Mid-Term Results of Popliteal-Pedal Inframalleolar Vein Bypasses in Chronic Limb-Threatening Ischemia Patients After Previous Failed Tibial Endovascular Recanalization

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Background: Inframalleolar bypass still preserves its role in the modern endovascular era. Aim of this study was to evaluate the mid-term outcomes of "short" inframalleolar vein bypasses in patients with chronic limb-threatening ischemia (CLTI) after the previously failed tibial endovascular recanalization.

Methods: Between January 2015 and December 2021,107 CLTI patients in 3 Italian Departments of Vascular Surgery underwent "short" inframalleolar vein bypass after failed tibial endovascular recanalization. Early (30-day) and 3-year outcomes were evaluated in terms of survival, primary patency, primary assisted patency, secondary patency, and amputation-free survival. Univariate analysis of the perioperative factors affecting outcomes were performed by the means of log-rank test. The associations of procedure variables were sought based on a multivariate Cox regression analysis.

Results: Distal anastomosis (inframalleolar) was mostly performed on dorsal pedis (64, 59.8%). At 30 days, bypass occlusion was recorded in 5 cases (4.6%). The mean follow-up period was 20.5 ± 17.9 months. The estimated 3-year overall survival was 66.7%. Three-year estimates of primary patency, primary assisted patency, secondary patency, and amputation-free survival were 68.5%, 70.1%, 70.2%, and 76.7%, respectively. Multivariate analysis showed a negative association of insulin treatment with primary patency (HR 4.3, $P = 0.04$), primary assisted patency (HR 5.1, $P = 0.02$), and secondary patency (HR 5.1, $P = 0.02$). The negative association of long-term corticosteroid use was also found with primary patency (HR 7.8, $P = 0.005$), primary assisted patency (HR 8.7, $P = 0.003$), secondary patency (HR 8.7, $P = 0.003$), and amputation-free survival (HR 3.9, $P = 0.05$).

Conclusions: Short" vein bypasses to the foot arteries in CLTI patients yielded good mid-term overall patency and limb salvage rates after a failed tibial endovascular recanalization. Insulin-dependent diabetes mellitus and long-term corticosteroid use seemed to affect the outcomes.

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INTRODUCTION

There are major limitations in the current state of evidence guiding treatment decisions in chronic limb-threatening ischemia (CLTI), particularly for severe anatomic patterns of disease treated via endovascular means.[1]

Open surgical bypass for long (>25 cm) infrainguinal arterial occlusions is the preferred first approach in patients with a life expectancy of more than 2 years when an autologous vein is available.[2] However, majority of CLTI patients have severe comorbidities with an increase of the overall perioperative morbidity and mortality risks.[3] For this reason, some authors advocated an endovascular-first approach, above all for the infrapopliteal vessel obstructive disease.[4]

Recently, Bypass versus Angioplasty in Severe Ischaemia of the Leg-2 (BASIL-2) trial suggested that more CLTI patients who required an infrapopliteal revascularization procedure to restore limb perfusion should be considered for a best endovascular treatment as ''first-revascularization strategy.''[5]

However, rates of restenosis and reocclusion after infrapopliteal endovascular interventions in patients with CLTI can reach up to 50% of the cases.[6] Therefore, endovascular approach has limitations in terms of long-term success, necessitating frequent repeat procedures.[7]

Inframalleolar bypass still preserves its role in the modern endovascular era[8–11]; however, in the Literature there is no agreement about the outcomes obtained with pedal bypasses after a previous endovascular tibial procedure. Indeed, some authors claim that bypass surgery after endovascular therapy (EVT) has lower primary patency rates in comparison with primary bypass, while others demonstrate that prior endovascular procedures are not detrimental to pedal bypasses for ischemic wounds.[12–14] ''Short'' distal bypasses starting from popliteal artery (PI) (popliteal-pedal bypasses) could represent a valid surgical alternative in case of failed endovascular approach.[15]

The aim of this study was to evaluate the midterm outcomes of ''short'' inframalleolar vein bypasses in CLTI patients after previous failed tibial endovascular recanalization.

MATERIAL AND METHODS

Study Population

We performed a retrospective multicenter data analysis of all patients with tibial occlusive disease who underwent ''short'' inframalleolar vein bypass after at least 1 failed tibial endovascular recanalization performed for CLTI in the period between January 2015 and December 2021, in 3 Italian Departments of Vascular Surgery.

Inclusion criteria were as follows:

1. Patients with CLTI with rest pain and/or ischemic lesions (Rutherford categories 4-5-6), with a history of failed tibial endovascular recanalization
2. Absence of stenosis or occlusion at the level of superficial femoral artery, with a triphasic flow at the level of popliteal artery
3. Calcified lesions involving at least two-third of the target tibial vessels, without an in-line flow from the groin to the foot
4. Availability of ipsilateral autologous saphenous vein in the limb to be operated on with a minimum diameter of not less than 1.6 mm
5. Proximal anastomosis located at the level of popliteal artery (including PI, PII, and PIII segments);
6. Distal anastomosis located at the level of one of the foot arteries.

The only exclusion criterion was aneurysmal disease of the lower limbs.

All data related to the procedures were prospectively collected in each center and then merged in a dedicated database. This included demographics, preoperative risk factors, clinical and diagnostic preoperative assessments, intraoperative features, and 30-day and follow-up data.

The analysis of the cohort study was retrospectively performed.

Institutional review board approval was waived due to the retrospective nature of the study. Written consent was obtained from each subject.

Timing Evaluations

Patient evaluations included a clinical examination and duplex scan at the following study timepoints: enrollment, procedure, 30 days, 6 months, 12 months, and yearly thereafter.

Risk stratification of all patients was based on wound, ischemia, and foot infection, according to the WIfI classification.[16] Beginning from July 2019 preoperative Global Anatomic Staging System (GLASS) was used to identify the preferred target artery path (TAP).[1]

In addition, a duplex scan was useful to evaluate the diameter of the great saphenous vein (GSV) in standing position; however, this was often not possible in patients with CLTI. In these cases, the

duplex scan was performed in the supine reverse Trendelenburg position (+15°).

Computed tomography angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography (DSA) were only performed on surgeon's discretion.

An intraoperative diagnostic evaluation to detect graft patency and to identify any technical defects was performed with different diagnostic tools (flowmeter, duplex scan, angiography, or a combination of them) on the basis of surgeon's discretion.

Intraoperative technical details (including anesthesia, operation time, and site of anastomosis) have been collected.

In all cases duplex surveillance was made to identify residual fistulas (in-situ vs. ex-situ configuration) and intra-graft or anastomotic stenoses.

Ischemic lesions or gangrene, whenever present, were treated according to the best standard of care according to the indications of International Working Group on the Diabetic Foot (IWGDF) guidelines.[17]

Definition, Outcome Measures, and Statistical Analysis

CLTI has been defined as objectively documented atherosclerotic peripheral arterial disease (PAD) in association with ischemic rest pain or tissue loss (ulceration or gangrene). Ischemic rest pain is typically described as affecting the forefoot and is often made worse with recumbency while being relieved by dependency. It should be present for >2 weeks and be associated with 1 or more abnormal hemodynamic parameters, such as ankle-brachial index or toe pressure.[1]

Other definitions of clinical events and/or imaging parameters were as per the reporting standards of the Society for Vascular Surgery for PAD.[18]

Technical success for peripheral revascularization was defined according to the Peripheral Academic Research Consortium guidelines, as the achievement of a final residual diameter stenosis <30% for stent and <50% for angioplasty or atherectomy by angiography at the end of the procedure (and without flow-limiting arterial dissection or hemodynamically significant translesional pressure gradient <10 mm Hg).[19] Any deviation from this definition was defined as a technical failure.

The primary outcome measures analyzed were primary patency [*defined as no evidence of restenosis of the target lesion during follow-up, namely a peak systolic velocity ratio (PSVR) ≥ 2.5 or occlusion of the target lesion, based on color-coded duplex ultrasonography*], secondary patency (*defined as target lesion patency maintained by repeat intervention after complete occlusion of the relevant lesion*), and amputation-free survival (*defined as absence of amputation ipsilateral to the target lesion above the level of the ankle joint*).

The secondary outcome measures analyzed were intraoperative survival, and primary-assisted patency (*defined as target lesion patency maintained by repeat intervention after not complete occlusion of the relevant lesion*).

Continuous data were expressed as the mean ± standard deviation (SD) or median ± interquartile range (IQR) values when necessary. Categorical data were expressed as percentages.

At follow-up, actual data in terms of death, vein graft occlusion, and major amputation were reported.

The estimated 3-year outcomes were evaluated in terms of survival, primary patency, primary assisted patency, secondary patency, and amputation-free survival by lifetable analysis (Kaplan—Meier test). Estimates were given with the 95% confidence intervals (CI).

Uni and multivariate analyses of the pre or intraoperative factors affecting primary patency, primary-assisted patency, secondary patency, major adverse limb events (MALEs), and amputation-free survival were performed by means of log-rank test and Cox regression analysis. The results of the regression analyses were presented as the hazard ratio (HR) and 95% CI.

Statistical significance was defined at the $P < 0.05$ level.

Statistical analysis was performed using SPSS software (version 24.0 for Apple; IBM Corporation, Armonk, NY, USA).

RESULTS

Demographic and Clinical Data

A total of 107 short bypasses to pedal arteries were performed in the analyzed period. The number of previous endovascular procedures was 1 in 99 cases (92.5%) and 2 in the remaining 8 cases (7.5%). The mean time between the last endovascular procedure and the vein bypass grafting was 5.7 ± 2.3 months.

Previous endovascular procedures did not modify the status of the run-off, so that at least 1 pedal artery was still patent in the whole cohort.

Patients were predominantly male (87, 81.3%), with a mean age of 71.7 ± 11.2 years. The demographic data are summarized in Table I.

According to Rutherford classification, patients were classified as class 4 in 6 cases (5.6%), class 5 in 93 cases (86.9%), and 8 in the remaining cases (7.5%).

Table I. Demographic data and preoperative clinical data

Variables	*n*. Patients (%)
Male	87 (81.3%)
Age, years	71.7
>80 years	28 (26.2%)
Clinical data	
Smoking (active)	9 (8.4%)
Smoking (former)	49 (45.8%)
Hypertension	89 (83.2%)
Hypercholesterolemia	58 (54.2%)
Diabetes mellitus	80 (74.8%)
Insulin treatment	21 (19.6%)
COPD	36 (33.6%)
Coronary artery disease	42 (39.3%)
Atrial fibrillation	25 (23.4%)
LVEF >40%	9 (8.4%)
Chronic kidney disease[a]	30 (28%)
Dialysis treatment	14 (13.1%)
Long-term corticosteroid use	13 (12.1%)

Continuous data are presented as the means; categorical data are given as the counts (percentage).
COPD, Chronic Obstructive Pulmonary Disease; LVEF, Left Ventricular Ejection Fraction.
[a]Glomerular filtration rate <30 mL/min.

According to the WIfI classification, stage 2 was identified in 4 cases (3.7%), stage 3 in 42 cases (39.3%), and stage 4 in 61 cases (57%).

Table II shows the preoperative medical therapy.

Previous open surgery on iliac or above-the-knee femoro-popliteal arteries has been performed in 4 patients (3.7%).

Preoperative diagnostic evaluation included the following: duplex scan alone (59, 55.1%), CTA (24, 22.4%), MRA (4, 3.7%), and DSA (20, 18.7%).

Intraoperative Data

Operations were performed under general anesthesia in 59 cases (55.1%) and loco-regional anesthesia in 48 cases (44.9%). The mean operation time was 299.1 ± 79.2 min. In 90 cases (4.1%), the operation time was longer than 240 min.

The location of the proximal anastomosis was above-the-knee PI in 24 cases (22.4%) and below-the-knee popliteal artery (PIII) in 83 cases (77.6%). In 9 cases, a bifurcated graft was performed. Table III summarizes the site of all distal anastomoses.

In all cases, a vein graft was used (GSV in 105 cases, 98.1%, and small saphenous vein in the remaining 2 cases, 1.9%). A reversed vein configuration was used in 12 cases (11.2%), while a nonreversed vein was used as graft in the remaining 95 cases (94 ''ex-situ technique'' and 1 ''in-situ technique'').

In 41 cases (38.3%), the distal anastomosis was performed with the use of tourniquets and the insertion of a temporary shunt ('no clamping technique') (intracoronary shunt, Axius Intracoronary Shunt, Getinge, Göteborg, Sweden).

A concomitant minor amputation was performed in 49 cases (5.8%).

Early Results (30 days)

The median intensive care unit (ICU) stay was 1 day (IQR 1−1), and the median overall postoperative hospital stay was 7 days (IQR 6−12).

At discharge, the postoperative antiplatelet or anticoagulant medical therapy was only acetylsalicylic acid in 52 cases (48.7%), dual antiplatelet therapy in 6 cases (33.6%), oral antiCoagulants (OAC) in 12 cases (11.2%), and direct oral antiCoagulants (DOAC) in the remaining 7 cases (6.5%).

At 30 days, 2 patients died due to acute coronary syndrome with an overall 30-day mortality rate of 1.9%. The overall rate of major adverse cardiac events (MACEs) was 4.7% (5 cases).

Overall, an early bypass occlusion was recorded in 5 cases (4.6%). Thirty-eight patients (35.5%) required a reintervention within 30 days from the index procedures, including minor amputation in 19 cases (17.8%), bypass thrombectomy or revision in 5 cases (4.7%), surgical revision for bleeding in 2 cases (1.9%), and surgical debridement and negative pressure wound therapy in 12 cases (11.2%).

Mid-term Results (3 years)

Follow-up was available in all patients with an overall median follow-up period of 19 months (IQR 4−30). During the follow-up, 24 bypass occlusions occurred with 17 subsequent major amputations. In addition, 22 deaths occurred; the causes of death were acute coronary syndrome in 7 cases, cancer in 5 cases, Covid-19 infection in 3 cases, pneumonia in 2 cases, pulmonary embolism in 1 case, and unknown in 4 cases.

The estimated 3-year overall survival was 70% (95% CI, 65.1% to 73.3%) (Fig. 1).

During the follow-up, two patients underwent angioplasty of the distal anastomosis due to stenosis, and 1 patient underwent endovascular thrombectomy due to graft occlusion, with complete flow restoration. Specifically, the first 2 patients developed an intimal hyperplasia at the point of the distal anastomosis on plantar artery, seemingly due to valve residues. We performed a drug-coated balloon (DCB) angioplasty of the lesions, obtaining optimal remodeling and

Table II. Preoperative medical therapy

Variables	*n*. Patients (%)
Acetylsalicylic acid	63 (58.9%)
Dual antiplatelet therapy	30 (28%)
Oral AntiCoagulants	8 (7.5%)
DOACs	4 (3.7%)
ASA + rivaroxaban 2.5 mg bid	2 (1.9%)
Statin	47 (43.9%)

Table III. Site of distal anastomoses

Variables	*n*. Patients (%)
Primary anastomosis	
Dorsal pedis artery	64 (59.8%)
Posterior tibial artery	18 (16.8%)
Lateral plantar artery	7 (6.5%)
Medial plantary artery	16 (15%)
Tarsal artery	2 (1.9%)
Secondary anastomosis (jump)	
Dorsal pedis artery	4 (44.5%)
Posterior tibial artery	0
Lateral plantar artery	1 (11.1%)
Medial plantary artery	2 (22.2%)
Tarsal artery	2 (22.2%)

good patency. The last patient, noncompliant to best medical therapy, developed a bypass occlusion, so he underwent a mechanical thrombectomy through a femoral percutaneous puncture.

The 3-year Kaplan–Meier estimates of primary patency, primary-assisted patency, secondary patency, and amputation-free survival were 68.5% (*n*. at risk: 16, 95% CI, 62.9–71.8%), 70.1% (*n*. at risk: 16, 95% CI, 64.3–72.5%), 70.2% (*n*. at risk: 17, 95% CI, 65.3–74.7%), and 76.7% (*n*. at risk: 18, 95% CI, 72.1–79%), respectively (Fig. 2).

Uni- and Multivariate Analyses

Table IV shows univariate analysis at 3 years.

Primary patency was affected by hypertension ($P = 0.04$), diabetes mellitus ($P = 0.01$), insulin treatment ($P < 0.001$), dialysis ($P = 0.003$), and long-term corticosteroid use ($P = 0.005$).

Primary-assisted patency was negatively associated with hypertension ($P = 0.05$), diabetes mellitus ($P = 0.02$), insulin treatment ($P < 0.001$), dialysis ($P = 0.002$), and long-term corticosteroid use ($P = 0.003$).

Even the variables affecting secondary patency included hypertension ($P = 0.05$), diabetes mellitus ($P = 0.02$), insulin treatment ($P < 0.001$), dialysis ($P = 0.002$), and long-term corticosteroid use ($P = 0.003$).

In addition, freedom from MALEs have been affected by insulin treatment ($P = 0.02$).

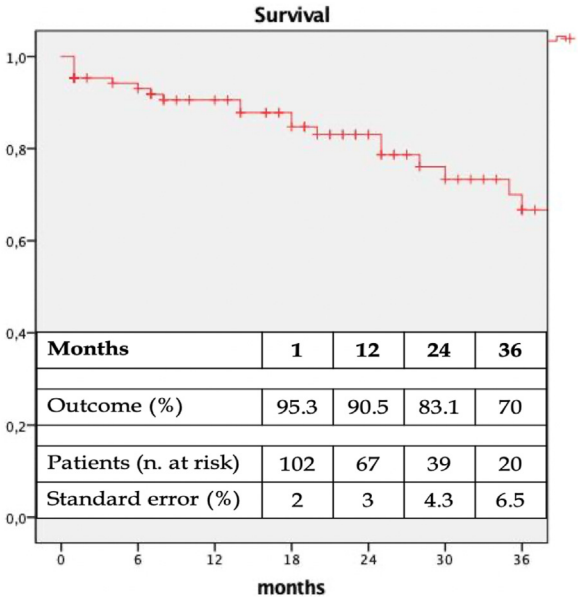
Finally, amputation-free survival was affected by hypertension ($P = 0.04$), insulin treatment ($P = 0.02$), dialysis ($P = 0.3$), and long-term corticosteroid use ($P = 0.05$).

Multivariate analysis of insulin treatment confirmed the negative association with primary patency (HR 4.3, 95% CI, 2.1 to 10.8, $P = 0.04$), primary-assisted patency (HR 5.1, 95% CI, 3.9–8.3, $P = 0.02$), and secondary patency (HR 5.1, 95% CI, 3.9–8.3, $P = 0.02$).

In addition, a negative association of long-term corticosteroid use was also confirmed with primary patency (HR 7.8, 95% CI, 4.6 to 11.2, $P = 0.005$), primary-assisted patency (HR 8.7, 95% CI, 5.2 to 12.6, $P = 0.003$), secondary patency (HR 8.7, 95% CI, 5.2 to 12.6, $P = 0.003$), and amputation-free survival (HR 3.9, 95% CI, 2.1 to 6.4, $P = 0.05$).

DISCUSSION

The massive expansion of endovascular treatment during last decades has sparked much debate among the best choice between open and EVT in CLTI patients. In this context, Best Endovascular vs Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI) trial reported a significantly lower incidence of MALEs or death for open bypass in patients with an adequate GSV.[20] However, most patients included suffered from femoro-popliteal disease, thereby leading to high level of outcomes' uncertainty for the infra-popliteal segment. Indeed, BASIL-2 trial was established to specifically overcome the scarcity of high-quality evidence regarding infrapopliteal revascularizations. This trial suggested that more patients with CLTI who required an infrapopliteal revascularization, should be considered for a best endovascular treatment first revascularization strategy.[5] However, restenosis and reocclusion in the infra-popliteal segment remain an issue and may somehow jeopardize the advocated superiority of the endovascular first approach.[6,21–23] In this scenario, inframalleolar bypass has emerged as a favourable bail-out procedure after failed tibial endovascular recanalization.[14,24] Even in the 3 centers participating in this retrospective study, the first approach is usually endovascular; however, patients are often switched to a distal bypass after failed



Months	1	12	24	36
Outcome (%)	95.3	90.5	83.1	70
Patients (n. at risk)	102	67	39	20
Standard error (%)	2	3	4.3	6.5

Fig. 1. Estimated 3-year survival (Kaplan-Meier curves with outcomes, numbers of patients at risk, and standard error values).

endovascular recanalizations when the autologous vein material is available. Nonetheless, a not negligible proportion of patients was considered high-risk, with either anticipated perioperative mortality >5% or anticipated 2-year survival <50%. In this group, another endovascular attempt may be justified, even though with scarce guarantees of technical and clinical success and durability of the procedure. On the other hand, striking a balance between extreme revascularization attempts and major amputation remains an issue. Therefore, high-risk patients may benefit from a conservative management, because a significant proportion of them will have limited survival and can potentially avoid unnecessary surgery and major amputations.[25] Another consideration should be done concerning the presence of a triphasic flow in the popliteal artery. This implies the patency of the femoro-popliteal segment that could be rare in CLTI patients, where a multilevel disease is more likely to be present. Given this restrictive criterion combined with a large proportion of high-risk patients, we experienced turndown rates up to 40%. This means that only highly selected patients may benefit from ultra-distal bypasses.

In our experience, patients treated with ''short'' inframalleolar bypasses demonstrated acceptable early outcomes, with an overall 30-day mortality of 1.9%. However, when considering early outcomes, the role of operation time needs to be addressed. Although performed by highly experienced surgeons, these types of bypasses imply long operative time (nearly 5 h) that only relatively fit patients can bear. In any case, there is no evidence to support the systematic avoidance of general anesthesia for lower-extremity bypass procedures.[26] Despite the low 30-day mortality, the rates of MACEs remain relatively high. However, a recent trial showed comparable results and demonstrated that patients who were deemed suitable candidates for open bypass surgery had similar periprocedural complications following either open or endo revascularization. Therefore, concern about the risk of MACEs should not be a deterrent in deciding revascularization.[3]

Then, we experienced an early bypass occlusion rate of 4.6%, which is in line with that reported in the Literature.[9] The seemingly high rates of bypass-related reintervention can be mainly related to an inadequate medical management. Specifically, patients who had undergone reintervention for early graft occlusion did not assume their antiplatelet therapy regularly and did not quit their smoke habit. Besides this specific occurrence potentially responsible of these results, similar rates of MALEs have already been described.[27]

Furthermore, the 3-year survival rate was similar to what was previously reported in the literature for CLTI patients.[28] During the entire follow-up, 24 bypass occlusions occurred, 17 of them needing for a major amputation as well as 22 deaths. These data may pose a doubt regarding the real benefit of performing this type of bypasses, especially considering the improvement in endovascular field, which has led to the ''endovascular first strategy.'' Indeed, the optimal strategy for revascularization in infrainguinal disease remains debatable. Comparative trials are scarce, and daily decisions are made based on low-quality evidence. A recent metanalysis showed improved patency for drug-eluting stents (DES) over bare-metal stents (BMS) in infrapopliteal arteries (primary patency: 73% vs. 50% at 1 year) and was at least comparable to balloon angioplasty (66% primary patency). Survival, major amputation, and amputation-free survival at 2 years were broadly similar between endovascular interventions and vein bypass.[29,30]

Similarly, we report rates of primary patency, primary-assisted patency, and secondary patency of 68.5%, 70.1%, and 70.2%, respectively, with a median follow-up of 19 months. Considering the mean follow-up period, having estimated outcomes up to 3 years could have reduced the generalizability of our analysis.

Nonetheless, satisfactory mid- and long-term graft patency rates for either femoro-popliteal or

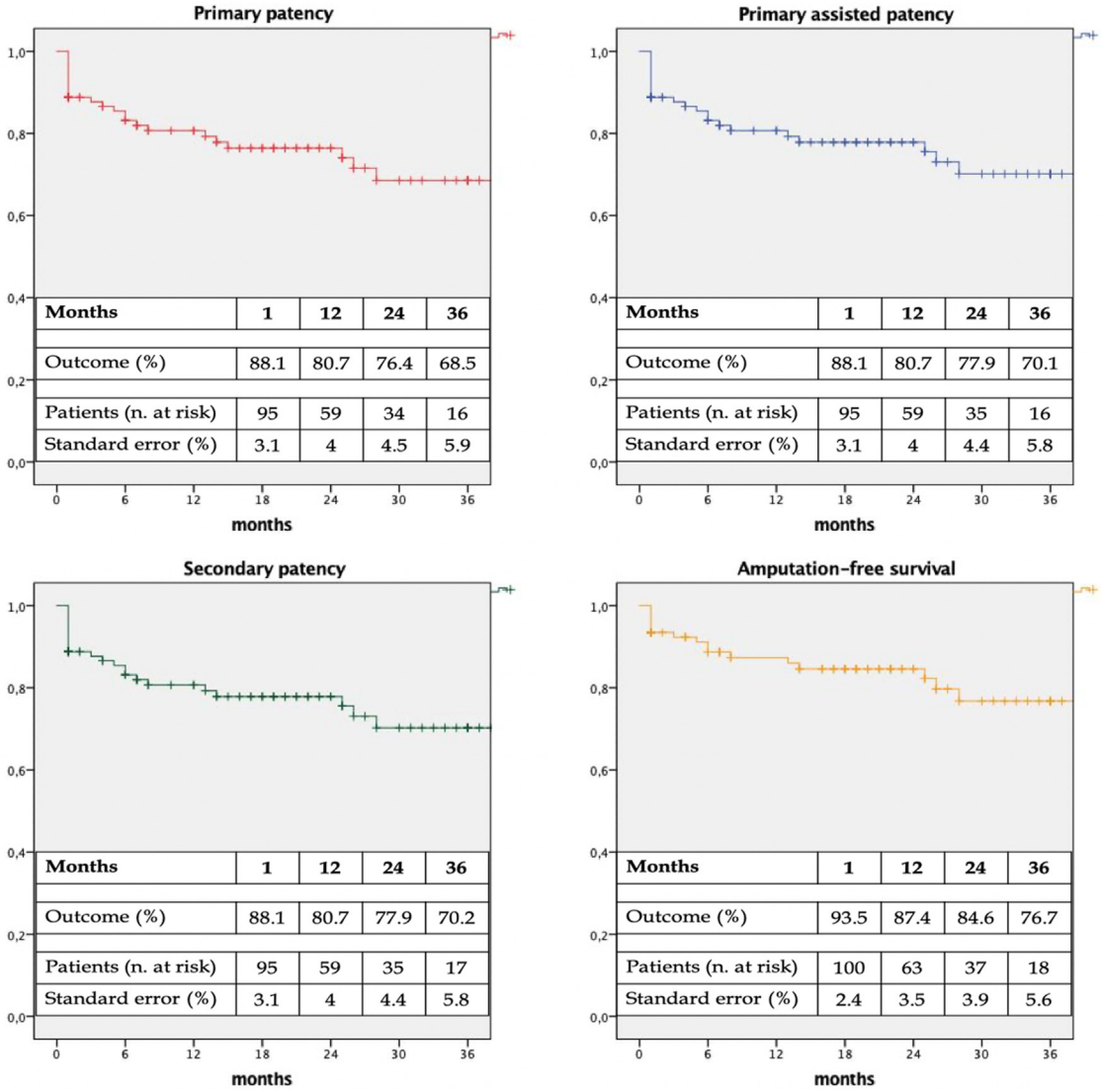


Fig. 2. Estimated 3-year primary patency, primary assisted patency, secondary patency, and amputation-free survival (Kaplan-Meier curves with outcomes, numbers of patients at risk, and standard error values).

femoro-tibial bypasses have already been demonstrated, especially when performed using a single-segment GSV.[31,32]

However, our results seem to suggest that inframalleolar short bypasses may represent a valid alternative to longer femoro-tibial bypasses for improving the inflow in the target runoff vessel in the presence of patent superficial femoral artery (SFA).[33]

Furthermore, the relatively high rate of limb salvage (76.7%) at 3 years presented in our cohort could be explained by the low rate of 30-day bypass occlusion. In fact, the graft patency should be sufficient for effective wound healing, decreasing the need for amputation. Due to this, patients who presented with extensive lesions, where a single runoff vessel would have not been sufficient to guarantee a rapid wound healing, underwent a bifurcated graft. Indeed, according to our analysis, patients classified as either Rutherford 5 or 6 may benefit for the most of this type of bypass. On the other hand, another point to consider, when performing inframalleolar surgical revascularizations, is the status of the upstream SFA. In case of stenosis or occlusion, the bypass patency may be compromised due to a poor inflow. In our cohort, only 2% of patients developed a nonhemodynamic stenosis (<70%) at the level of the SFA, which did not affect the distal runoff. In any case, a strict follow-up is mandatory to promptly diagnose and

Table IV. Univariate analysis at 3 years

Variables	Primary patency (%)	*P*	Primary assisted patency (%)	*P*	Secondary patency (%)	*P*	Freedom from MALEs (%)	*P*	Amputation-free survival (%)	*P*
Sex		0.23		0.28		0.28		0.71		0.73
Male	66.7%		68.7%		68.9%		65.9%		76.9%	
Female	74.5%		74.5%		74.5%		65.1%		74.5%	
Age		0.75		0.94		0.94		0.76		0.87
<80 years	66.8%		66.8%		67.1%		62.8%		73.8%	
>80 years	69.8%		75.6%		75.6%		72.5%		81.9%	
Active smoking		0.55		0.50		0.52		0.44		0.60
No	69.8%		71.5%		71.5%		66.5%		77.6%	
Yes	58.3%		58.3%		58.3%		54.8%		66.7%	
Former smoking		0.38		0.53		0.53		0.88		0.78
No	73.7%		73.7%		73.7%		65.5%		77.4%	
Yes	61.5%		65.5%		65.5%		64.5%		74.9%	
Hypertension		**0.04**		**0.05**		**0.05**		0.07		0.07
No	93.3%		93.3%		93.3%		90.2%		100%	
Yes	62.5%		64.6%		64.6%		63.4%		71.4%	
Hypercholesterolemia		0.09		0.14		0.14		0.33		0.29
No	79.4%		79.4%		79.4%		73.5%		84.1%	
Yes	58.7%		61.9%		61.9%		60.4%		69.8%	
Diabetes mellitus		**0.01**		**0.02**		**0.02**		0.25		0.27
No	92.1%		92.1%		92.1%		78.5%		87.9%	
Yes	58.8%		61.2%		61.5%		60.1%		70.8%	
Insulin treatment		**< 0.001**		**< 0.001**		**< 0.001**		**0.02**		**0.02**
No	80.7%		82.6%		82.6%		75.1%		84.1%	
Yes	24.7%		24.7%		24.7%		31.1%		37.3%	
COPD		0.39		0.24		0.25		0.88		0.91
No	68.7%		68.7%		68.7%		67.5%		78.5%	
Yes	71.2%		75.6%		75.6%		65.4%		75.8%	
CAD		0.50		0.71		0.70		0.48		0.43
No	71.3%		71.3%		71.3%		70.4%		79.4%	
Yes	64.9%		69.4%		69.4%		63.4%		73.5%	
Atrial fibrillation		0.09		0.11		0.12		0.11		0.07
No	64.8%		66.8%		66.8%		62.5%		73.7%	
Yes	82.6%		82.6%		82.6%		75.6%		88.9%	
LVEF <40%		0.18		0.15		0.15		0.54		0.62
No	72%		73.8%		73.8%		68.5%		79.3%	
Yes	43.2%		43.2%		43.2%		50.3%		55.6%	
Chronic kidney disease		0.42		0.33		0.32		0.92		0.98

(*Continued*)

Table IV. Continued

Variables	Primary patency (%)	*P*	Primary assisted patency (%)	*P*	Secondary patency (%)	*P*	Freedom from MALEs (%)	*P*	Amputation-free survival (%)	*P*
No	70.6%		72.9%		72.9%		65.4%		77%	
Yes	63.9%		63.9%		63.9%		67.8%		77%	
Dialysis treatment		**0.003**		**0.002**		**0.002**		0.07		**0.03**
No	74.7%		76.6%		76.6%		70.3%		81.4%	
Yes	37.5%		37.5%		37.5%		48.4%		50%	
Long-term corticosteroid		**0.005**		**0.003**		**0.003**		0.07		**0.05**
No	71.9%		73.8%		73.9%		68.3%		78.4%	
Yes	44%		44%		44%		55.3%		64.1%	
Prev endovasc proced		0.23		0.35		0.40		0.58		0.55
1	73.1%		73.1%		73.7%		64.3%		71.7%	
2	63.5%		65.1%		66.4%		72.3%		70.9%	
Rutherford class		0.12		0.08		0.10		0.07		0.07
4	73.3%		75.5%		74.2%		73.5%		83.1%	
5	69.4%		70.9%		67.5%		69.2%		79.4%	
6	41.7%		41.7%		41.7%		42.8%		51.7%	
WIfI stage		0.26		0.39		0.39		0.19		0.15
2−3	74.1%		74.1%		74.3%		62.8%		71.5%	
4	62.3%		65.8%		65.8%		73.5%		81.6%	
Preoperative imaging		0.16		0.11		0.11		0.35		0.47
Duplex scan	76.3%		78.6%		78.8%		73.5%		81.8%	
Other	49.9%		49.9%		49.9%		54.1%		63.5%	
Proximal anastomosis		0.34		0.41		0.41		0.63		0.59
Popliteal AK	81.7%		81.7%		81.7%		74.4%		85.7%	
Popliteal BK	65.6%		68%		68%		67.1%		75.2%	
Outflow		0.63		0.46		0.45		0.88		0.95
Dorsal	68.2%		68.2%		68.2%		68.3%		77.9%	
Plantar	70.1%		73.8%		73.8%		64.1%		75.7%	
Surgical technique		0.50		0.55		0.56		0.87		0.96
Reversed	81.5%		81.5%		81.5%		74.1%		85.3%	
Non reversed	66.3%		68.1%		68.3%		65.8%		77.8%	
No clamping technique		0.54		0.75		0.75		0.65		0.78
No	70.5%		74%		74%		71.1%		80.9%	
Yes	66.3%		66.3%		66.3%		64.2%		73.4%	
Time >240 min		0.40		0.46		0.47		0.22		0.18
No	82.4%		82.4%		82.4%		83.5%		94.1%	
Yes	64.8%		66.9%		67.1%		63.8%		72.8%	

Anesthesia		0.42		0.58		0.58		0.58		0.69
General	67.7%		67.7%		68.4%		60.6%		70.2%	
Loco-regional	66.2%		69.7%		69.7%		72.5%		81.1%	
Postop statin use		0.54		0.42		0.43		0.38		0.31
No	72.8%		75.4%		75.4%		71.1%		82.4%	
Yes	61%		61%		61%		55.5%		66.1%	
Postop OAC/DOAC		0.43		0.14		0.15		0.12		0.15
no	65.6%		65.6%		65.8%		69.5%		72.4%	
yes	82.5%		88.8%		88.8%		84.3%		94.7%	

Bold values indicate statistically significant ($P < 0.05$).
MALE, major adverse limb event; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; AK, above-the-knee; BK, below-the-knee; OAC, oral anticoagulants; DOAC, direct oral anticoagulants; CAD, coronary artery disease.

perform the intervention, if necessary, to prevent bypass occlusion.

In our study, the majority of patients presented with diabetes mellitus, which is a well-known factor negatively affecting outcomes.[34,35] Similarly, patients with end-stage renal disease (ESRD) are recognized to suffer from poor patency and low amputation-free survival rates due to extensive calcifications of tibial arteries and high susceptibility to infections.[36] In our series, patients with diabetes mellitus or on dialysis had significantly worse overall patency and amputation-free survival rates, compared with those who did not present the aforementioned risk factors. Furthermore, long-term corticosteroid use seems to be a strong predictor of poor patency and limb salvage. These data are in contrast with that recently reported by Romary et al.,[37] who demonstrated that chronic systemic immunosuppression with corticosteroid did not have a significant effect on late outcomes following lower extremity revascularization, in terms of primary patency, reintervention, or major amputation. Conversely, our results highlight the negative impact on outcomes of chronic corticosteroid use, in terms of immunosuppression and wound healing delay because of both local and systemic effects.[38,39] Moreover, in our study, another factor negatively affecting mid-term patency is insulin treatment. Indeed, a strong association between perioperative glucose control and 30-day mortality, in addition to multiple other postoperative outcomes, has already been demonstrated.[35] However, it is yet to be determined, which is the better hypoglycemic regimen to reach the target glycemic level. In fact, some studies reported lower amputation-free survival rates in both insulin and noninsulin-treated patients.[40] On the other hand, patients under an insulin regimen are the most generally ill of all CLTI patients, so that worse outcomes in terms of overall patency can be expected. Nonetheless, Dosluoglu et al.[41] showed nearly identical survival and limb salvage rates of patients controlled with diet or oral medications (OM) to nondiabetics. Furthermore, both these outcome measures were significantly better in patients treated without insulin, so that being on insulin regimen was independently associated with decreased survival and limb loss but not primary patency. Above all, we further underlined that insulin treatment may also decrease overall patency rates. This may be of particular interest for preoperative medical assessment and management of patients who are candidates for inframalleolar bypass. It could be reasonable to speculate whether in the perioperative period, it may be worth to prefer a lower glycemic control obtained with OM rather than a higher

control based on insulin regimen. Given the aforementioned factors and the satisfactory 3-year patency rate, we are encouraged to safely perform a short inframalleolar bypass after a single upfront failed endovascular attempt. Obviously, before deciding to proceed with the intervention, consideration should be done on cost-effectiveness. Recent evidence from BASIL-2 trial demonstrated that infrapopliteal bypasses are more expensive than best EVT, in terms of both procedural human resources and total in-hospital costs.[42,43] On the other hand, in cases of challenging endovascular procedures where the foreseen devices would be used and related costs would be too high, performing a short distal bypass with the GSV may represent an alternative that somehow can limit the costs. This approach can translate into a shorter hospital stay, thanks to the reduced number of surgical wounds that allow an early recovery and the low rate of reintervention due to satisfactory primary patency rates.

This study has several limitations. First of all, it is a retrospective study and as such it owns inherited selection bias. Secondly, the small sample size reduces the sensitivity of subgroup and multivariate analyses. Third, the study group lacks of a comparative group; in fact, the policy of the 3 centers participating in this retrospective study is to offer a ''first-endovascular'' approach, and then to switch to a distal bypass when the autologous vein material is available. Eventually, it is to be considered that not all centers are able to perform this type of procedures, so that results are not easily reproducible on a large scale.

CONCLUSION

This multicenter experience demonstrated that ''short'' vein bypasses to the foot arteries yielded excellent mid-term patency and good limb salvage rates after a failed tibial endovascular recanalization. These outcomes should be necessarily compared to those obtained with the modern endovascular approaches. Insulin-dependent diabetes mellitus and long-term corticosteroid use seemed to affect the outcomes. Further studies with bigger population sizes are needed to validate these outcomes.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Nicola Troisi: Writing – original draft, Visualization, Validation, Supervision, Formal analysis, Data curation, Conceptualization. **Francesco Stilo:** Validation, Supervision, Data curation, Conceptualization. **Daniele Adami:** Validation, Supervision, Formal analysis. **Giovanni De Caridi:** Visualization, Validation, Supervision. **Nunzio Montelione:** Visualization, Validation, Supervision, Methodology, Investigation, Data curation. **Giulia Bertagna:** Writing – original draft, Visualization, Data curation, Conceptualization. **Chiara Barillà:** Validation, Data curation. **Raffaella Berchiolli:** Writing – review & editing, Visualization, Validation, Supervision. **Francesco Spinelli:** Validation, Supervision, Conceptualization. **Filippo Benedetto:** Visualization, Validation, Supervision, Methodology, Data curation.

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