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Clinical Outcomes and Cost Implications of Recanalization for Complex Femoropopliteal Occlusive Disease Using a Retrograde Tibial Approach After Failed Infragenicular Bypass

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Abstract

Purpose: We report the mid-term outcomes of the Controlled Antegrade Retrograde Subintimal Tracking (CART) or reverse CART (r-CART) technique in patients who underwent recanalization for femoropopliteal occlusive disease after an occluded infragenicular bypass and the cost-effectiveness of the retrograde approach.

Methods: A case-series study was performed in all patients who underwent retrograde recanalization for complex femoropopliteal occlusive disease at our centre, with data prospectively collected from November 2015 to April 2018. The assigned costs for the economic evaluation were the initial hospitalization and all perioperative admission-related complications.

Results: A total of 185 patients underwent femoral and/or popliteal artery intervention. Fifty-five patients were identified as suitable for the retrograde approach after failed antegrade recanalization and were included in this registry. A total of 40 patients underwent a retrograde approach but never had infragenicular bypass surgery (group A patients), whereas 15 patients underwent previous placement of an infragenicular bypass graft that occluded despite patent tibial vessel run-off (group B patients); the mean lesion lengths were 24.4 ± 8.1 cm *vs.* 34.9 ± 3.7 cm, respectively, and this difference was significant (P=0.03). The overall median procedure time in both groups was 107.7 ± 49.8 minutes (range, 175 min to 503 min), with an overall median fluoroscopy time of 27.7 ± 12.1 minutes (range, 38 min to 105 min) and a contrast volume of 133.2 ± 63.7 mL (range, 31 mL to 121 mL). However, the duration of fluoroscopy was significantly different between the two groups of patients (30.4 ± 12.0 minutes *vs.* 20.8 ± 9.6 minutes; P= 0.01). The retrograde approach cost ($25106 ± 8700) was significantly higher than the cost for patients who underwent the antegrade approach ($17337 ± 7827, *P*=0.002). The average total cost per patient after procedural admission was 1.5-fold higher for the retrograde approach than for the antegrade approach (P<0.001).

Conclusion: We suggest that retrograde revascularization should be considered a part of the complete armamentarium in the management of femoropopliteal occlusive disease, primarily in long and heavily calcified lesions after failure of the antegrade approach, even in patients with failed previous infragenicular bypass surgery. The increased initial treatment costs can be offset by the benefits of this procedure.

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Introduction

Peripheral artery disease has been considered an increasingly important medical problem that affects approximately 12% of people over the age of 60 [1,2]. An endovascular approach is associated with lower morbidity and is preferable to open surgical techniques for comparable lesions [3].

As first reported by Spinosa et al. [4], the subintimal arterial flossing with Controlled Antegrade Retrograde Intervention (CART) recanalization technique has become an important addition to the endovascular armamentarium. It is principally indicated when antegrade passage of a wire through a lesion is unsuccessful [5-8]. This has resulted in lesions previously deemed not amenable to endovascular therapy now being successfully treated *via* the incorporation of this technique either *via* the popliteal artery or the pedal/tibial vessels [9-14].

There is no published data reporting the outcomes of this technique in patients with previous bypass surgery despite all publications supporting the use of this technique in patients with *de novo* complex arterial lesions. It is uncertain whether these patients have as good outcomes as those with *de novo* arterial lesions, or if the presence of a failed bypass/anastomosis jeopardizes technical and patency outcomes. Concomitantly, the cost of employing the CART technique remains unclear and unreported.

The primary aim of our study was to report the safety and mid-term outcomes of the CART technique in patients who underwent recanalization for femoropopliteal occlusive disease after occluded infragenicular bypass compared with those who underwent a *de novo* procedure after failed antegrade recanalization. The secondary aim was to report the overall cost of the CART technique compared with that of an antegrade alone technique.

Materials and Methods

Patients

A review of all patients who underwent a retrograde pedal/ tibial approach to treat femoral and/or popliteal arterial occlusive disease was performed between November 2015 and April 2018 at Royal Perth Hospital (RPH), Western Australia. Lower extremity Computed Tomography Angiography (CTA) was performed in all patients who had previously undergone infragenicular bypass surgery, unless the eGFR was <30 mL/min prior to any intervention. An antegrade recanalization approach was attempted in all patients. In cases of technical antegrade failure, the primary operator decided to identify whether crural vessel run-off was suitable for a retrograde attempt [defined as a Patent Posterior Tibial Artery (PTA) crossing the ankle joint and/Oran Anterior Tibial Artery (ATA) in continuity with a patent Dorsalis Pedis Artery (DPA)]. In suitable cases, retrograde revascularization was attempted during the same procedure. A total of 185 patients underwent femoral and/or popliteal artery intervention. Fifty-five patients' were identified as suitable for a retrograde approach after failed antegrade recanalization. Of these, 15 patients had undergone previous placement of an infragenicular bypass graft that occluded despite patent run-off (group B). Group A consisted of patients who underwent a retrograde approach but never had infragenicular bypass surgery (n=40). All patients were followed according to the protocol after peripheral angioplasty and/or clinical stenting, Ankle Brachial Index (ABI) testing, duplex scanning and CTA if deemed necessary.

Data collection

Baseline demographic information and procedural characteristics were retrieved 6 from clinical notes as well as vascular department and operating theatre databases. The information recorded included age, ethnicity, smoking status, and medical history. Most importantly, information was obtained on the current intraoperative findings, post-operative follow-up, perioperative complications and patency rate after successful recanalization. Information relating to the economic evaluation were collected *via* RPH accounting office. This included all direct costs related to the surgical or interventional radiologic procedure in addition to the indirect costs of overhead that were allocated to the treating department. Direct costs, some of which were based on an hourly rate, included all labor and supplies related to the delivery of the procedure. Indirect costs included the expenses of cost centers that were administrative or ancillary in nature, as well as expenses such as utilities that were allocated on the basis of square footage of the providing department. Professional fees were based on current Medicare reimbursement in Australia for surgical reconstruction or stent deployment. All other data were obtained retrospectively through review of the hospital records and outpatient clinical charts. The hospital ethics committee approved the study protocol.

Primary endpoints

The endpoint in this study was primary patency at 6 and 12 months using DUS and/or CTA and assigned cost of the procedure. The loss of primary assisted patency was defined as the first occurrence of occlusion of the treated arterial segment by DUS or CTA or surgical bypass of the treated arterial segment in treatment areas that demonstrated an increase in the Peak Systolic Velocity Ratio (PSVR) ≥ 3.0 (PSVR within the area of stenosis divided by peak systolic velocity in a normal adjacent proximal artery segment). Lesions occurring within 5 mm of the proximal or distal ends of the stented segment were part of the treated arterial segment for analytical purposes. The assigned costs for the economic evaluation were the initial hospitalization and all perioperative admission-related complications.

Secondary endpoints

Secondary endpoints included changes in post-operative ABI improvement by 1.0 or greater above baseline that did not deteriorate by >0.15 from the maximum early post-procedure level), major and minor amputation rates, limb salvage, 30-day mortality and morbidity and complications. Complications included those that were access-related, such as hematoma, pseudo aneurysm and arteriovenous fistula formation; as well as systemic, such as perioperative myocardial infarction and contrast-induced nephropathy. Technical success was defined as a residual stenosis post-intervention of less than 30% of the final residual luminal stenosis measured at the narrowest point of the vascular lumen [15].

Hemodynamic success was defined as a 0.10 improvement in the ABI from pre-procedure to immediately post-procedure (discharge). ABI values were recorded prior to intervention, pre-discharge, at 1, 3, 6, and 12 months and yearly post-procedure. Clinical success was defined as the relief or improvement of the presenting symptoms with an improvement of at least one Rutherford category [15]. Based on fluoroscopic visualization, calcification was classified as minor (i.e., calcification involving less than half of the circumferential vessel wall), moderate (i.e., calcification involving more than half the vessel wall), or major for deposits filling the entire vessel diameter [16,17].

Technique

All patients underwent ABI measurements either with or without a dynamic treadmill exercise test if indicated and feasible, a lower limb arterial duplex and/or CTA prior to their vascularization procedure. All patients were taking aspirin (100 mg to 150 mg daily) on admission.

Procedures were performed either with local anesthetic with intravenous sedation or under general anesthesia. Access to the infrainguinal recanalization site was obtained through US-guided puncture of the contralateral or ipsilateral common femoral artery [18,19]. If the proximal 5 cm to 10 cm of the Superficial Femoral Artery (SFA) was involved, our initial means of endovascular

Table 1: Demographic and clinical characteristic of the patients.

Characteristics	All Patients	Group A	Group B	P-value
	(N=55)	(N=40)	(N=15)	
Age (year)*	72.5 ± 10	71.0 ± 9.5	76.4 ± 10.5	0.08
Male sex-no. (%)	45 (82)	33 (83)	12 (80)	0.83
Smoking at baseline - no. (%)	28 (51)	22 (55)	6 (40)	0.33
Hyperlipidaemia -no. (%)	32 (58)	26 (65)	6 (40)	0.1
Diabetes mellitus -no. (%)	28 (51)	20 (50)	8 (53)	0.83
Coronary artery disease -no. (%)	31 (56)	24 (60)	7 (47)	0.38
Chronic kidney disease -no. (%)	10 (18)	7 (18)	3 (20)	0.83
Hypertension - no. (%)	45 (82)	36 (90)	9 (60)	0.01
Cerebrovascular disease - no. (%)	2 (4)	2 (5)	0	0.39
Rutherford-Baker classification of PAD - no. (%) ‡				
R-B III	12 (22)	10 (25)	2 (13)	0.36
R-B IV	28 (51)	19 (48)	9 (60)	0.42
R-B V	15 (27)	11 (28)	4 (27)	0.95
Target vessel - no. (%)				
SFA only	46 (84)	32 (80)	14 (93)	
Popliteal artery with or without SFA	9 (16)	8 (20)	1 (17)	
Baseline ABI*	0.40 ± 0.13	0.44 ± 0.14	0.31 ± 0.05	
Treated side - no.				
Left	30 (55)	24 (60)	6 (40)	N/A
Right	25 (45)	16 (40)	9 (60)	N/A

*Plus-minus values are means ± SDs

‡Rutherford-Becker stage 3 corresponds to incapacitating claudication, stage 4 to ischemic pain while the patient is resting, and stage 5 to ischemic ulcers

treatment for SFA occlusion was the contralateral retrograde femoral approach. If the proximal SFA was intact, we chose the ipsilateral antegrade femoral artery approach. If antegrade recanalization of the target infrainguinal artery failed, the leg and foot were prepared in a sterile manner, and local anesthesia was administered. A suitable crural vessel was therefore identified as the target vessel for the pedal puncture. If the peroneal artery was the only patent or disease-free vessel, then the bypass decision was made (this was considered an exclusion criterion in our registry).

The tibial artery was punctured using a 21-gauge EchoTip® needle (Micropuncture® PedalAccess Set, Cook Medical, Bloomington, USA) under ultrasound guidance using an 18-Hz 'Hockey stick' transducer (General Electric HealthCare, Waukesha, WI, USA). An introducer sheath was not placed in the tibial artery unless it was deemed necessary by the operator.

However, if it was deemed necessary, a 4F micropuncture sheath with a Check-Flo® haemostatic valve was placed into the vessel, and 5000 IU heparin was administered intra-arterially. From the pedal approach, a 0.014-inch (PT2, Boston Scientific Corporation, Natick, MA, USA) or 0.018-inch (V-18™ ControlWire® Guidewires, Boston Scientific Corporation) and Hi-Torque Connect 250T, Abbott Vascular, Santa Clara, California, USA) wire was used to negotiate the occluded femoropopliteal vessels with a Quick Cross® support catheter (Spectranetics Corporation, Colorado Springs, USA) or a CXITM support catheter (Cook Medical Incorporation, Bloomington, USA). The occluded vessel was either crossed easily or was crossed using adjunct techniques as a rendezvous technique or the CART technique [4,20,21]. In most cases, the tibial wire was snared from the femoral access side. Predilation was performed in all cases before either angioplasty with Drug-Eluting Balloons (DEBs) or stenting of the lesion. A variable dose of 100 μ to 500 μ Gintra-Arterial Glyceryl Trinitrate (GTN) was administered selectively into the tibial arteries according to the systemic blood pressure to resolve vasospasm before removal of the pedal sheath. An angiography was performed at the end of the procedure to demonstrate the integrity of the reanalyzed vessel and the crural puncture site. If contrast extravasation persisted from the pedal puncture site, prolonged digital pressure was performed (Figure 1a-1c), and if unsuccessful, this was followed by angioplasty of the distal vessel (Figure 2a, 2b). A completion angiogram was performed to identify the integrity of the puncture vessel site and the plantar arch (Figure 2c). An ABI and, if possible, absolute toe pressure and toe-brachial index measurements were performed before discharge and at each follow-up to assess the integrity of the puncture vessel site and the durability of the reanalyzed femoropopliteal vessel. The femoral lesions were treated with a Passeo-18 Lux DEB (Biotronik AG, Bülach, Switzerland) and/or bare metal self-expandable stents (BM-SES; Pulsar-18 SE Nitinol Stent, Complete™ SE vascular stent and Absolute Pro® vascular self-expanding stent system) according to the physician's clinical judgment. A senior operator (BPM) performed all retrograde puncture case procedures. The patients were moved to the ward for an overnight stay. They were discharged the following day with dual antiplatelet therapy (100 mg aspirin and 75 mg clopidogrel once daily after a loading dose of 300 mg, unless the patient was already on clopidogrel). Dual antiplatelet therapy was continued for at least 6 months.

Table 2: Baseline angiographic and interventional data.

Variables	**All Patients** (N=55)	**Group A** (N=40)	**Group B** (N=15)	**P-value**
Length of treated segment* - cm	27.2 ± 8.6	24.4 ± 8.1	34.9 ± 3.7	0.03
TASC classification				0.08
B	3 (5.5)	3(7)	0	
C	8 (14.5)	8 (20)	0	
D	44 (80)	29 (73)	15 (100)	
Target-lesion calcification - no. of patients (%) ‡				0.69
Moderate	13 (24)	10 (25)	3 (20)	
Severe	42 (76)	30 (75)	12 (80)	
No. of crural run-off vessels - no. of patients (%)				0.32
1	4 (7)	3 (8)	1(7)	
2	17 (31)	11 (27)	6 (40)	
3	34 (62)	26 (65)	8 (53)	
Radiation dose	23.754 ± 17.144	26.093 ± 19.326	17.518 ± 5.992	0.1
Duration of fluoroscopy - min	27.7 ± 12.1	30.4 ± 12.0	20.8 ± 9.6	0.01
Amount of contrast agent - ml	133.2 ± 63.7	140.6 ± 66.1	113.4 ± 53.9	0.16
Preoperative creatinine	108.7 ± 94.2	116.6 ± 108.9	87.6 ± 22.5	0.31
Procedure duration - min	107.7 ± 49.8	104.1 ± 42.8	117.3 ± 65.9	0.39
Pedal sheath duration - min	12.9 ± 4.3	12.5 ± 4.0	14.2 ± 4.7	0.18
Heparin dose-units	6636.4 ± 2163.4	6800 ± 2344.7	6200 ± 1567.5	0.37
GTN dose -mcg§	233.6 ± 113.1	215.0 ± 113.3	283.3 ± 99.4	0.05
Major complication - no. of patients (%)	4 (7)	3 (8)	1 (6)	0.42

*Plus-minus values are means ± SDs
‡Calcifications were determined either by pre-operative CT (Computed Tomography) angiography or by fluoroscopy
§GTN denotes Glyceryl Trinitrate expressed in micrograms (mcg)

Table 3: Breakdown of resource usage and costs (2015-2018 Australian dollar) during procedural hospitalization comparing both groups of retrograde patients.

Cost centres	Mean (SD), cost per patient		Mean cost difference	P-value*
	Group A (N=40)	Group B (N=15)	(95% CI)	
Operating room	3122 (1284)	3520 (1977)	975 (-720 to 1590)	0.43
Devices**	12395 (3419)	15659 (3920)	4458 (993 to 6274)	0.006
Medical personnel	3831(2159)	3852 (1771)	505 (-868 to 1505)	0.84
Nursing staff†	653 (230)	715 (236)	-50 (-93 to 210)	0.51
Allied health services	131 (112)	321 (242)	168 (9 to 421)	0.01
Laboratory services	1070 (382)	1092 (545)	-8.5 (-260 to 290)	0.74
Radiology services	339 (186)	445 (164)	95 (9 to 198)	0.03
Pharmacy services††	373 (175)	501 (244)	59 (-13 to 227)	0.08
Ward consumables and other expenses§§	1980 (1180)	2115 ± 1196	5148 (1768 to 13284)	0.85
Total	23894 (8065)	28220 (9195)	13516 (9345 to 17890)	0.06

CI: Confidence Interval; SD: Standard Deviation. *A two-tailed test was used (Mann-Whitney test).
**Devices, including stents, wires, sheaths, drug-eluting balloons and any other devices (implantable or non-implantable) used
†ward nursing from the ward only. Nursing costs were based on the average per diem cost for the specific patient care unit multiplied by the length of stay on the unit
††Pharmaceutical services include all pharmaceutical costs provided by the hospital in areas such as wards and high-dependency units except operating theatres
§§Administrative and hospital room costs (based on the average per diem cost for the specific patient care unit multiplied by the length of stay on the unit)

Statistical analysis

Patient demographics and outcomes between the two groups of patients are reported as absolute numbers and percentages, and continuous values are expressed as the means (± SDs), along with medians and ranges if necessary. Primary patency, primary assisted patency and freedom from TLR were determined using Kaplan-Meier analysis. A log-rank test was used to compare patency estimates when the patency endpoints were stratified, and one-way ANOVA was used for multiple comparison analysis. For comparative analyses, a P value of 0.05 or less was considered to represent a significant difference.

A cost-effectiveness analysis of the overall procedures was performed. The estimated cost was compared with the overall cost for the subset of patients who underwent successful antegrade recanalization of the femoropopliteal disease segment. Analyses were conducted using PASW 18 (SPSS, Chicago, Ill) and SAS 9.2 (SAS Institute Inc., Cary, NC) statistical software.

Table 4: Breakdown of resource usage and costs (2015-2018 Australian dollar) during procedural hospitalization comparing retrograde and antegrade cases.

Cost centres	Mean (SD), cost per patient		Mean cost difference	P-value*
	Retrograde group (N=55)	Conventional antegrade group (N=130)	(95% CI)	
Operating room	3231 (1495)	2009 (756)	1000 (750 to 1750)	<0.0001
Devices**	13285 (3818)	7662 (5131)	6436 (4434 to 7556)	<0.0001
Medical personnel	3837 (2045)	3244 (984)	308 (-698 to 378)	0.67
Nursing staff†	670 (231)	658 (183)	-62 (-91 to 60)	0.73
Allied health services	183 (178)	170 (153)	0 (-20 to 20)	0.99
Laboratory services	1076 (428)	872 (225)	112 (1 to -322)	0.04
Radiology services	368 (185)	320 (100)	–4 (-72 to 16)	0.35
Pharmacy services††	408 (202)	397 (191)	-3 (-65 to 52)	0.87
Ward consumables and other expenses§§	2048 (1180)	2005 (1004)	1(-760 to 886)	0.97
Total	25106 (8700)	17337 (7827)	13516 (9345 to 17890)	0.002

CI: Confidence Interval; SD: Standard Deviation

*A two-tailed test was used (Mann-Whitney test), **Devices, including stents, wires, sheaths, drug-eluting balloons and any other devices (implantable or non-implantable) used, †ward nursing from the ward only, ††Pharmaceutical services include all pharmaceutical costs provided by the hospital in areas such as wards and high-dependency units except operating theatres §§Administrative and hospital room costs

Results

Patient demographic and clinical characteristics

From November 2015 to April 2018, 185 patients underwent femoral and/or popliteal artery intervention. Fifty-five patients were identified as suitable for a retrograde approach after failed antegrade recanalization and were included in this registry; 40 patients underwent a retrograde approach but never received infragenicular bypass surgery (group A patients), whereas 15 patients underwent previous placement of an infragenicular bypass graft that occluded despite patent tibial vessel run-off (group B patients). Most patients in both groups were male, with a mean age of 71.0 ± 9.5 years and 76.4 ± 10.5 years for group A patients and group B patients, respectively (Table 1).

Procedure data

The technical success rate was 100% in group B patients; however, two patients experienced failure in group A because of the extensive calcification and inability to pass the guide wire intraluminally or to re-enter the true lumen after the occluded segment. These patients underwent placement of a femoral below-the-knee popliteal bypass graft and were included in the follow-up data of the registry and in the intention to treat analysis. The details of the procedural lesion characteristics are summarized in Table 2. The mean lesion length (by the normal-to-normal site method) was significantly different [24.4 ± 8.1 cm *vs.* 34.9 ± 3.7 cm] between groups A and B, respectively (P=0.03), with all patients in group B presenting with only TASC D lesions. The overall median procedure time (from skin incision to skin closure) in both groups was 107.7 ± 49.8minutes (range, 175 min to 503 min), with an overall median fluoroscopy time of 27.7 ± 12.1 minutes (range, 38 min to 105 min) and a contrast volume of 133.2 ± 63.7 mL (range, 31 mL to 121 mL). However, the duration of fluoroscopy was significantly different between the two groups of patients (30.4 ± 12.0 min *vs.* 20.8 min ± 9.6 min; P=0.01). The radiation dose was comparable between the two groups of patients: 26.093 ± 19.326 Gy cm^2 *vs.* 17.518 ± 5.992 Gycm^2 (P=0.10).

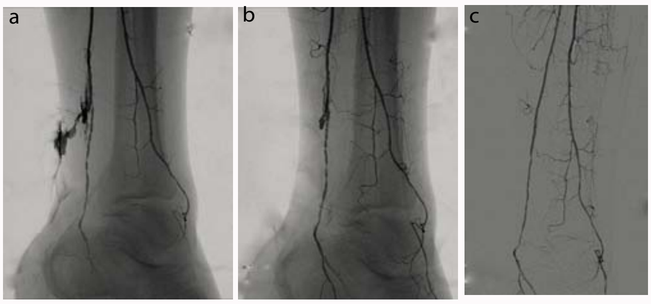


Figure 1: Angiographic imaging of a 70-year-old man with Rutherford 4 classification. **(a)** The posteriortibial artery was the target access vessel, and the final run-off imaging post-removal of the tibial sheath demonstrated extravasation of contrast through the puncture site. **(b)** After 5 minutes of digital pressure, there was a decrease in contrast extravasation at the tibial puncture site. **(c)** After 10 minutes of digital pressure, hemostasis was established with no evidence of residual stenotic lesions at the tibial puncture site.

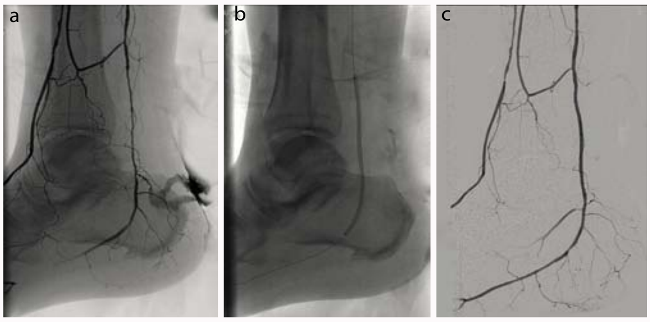
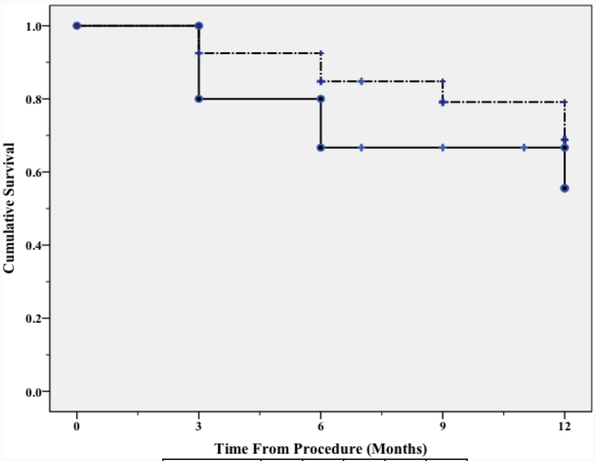


Figure 2: Angiographic imaging of a patient with an ischemic leg (RB 5). **(a)** Final angiographic runs after removal of the sheath at the end of recanalisation of the heavily calcified SFA and stenting demonstrate extravasation of contrast at the puncture site. **(b)** Balloon-assisted hemostasis angioplasty of the PTA with a 3 mm 100 mm Fox SV 0.18 balloon, inflated over 90 seconds. **(c)** Final angiographic run-off showing that hemostasis was achieved successfully with the PTA remaining patent with no evidence of residual stenosis.

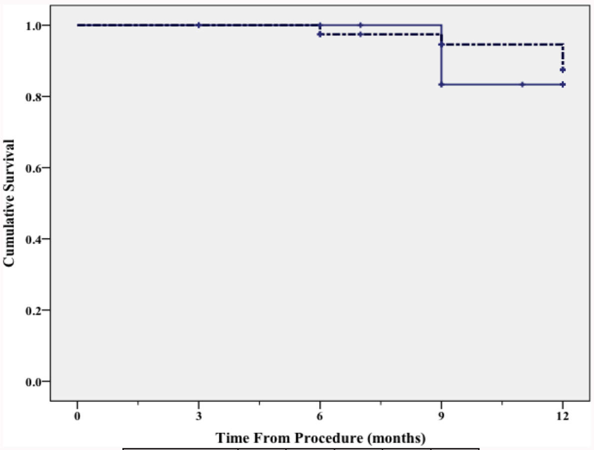
Primary endpoints

Primary patency was also evaluated by the Kaplan-Meier time-to-event method, as shown in Figure 3. For this analysis, the time to loss of patency was evaluated for all patients irrespective of the timing of their follow-up visits, thereby incorporating all available data. Under this method, the primary patency at 1 year was 73% in group A



N at Risk	0	3	6	9	12
Group A	40	36	31	23	19
Group B	15	12	9	7	4

Figure 3: Kaplan-Meier analysis of primary patency rates comparing both groups of retrograde patients (de novo occluded femoropopliteal segment and patients with failed bypass surgery). Log-Rank (Mantel-Cox), P=0.27. Kaplan-Meier curve of primary patency between patients who underwent retrograde recanalisation via the tibial approach at the level of the ankle for primary occluded long SFA segments (with or without previous stenting) (group A, dotted blue line), with a primary patency of 73%, and patients with failed infragenicular bypass (group B, straight blue line), with a primary patency of 60%. The overall primary patency was 69%.



N at Risk	0	3	6	9	12
Group A	40	39	37	32	24
Group B	15	14	13	8	6

Figure 4: Kaplan-Meier curve of primary assisted patency rates comparing both groups of retrograde patients (de novo occluded femoropopliteal segment and patients with failed bypass surgery). Log-rank (Mantel-Cox), P = 0.61. Kaplan-Meier curve of primary assisted patency between patients who underwent retrograde recanalization *via* the tibial approach at the level of the ankle for primary occluded long SFA segments (with or without previous stenting) (group A, dotted blue line), with a primary assisted patency at the 12-month follow-up of 90%, and patients with failed infragenicular bypass (group B, straight blue line), with a primary assisted patency at the 12 month-follow-up of 86.7%.

patients (95% CI, 9.8% to 11.6%) *vs.* 69% in group B patients (95% CI, 7.3% to 11.5%, P=0.27) (Figure 3). Upon further analysis, the 1-year assisted primary patency was 90% in group A patients (95% CI, 11.4% to 12.1%) *vs.* 86.7% in group B patients (95% CI, 10.9% to 12.1%, P=0.60) (Figure 4).

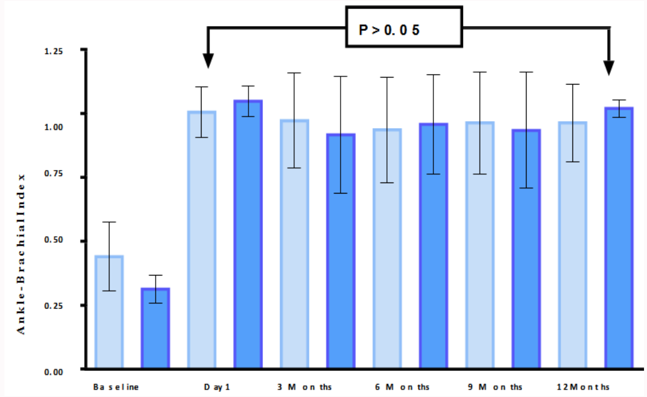


Figure 5: Graph showing the improvement in the ABI in both groups after the intervention. The ABI changed from a mean of 0.44 (95% CI, 0.39 to 0.48) preoperatively to a mean of 1.01 (95% CI, 0.97 to 1.04) prior to discharge from the hospital in group A, while in group B, the mean ABI changed from 0.31 (95% CI, 0.28 to 0.34) preoperatively to 1.05 (95% CI, 1.01 to 1.08) prior to discharge.

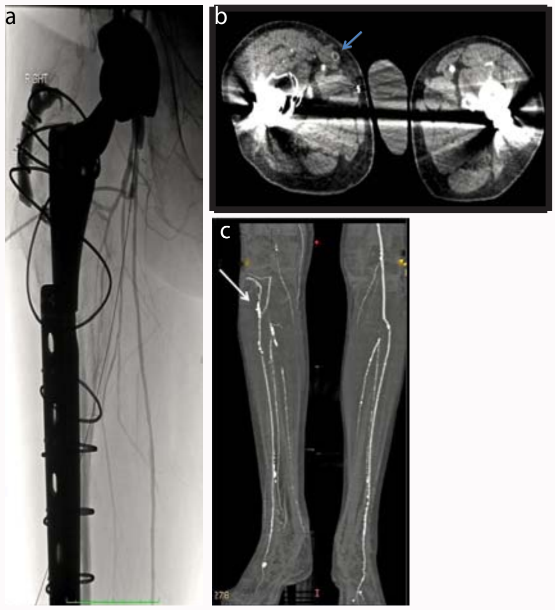


Figure 6: Angiographic imaging of a 70-year-old patient who previously underwent a femoral to anterior tibial artery bypass. **(a)** There was a stump from a previous bypass graft with a patent proximal SFA (yellow arrow). **(b)** The bypass graft was occluded (blue arrow), as shown in the axial CTA. **(c)** Reformatted CTA demonstrates that the anterior artery tibial artery has an in-line flow to the foot. The stump of the distal anastomosis of the previous femoro-distal bypass graft is easily identifiable (white arrow).

Log-rank (Mantel-Cox), P=0.61. Kaplan-Meier curve of primary assisted patency between patients who underwent retrograde recanalization *via* the tibial approach at the level of the ankle for primary occluded long SFA segments (with or without previous stenting) (group A, dotted blue line), with a primary assisted patency at the 12-month follow-up of 90%, and patients with failed infragenicular bypass (group B, straight blue line), with a primary assisted patency at the 12 month-follow-up of 86.7%.

Secondary endpoints

In group A, the mean ABI increased from 0.44 ± 0.14 (95% CI, 0.39% to 0.48%, range 0.1 to 0.63) at baseline to 1.0 ± 0.1 (95% CI, 0.97% to 1.04%, range 0.67 to 1.30) pre-discharge from the hospital

Figure 7: Angiographic imaging of a 70-year-old patient (see Figure 6) who previously underwent a femoral to anterior tibial artery bypass. Imaging post-retrograde recanalisation of the SFA and popliteal arteries. **(a)** The SFA was stented, and angioplasty was performed with a paclitaxel-coated drug-eluting balloon. **(b)** There are now two satisfactory vessel run-offs to the foot (the ATA and peroneal artery). The tibioperoneal and proximal peroneal arteries were subjected to angioplasty with a paclitaxel-coated drug-eluting balloon.

(Figure 5). In group B, the mean ABI increased from 0.31 ± 0.05 (95% CI, 0.28% to 0.34%, range 0.22 to 0.38) at baseline to 1.05 ± 0.06 (95% CI, 1.01% to 1.08%, range 0.92 to 1.13) pre-discharge from the hospital. There were no significant differences noted in the mean ABI values between the study groups at the 12-month follow-up after re-intervention in well-identified patients with significant rest enosis (Figure 5): 0.96 ± 0.15 (95% CI, 0.91% to 1.02%, range 0.48 to 1.10) and 1.02 ± 0.03 (95% CI, 0.99% to 1.05%, range 0.99 to 1.10).

Repeat interventions

There was a significant difference in the re-intervention rates (Table 2) between both groups (15% *vs.* 33.3%). The re-intervention technique was either the use of other stents (two stents *vs.* no stents) and/or DEB (six balloons *vs.* five balloons). There were no per procedural deaths, and freedom from Major Adverse Events (MAEs) was achieved in 92% of the patients in group A and 94% of the patients in group B. Myocardial infarction was reported in one patient in group A. All instances of hematoma at the puncture site required only conservative management. One patient in each group developed a pseudo aneurysm of the femoral artery, and both of these patients required surgical management because there were no candidates for thrombin injection. One patient developed a retroperitoneal hematoma requiring surgical evacuation and repair of the Common Femoral Artery (CFA). One patient in group A developed contrast-induced nephropathy and subsequently required dialysis for one week. His acute renal insufficiency was transient, and he no longer required dialysis at discharge.

As seen in Table 3, the average cost per patient in the subcategory's radiological services and devices were significantly higher in patients in Group B than those in Group A after failed infragenicular bypass. However, the total mean cost between both groups did not differ significantly ($23894 ± 8065 *vs.* $28220 ± 9195, P=0.06, two-tailed test). We did compare the overall cost of all retrograde patients with the patients who underwent successful recanalization through the antegrade approach based on a historical cohort of patients.

As demonstrated clearly in Table 4, the retrograde approach cost ($25106 ± 8700), which was significantly higher than the cost for patients who underwent the antegrade approach ($17337±7827, P=0.002, two-tailed test). The average total cost per patient after procedural admission was 1.5-fold higher in the event of a retrograde approach than of an antegrade approach (P<0.001). A significantly higher percentage of total hospital costs were related to the following subcategories: Operating room, devices and laboratory service costs.

Discussion

We have demonstrated here acceptable technical and patency outcomes, particularly in more complex patients with a previous history of surgical bypass. Despite having more complex lesions and presentations, patients with a previous history of surgical bypass have outcomes equivalent to those presenting with *de novo* arterial lesions. The CART technique is considerably more expensive than the antegrade technique.

The primary patency in both groups was not significantly different (60% in the failed infragenicular bypass group versus 73% in the simple retrograde group, P=0.27). The primary patency was also not significantly different between the two groups. These results compare favorably with those of published studies that report 1-year primary patency rates between 45% and 84.2% [22].

Retrograde revascularization is most often indicated in anatomically suitable patients following unsuccessful antegrade endovascular procedures [8,23]. These patients often have complete occlusions or multiple diffuse stenotic lesions that prevent antegrade wire passage. The improved success with a retrograde approach has been attributed to the tapering of the distal occlusion stump, which subsequently increases the chance of intraluminal guide-wire seating [6,17,24]. In the current study, the lesions that had undergone a failed antegrade approach were more severely calcified, which significantly influenced the application of the retrograde approach. Lesion length was also a significant factor that favored the retrograde pedal approach, as most of the lesions that experienced failure with the antegrade approach were TASC D lesions. All these factors are important considerations when considering a patient for endovascular revascularization.

Montero-Baker et al. [23] published one of the largest studies on the use of the retrograde approach for infragenicular lesions in 2008. Retrograde access was achieved *via* the ATA, the DPA or the PTA under 'road-map' imaging or contrast angiography. In 36 patients, no introducer was used to minimize vessel trauma (i.e., wire-balloon-only technique), whereas in nine patients, a 4-Frintroducer sheath was inserted. The remaining six patients underwent a trans-collateral retrograde loop technique as described by Fusaro et al. [10], the authors felt that a combination of factors, including the size of the 4-Fr sheath causing vessel trauma and the low-flow state exacerbated by revascularization failure, contributed to the formation of acute puncture site thrombosis, and they subsequently abandoned the use of 4-Fr sheaths for distal access. In our study, all retrograde vessel approaches were achieved under ultrasound imaging using a high-frequency Hockey stick probe.

Endovascular treatment of patients with a previous history of surgical bypass may result in problems. Scarring of the groin may make vascular access difficult; as such an alternative access point such as the contralateral groin may need to be planned. Conformation of the proximal and distal anastomoses also needs to be considered. A proximal anastomosis that is configured end-to-side will allow recanalization of the SFA. However, on control angiography, a sharp anterior oblique angle is required to differentiate the SFA origin from the anastomotic hood. If a proximal end-to-end anastomosis has been constructed, the SFA origin is usually excised. In this scenario, revascularization of the limb *via* passage of the wire through the graft will need to be attempted. Distal anastomosis also poses similar problems.

Again, an end-to-side configuration will allow access to the SFA in both the antegrade and retrograde directions. However, if an end-to-end distal anastomosis has been performed, then wire passage will occur through the bypass graft. Despite the technical difficulties that may be countered in revascularizing the post-bypass limb, we have demonstrated here a technical success rate of 100%, achieved via the retrograde technique. Importantly, the lack of difference in outcomes between the bypass and non-bypass groups suggests that the presence of bypass should not hamper attempts to revascularize the limb using endovascular means. This has been demonstrated clearly in the case illustrated in Figures 6a-6c and Figures 7a-7c.

In the economic analysis of the retrograde approach for recanalization of an occluded femoropopliteal arterial occlusive lesion, it was found that the retrograde approach increased initial hospital costs by $7769 per patient compared with antegrade approach recanalization. The higher costs were related to several factors, including the costs of and number of stents themselves, other disposable equipment (more than three wires and balloons used per case in the retrograde group) used in the catheterization laboratory, longer procedure durations, and higher physician costs. Nonetheless, such treatments can be cost-effective if they result in substantial and sustained improvements in quality of life (e.g., by improving claudicating or preventing amputation) or if applied to patients with a high likelihood of requiring peripheral bypass (OR Redo-Bypass) surgery in the event of primary or secondary treatment failure (previous failed bypass surgery subgroup).

Study Limitations

This study has several limitations. The sample size for this economic study was relatively small. Moreover, the duration of the economic analysis was brief and limited to only in-hospital costs. Further studies will be necessary to better define the short- and long-term costs associated with this therapeutic procedure. Formal cost-effectiveness analyses incorporating in-hospital and long-term quality of life benefits will be crucial for understanding the overall value of the retrograde approach.

Conclusion

We suggest that retrograde revascularization should be considered as a part of the complete armamentarium in the management of femoropopliteal occlusive disease, primarily for long and heavily calcified lesions after failure of the antegrade approach, even in patients with previous failed infragenicular bypass. The increased initial treatment costs can be offset by the benefits of this procedure.

Data Availability

Patient level data used for statistical analysis and to support the findings of this study are available from the corresponding author upon request.

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