.91 (6)

Table 3 Unadjusted comparisons regarding outcome measures between both groups

	Group A (n = 285)	Group B (n = 29)	*p-values
Major amputation, % (n)	3.86 (11)	24.14 (7)	< 0.0001
Minor amputation, % (n)	52.98 (151)	34.48 (10)	0.058
Length of hospital stay, days (mean, SD)	81.37 ± 88.41	60.86 ± 61.40	0.2834
Repeat interventions, % (n)	11.93 (34)	27.57 (8)	0.0185
Mortality, % (n)	15.79 (45)	17.24 (5)	0.6466
Wound healing			< 0.0001
Complete cure, % (n)	53.74 (151)	20.69 (6)	
Partial improvement, % (n)	23.49 (66)	17.24 (5)	
Stable wounds, % (n)	20.28 (57)	27.59 (8)	
Worsening, % (n)	2.49 (7)	34.48 (10)	

*Statistical test used was the Clopper–Pearson

comparing Group A versus Group B, major amputation rates were: 3.9% versus 27.5% at 1 year; 4.6% versus 27.5% at 2–5 years ($p < 0.0001$). Age at baseline also had a significant impact in overall mortality ($p < 0.0001$) and major amputation rates ($p = 0.0058$) (Fig. 3). Multivariate regression analysis evaluating predictors for major amputation and mortality are depicted in Tables 4 and 5, respectively. Significant predictors for major amputation included failed revascularization ($p < 0.0001$), older age ($p = 0.0394$), prior stroke ($p = 0.0018$) and dialysis (0.0476). Significant predictors for mortality included older age ($p < 0.0001$) and coronary artery disease (0.0388). Baseline Wagner classification 4 or 5 was a significant predictor for any (minor plus major) amputation [odds ratio (OR) 1.6, 95% confidence Interval (CI) 1.26–2.1, $p = 0.0034$]. Other predictors for any amputation were the presence of iliac artery disease (OR 1.9, 95% CI 1.2–2.9, $p = 0.0051$) and chronic kidney disease (OR 1.4 95% CI 1.02–1.93, $p = 0.0375$).

Adverse events following endovascular revascularization were major in one patient from Group A (0.4%) and in another patient from Group B (3.5%; $p = 0.0017$; overall rate of 0.6%) and included 2 patients with active bleeding from the femoral access site requiring emergent management with percutaneous ultrasound-guided thrombin injection into femoral artery pseudoaneurysms. Both patients recovered from these events without sequela (Grade 3). Minor adverse events were registered in 10 patients from Group A (3.5%) and 2 patients from Group B (6.9%; $p = 0.3654$; overall rate of 3.8%). Minor adverse events included (Grades 1 or 2): self-limited puncture site femoral hematoma ($n = 4$); hypertensive crisis on the day following the intervention ($n = 2$); self-limited worsening of renal function not requiring dialysis ($n = 2$); glycemic dysregulation needing medical adjustment ($n = 2$); urinary tract infection medically managed ($n = 1$); worsening of chest pain in a patient with unstable angina managed medically ($n = 1$).

Discussion

There is plenty of research showing that a multidisciplinary team can greatly improve outcomes, mostly avoiding major lower limb amputations even in severe cases [10]. In this study, a multidisciplinary approach with experienced and dedicated foot surgeons together with endovascular specialists allowed for a limb salvage rate of 94%. Of note that all major amputations occurred within the first 2 years after revascularization, proving the long-term (up to 5 years) impact of this multidisciplinary approach for DFU healing. No relapsing DFUs requiring major amputation occurred

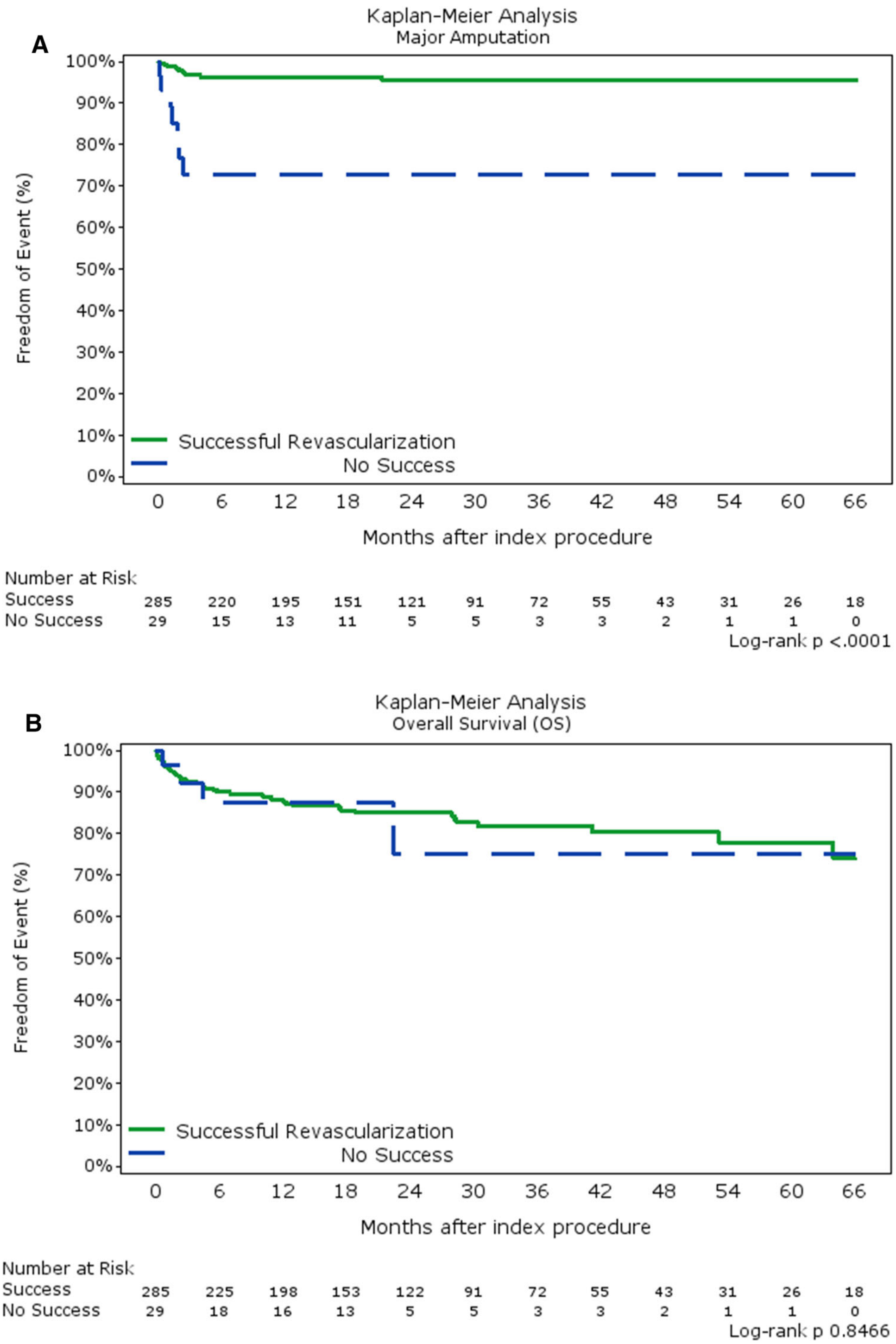

Fig. 2 Kaplan–Meyer curves comparing the two groups regarding major amputation **A** and mortality **B** after revascularization

during the 5 years of follow-up after revascularization, even though repeat revascularization was needed in 12% of patients. Most repeat revascularizations in patients with a successful revascularization were due to relapse of the previously treated arterial lesions and were usually performed 1 year after the first revascularization. Most repeat revascularizations in patients with a failed revascularization were performed within the first month to avoid a major amputation.

Few controlled studies have reported the impact of revascularization (versus no treatment) on limb salvage and ulcer healing [2]. The impact of a successful revascularization was significant, reducing the major amputation rate from 28% to 5% (limb salvage rate of 95% versus 72%) and allowing a rise in complete DFU healing from 21% to

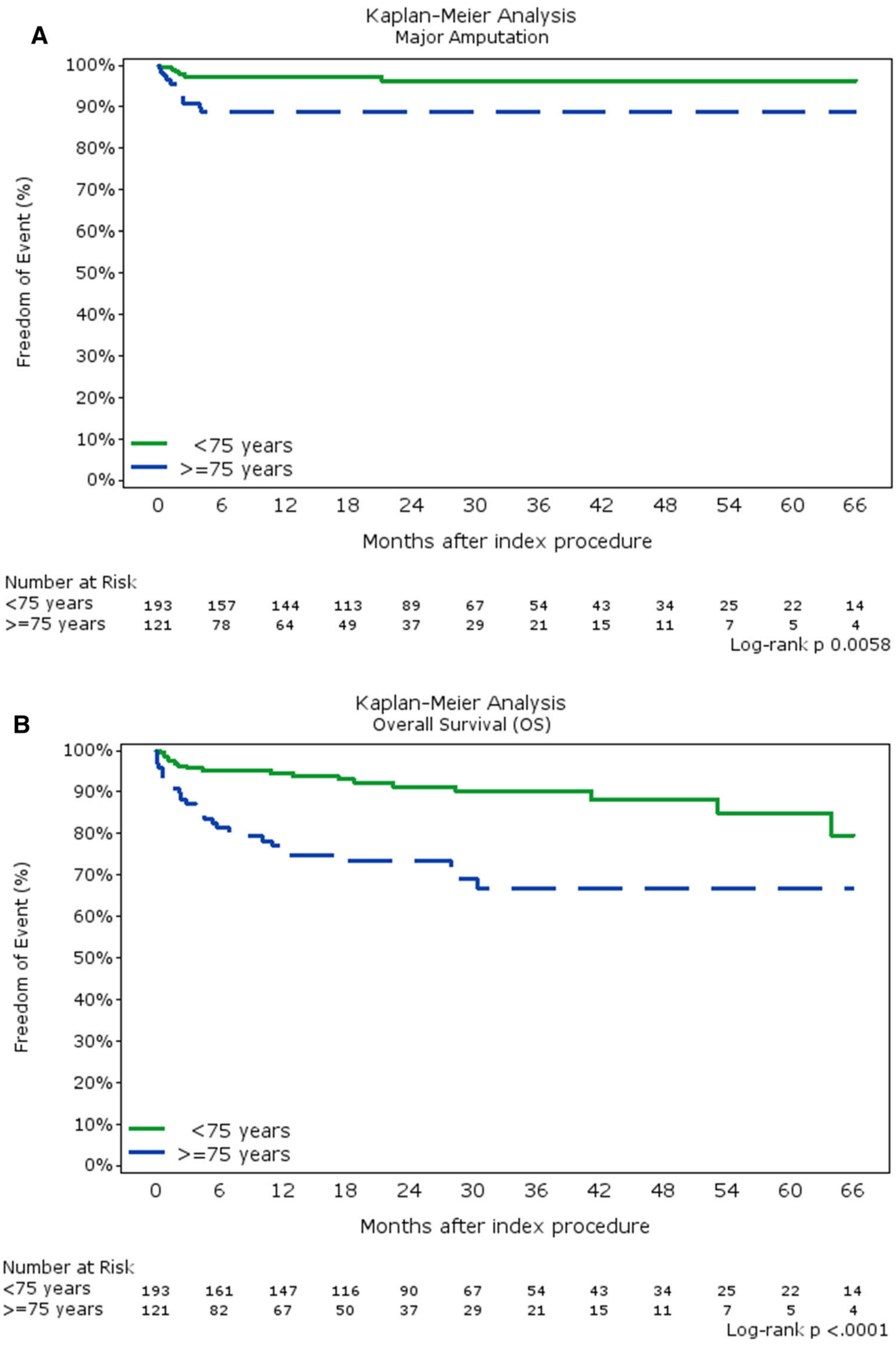

Fig. 3 Kaplan–Meyer curves comparing patients older versus younger than 75 years old regarding major amputation **A** and mortality **B** after revascularization

54%. The vast majority of these patients were revascularized endovascularly with less than 2% of patients being considered upfront for bypass surgery. The timing for revascularization was also important, with patients presenting with severe infection and/or DFUs being revascularized 1–3 days after surgical debridement. All patients with failed endovascular revascularization were considered poor candidates for bypass surgery and were, thus, left without any kind of revascularization. Of note, that surgical expertise when dealing with DFU is essential: approximately 72% of patients with DFU and failed revascularization were able to avoid major amputation. This was possible due to the dedication and perseverance of the foot surgeons. This has obvious drawbacks such as lengthy hospital stays, with a mean of 60 to 80 days in this study. The included patients had severe DFUs (mean Wagner

Table 4 Multivariate regression analysis evaluating predictors for major amputation

Parameter	Odds ratio	95% Lower confidence limit for OR	95% Upper confidence limit for OR	*p*-value
Full multivariate model				
Successful revascularization	0.042	0.007	0.242	0.0004
Male gender	2.724	0.492	15.063	0.2509
Age (per 10 years)	1.974	1.034	3.769	0.0394
Iliac diseased	0.104	0.005	2.195	0.146
Femoropopliteal diseased	1.707	0.224	12.997	0.6056
Number of infragenicular vessels diseased	1.019	0.564	1.84	0.9508
Iliac treated	10.745	0.336	343.757	0.1793
Femoropopliteal treated	1.57	0.241	10.235	0.6374
Number of infragenicular vessels treated	0.97	0.419	2.246	0.944
Length of stay index procedure	1.002	0.996	1.008	0.5013
Smoker	0.745	0.16	3.461	0.7074
Dyslipidemia	1.908	0.544	6.695	0.3128
Hypercholesterolemia	1.455	0.306	6.924	0.6375
Hypertension	2.918	0.408	20.884	0.2863
Coronary artery disease	2.058	0.581	7.292	0.2634
Chronic obstructive pulmonary disease (COPD)	1.883	0.32	11.083	0.4842
Prior stroke	5.567	1.516	20.442	0.0097
Obesity	0.74	0.078	7.055	0.7936
Chronic kidney disease	0.502	0.101	2.496	0.3999
Dialysis	7.377	0.907	60.002	0.0617
Prior arterial limb bypass	0.755	0.106	5.364	0.7786
Wagner classification 4 or more	1.279	0.288	5.680	0.7466
Wound infection classification 3	2.843	0.498	16.243	0.2400
Wound infection classification 4	2.919	0.185	46.142	0.4468
Multivariate stepwise selection model: entry and stay *p*-values of $p = 0.40$ and $p = 0.15$				
Successful revascularization	0.137	0.053	0.353	< 0.0001
Prior stroke	4.466	1.745	11.434	0.0018
Dialysis	2.872	1.011	8.157	0.0476

scores of 3.2) and many had been proposed for major amputation before consulting this diabetic foot unit.

About 60% of DFUs will become infected [11] in variables degrees of severity, not uncommonly putting at-risk the limb, or even the life, of the patient. In this cohort, infection was present in more than 70% of treated patients with the vast majority (78%) having moderate-to-severe infection requiring hospital admission to control the infection of the DFUs. Management of diabetic foot infections should be performed by an experienced surgeon, with deep knowledge in surgical anatomy and biomechanics of the foot [12, 13]. It should be kept in mind that "time is tissue" in these patients, so early recognition and treatment of acute presentations are necessary to prevent further unwarranted morbidity and even mortality [14]. The use of Dakin's solution at 0.5%, instilled into the wound bed is part of the surgical management protocols [15]. However, aggressive debridement should be avoided initially and revascularization performed urgently [14].

This study presents several limitations. Firstly, this analysis is retrospective and the two groups being compared were very different in size. However, there were no significant differences at baseline between both groups regarding all measured parameters. Transcutaneous partial pressure of oxygen (TcPO2) and post-PTA patency analyses were not available. The goal of this study was to assess clinical outcomes, mainly limb salvage and overall survival and not patency rates or TcPO2 improvements after PTA for patients with DFUs. Disease-specific outcomes are much more relevant than procedure-specific

Table 5 Multivariate regression analysis evaluating predictors for mortality

Parameter	Odds ratio	95% Lower confidence limit for OR	95% Upper confidence limit for OR	*p*-value
Full multivariate model				
Any occurrence of major amputation	1.004	0.338	2.983	0.9948
Successful revascularization	1.38	0.294	6.47	0.6831
Male gender	1.862	0.803	4.319	0.1474
Age (per 10 years)	1.965	1.367	2.824	0.0003
Procedure is a re-intervention	0.148	0.02	1.115	0.0637
Iliac diseased	1.287	0.271	6.113	0.7507
Femoropopliteal diseased	1.332	0.427	4.155	0.6209
Number of infragenicular vessels diseased	1.201	0.847	1.705	0.3037
Iliac treated	0.66	0.082	5.305	0.6956
Femoropopliteal treated	0.668	0.211	2.115	0.4928
Number of infragenicular vessels treated	0.83	0.495	1.394	0.4814
Length of stay index procedure	1	0.997	1.004	0.9446
Smoker	0.956	0.43	2.123	0.9115
Dyslipidemia	0.75	0.372	1.512	0.4218
Hypercholesterolemia	1.366	0.455	4.103	0.5779
Hypertension	0.576	0.283	1.171	0.1275
Coronary artery disease	1.75	0.899	3.408	0.0998
Chronic obstructive pulmonary disease (COPD)	0.664	0.202	2.18	0.4997
Prior stroke	1.303	0.638	2.658	0.4677
Obesity	2.317	0.908	5.914	0.0788
Chronic kidney disease	1.192	0.571	2.49	0.6394
Dialysis	0.926	0.316	2.718	0.8891
Prior arterial limb bypass	0.624	0.144	2.71	0.5291
Wagner classification 4 or more	1.444	0.716	2.911	0.3047
Wound infection classification 3	1.261	0.555	2.864	0.5801
Wound infection classification 4	0.611	0.122	3.049	0.5481
Multivariate stepwise selection model: Entry and Stay *p*-values of $p = 0.40$ and $p = 0.15$				
Age (per 10 years)	1.969	1.439	2.695	< .0001
Procedure is a re-intervention	0.143	0.02	1.042	0.055
Hypertension	0.57	0.296	1.094	0.0912
Coronary artery disease	1.847	1.032	3.306	0.0388

outcomes [2]. Significant predictors for mortality included older age and coronary artery disease as many of the deaths were related to cardiac events during follow-up as previously shown [16]. Significant predictors for major amputation in this study included failed revascularization, older age, prior stroke and dialysis. Some of these predictors have been previously identified [17]; however, the potential benefit of revascularization in older patients with a history of stroke and limited mobility and/or on dialysis should be discriminated as these patients have a higher rate of major amputation regardless the outcome of revascularization.

Conclusion

The present study showed that a multidisciplinary approach including experienced foot surgeons and interventional radiologists amongst other physicians for the treatment of patients with DFUs allows for a limb salvage rate of 94% following revascularization that is sustained during long-term follow-up up to 5 years. The low rate of adverse events (< 1%) due to the endovascular revascularization and significant impact on limb salvage justify an aggressive endovascular revascularization approach for all patients with DFUs and evidence of peripheral artery disease, shortly after the initial surgical debridement.

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Compliance with Ethical Standards

Conflict of interest Tiago Bilhim is a paid consultant for Merit Medical and has received speaker fees for Philips Medical, Cook Medical, Terumo and is a stock holder for EmbolX.Nuno Vasco Costa is a paid consultant for Merit Medical.Filipe Veloso Gomes is a paid consultant for Terumo.

Ethical Approval Institutional review board approval was waived to perform this retrospective analysis.

Informed Consent Informed Consent was obtained from all patients.

Consent for Publication Consent for Publication was obtained.

References

1. Schaper NC, van Netten JJ, Apelqvist J, et al. Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. 2020 Mar;36(Suppl 1):e3266. https://doi.org/10.1002/dmrr.3266.
2. Hinchliffe R, et al. Effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. Diabetes Metab Res Rev. 2016;32(Suppl. 1):136–44.
3. Odink H, et al. Technical and clinical long-term results of infrapopliteal percutaneous transluminal angioplasty for critical limb ischemia. J Vasc Interv Radiol. 2012;23:461–7.
4. Peregrin J, et al. PTA of Infrapopliteal arteries: long-term clinical follow-up and analysis of factors influencing clinical outcome. Cardiovasc Intervent Radiol. 2010;33:720–5.
5. Hinchliffe RJ, Forsythe RO, Apelqvist J, et al. Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020 Mar;36(Suppl 1):e3276. https://doi.org/10.1002/dmrr.3276.
6. Fossaceca R, et al. Endovascular treatment of diabetic foot in a selected population of patients with below-the-knee disease: is the angiosome model effective? Cardiovasc Intervent Radiol. 2013;36:637–44.
7. Wagner FW Jr. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle. 1981;2:64–122.
8. Lavery LA, Armstrong DG, Murdoch DP, Peters EJ, Lipsky BA. Validation of the Infectious diseases society of America's diabetic foot infection classification system. Clin Infect Dis. 2007;44:562–5.
9. Filippiadis DK, Binkert C, Pellerin O, Hoffmann RT, Krajina A, Pereira PL. Cirse quality assurance document and standards for classification of complications: the cirse classification system. Cardiovasc Intervent Radiol. 2017 Aug;40(8):1141–6.
10. Musuuza J, et al. A systematic review of multidisciplinary teams to reduce major amputations for patients with diabetic foot ulcers. J Vasc Surg. 2019. https://doi.org/10.1016/j.jvs.2019.08.244.
11. Mendes JJ, Neves J. Diabetic foot infections: current diagnosis and treatment. J Diabetic Foot Complic. 2012;4(2):26–45.
12. Lipsky BA, Berendt AR, Cormia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132–e173173.
13. Highlander P, Shinabarger AB. Perioperative laboratory assessment of diabetic infections undergoing amputation: a systematic review. Foot Ankle Spec. 2013;6(6):465–70.
14. Schper NC, Andros G, Apelqvist J, et al. Specific guidelines for the diagnosis and treatment of peripheral arterial disease in a patient with diabetes and ulceration of the foot 2011. Diabetes Metab Res Rev. 2012;28(suppl 1):236–7.
15. Duarte B, Formiga A, Neves J. Dakin's solution in the treatment of severe diabetic foot infections. Int Wound J. 2019;17(2):277–84.
16. American Diabetes Association. Diabetes 1996 vital statistics. Alexandria, VA: American Diabetes Association; 1996.
17. Sen P, Demirdal T, Emir B. Meta-analysis of risk factors for amputation in diabetic foot infections. Diabetes Metab Res Rev. 2019;35(7):e3165. https://doi.org/10.1002/dmrr.3165.