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ORIGINAL ARTICLE

Cost Analysis of Target Lesion Revascularisation in Patients With Femoropopliteal In Stent Re-Stenosis or Occlusion: The COSTLY-TLR Study

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WHAT THIS PAPER ADDS

Target lesion revascularisation (TLR) is common following intervention(s) for femoropopliteal steno-occlusive peripheral artery disease (PAD). The precise cost of TLR has not been clearly defined in the literature, either from a monetary point of view or from the associated clinical events and complications. This multicentre international series found that the cost of TLR, from a healthcare payer's perspective, is high and mostly driven by operating time. This is novel important information for future PAD related health economic analyses; it provides justification for investigating and using techniques or types of intervention associated with reduced TLR when dealing with femoropopliteal PAD.

Objective: To report the cost of target lesion revascularisation procedures (TLR) for femoropopliteal peripheral artery disease (PAD) following stenting, from a healthcare payer's perspective.

Methods: European multicentre study involving consecutive patients requiring femoropopliteal TLR (January 2017 — December 2021). The primary outcome was overall cost (euros) associated with a TLR procedure from presentation to discharge. Exact costs per constituent, clinical characteristics, and early outcomes were reported.

Results: This study included 482 TLR procedures (retrospectively, 13 hospitals, six countries): 56% were female, mean age was 75 ± 2 years, 61% were Rutherford class 5 or 6, 67% had Tosaka class 3 disease, and 16% had common femoral or iliac involvement. A total of 52% were hybrid procedures and 6% involved open surgery only. Technical success was 70%, 30 day mortality rate was 1%, and the 30 day major amputation rate was 4%. Most costs were for operating time during the TLR (healthcare professionals' salaries, indirect and estate costs), with a mean of: €21 917 ± €2 110 for all procedures; €23 337 ± €8 920 for open procedures; €12 903 ± €3 108 for endovascular procedures; and €22 806 ± €3 977 for hybrid procedures. In a regression analysis, procedure duration was the main parameter associated with higher overall TLR costs (coefficient, 2.77; standard error, 0.88; $p < .001$). The mean cost per operating minute of TLR (indirect, estate costs, all salaried staff present included) was €177 and the mean cost per night stay in hospital (outside intensive care unit) was €356. The mean cost per overnight intensive care unit stay (minimum of 8 hours per night) was €1 193.

Conclusion: The main driver of the considerable peri-procedure costs associated with femoropopliteal TLR was procedure time.

Keywords: Cost effectiveness, Peripheral artery disease, Revascularisation
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INTRODUCTION

Peripheral artery disease (PAD) is a major health problem and the main cause of lower limb amputation.[1,2] Endovascular revascularisation procedures are now common amongst those with PAD, especially amongst patients with symptomatic femoropopliteal steno-occlusive disease. New technologies (e.g., drug coated balloons, atherectomy, and intravascular lithotripsy) aim to improve outcomes following endovascular treatment by reducing the need for target lesion revascularisation (TLR). Some randomised controlled trials (RCTs) and other studies have provided useful data regarding the clinical efficacy or effectiveness of such technologies compared with surgical revascularisation or plain balloon angioplasty;[1,3–7] however, they have not provided exhaustive cost effectiveness information. Recent work has highlighted that cost utility analyses in chronic limb threatening ischaemia are in their infancy. Revascularisation in infrainguinal disease may be favoured over major lower extremity amputation or conservative management; however, data are inadequate to support recommendations for any specific treatment.[8] A contemporary in depth and large scale pragmatic evaluation of the cost effectiveness of modern PAD endovascular devices cannot be performed using data from existing RCTs[7,9,10] because the actual cost of a TLR procedure from a healthcare payer's perspective for a patient with prior femoropopliteal endovascular intervention has not been comprehensively assessed in the existing literature using contemporary data. Furthermore, randomised data do not always reflect routine clinical care pathways,[11] which greatly impact the assessment of cost effectiveness. These reasons highlight the need for pragmatic and current data regarding the actual costs of femoropopliteal TLR in allcomers across countries and institutions. This will enable future work to provide a better understanding of the cost effectiveness of new endovascular therapies, especially since the actual cost of TLR in this context remains unknown. The most recent European guidance for the management of PAD,[12] as well as international guidance for the management of diabetic foot ulceration, especially amongst those with PAD,[12,13] have highlighted this as an area for future research.

Therefore, this multicentre series aimed to precisely define and report the actual cost(s) associated with a TLR procedure in consecutive patients presenting with femoropopliteal in stent re-stenosis (ISR) and or occlusion across several institutions in Europe.

METHODS

This was a multicentre observational study across 13 vascular centres (hospitals). All participating hospitals were regional referral centres for arterial disease based in academic teaching hospitals in Western healthcare systems. All consecutive patients treated by endovascular, hybrid, or open surgery for symptomatic ISR, occlusion, or stent thrombosis involving the superficial femoral artery (SFA) and or popliteal artery (PA) between January 2017 — December 2021 were identified at each participating centre (sites and number of participants per site are listed in Supplementary Table S1) and eligible patients (see below) only were included in this report. Patients presenting with isolated below the knee or iliac in stent re-stenosis requiring intervention were excluded; inflow and outflow procedures were not considered as part of the exclusion criteria. Data were collected retrospectively using a purpose built electronic case report form. No patient identifiable information was collected or exchanged. Patients were identified retrospectively once the TLR procedure had taken place at each study site. Costs and clinical information were obtained at each site by the local lead or collaborator, for each TLR procedure, who was also responsible for data quality and control.

The following were documented: the exact cost of each endovascular device or surgical equipment used or implanted during the procedure; duration of the TLR procedure in minutes; location of the TLR procedure (operating theatre, hybrid suite, angioplasty or cardiology suite, or other setting); seniority and cost per minute of members of staff present during the TLR procedure; daily costs per hospital for each hour spent as an inpatient; all postoperative events (until discharge); and all medical treatments administered. The costs of devices, all equipment, tools, per-minute payments (salaries) to healthcare professionals, and indirect and estate costs were obtained directly from the institution or centre where the TLR took place by each centre's collaborator, using the exact payments made per patient by the insurer or healthcare provider (e.g., the National Health Service). Anatomical, clinical, and demographic data were reported based on medical notes and clinical letters, accessed by each site collaborator.

Data queries were resolved via correspondence with each local investigator by AS, KS, and YC. The site investigator was also responsible for local or regional approval (Supplementary Table S1). AS, GT, and KS collated data and assessed for accuracy and missing information. In the case of missing data ($<$ 3% of the dataset) relating to baseline characteristics and the key outcomes of interest (i.e., actuarial costs), the sites' investigators and collaborators were contacted and the missing data were obtained accordingly. No imputation was necessary in this report. All site investigators were identified via the Research Collaborative for Peripheral Arterial Disease (RCPAD). Adjudication of data and missing data queries were addressed locally at each participating site by the main RCPAD investigator and an additional collaborator. AS and KS managed data centrally and checked for consistency and erroneous figures, with the aid of an independent statistician and health economic expert at the National Institute of Health and Care Research (NIHR) Leicester Biomedical Research Centre (BRC). The funder was not involved in data collection or adjudication.

Ethical and regulatory approval

Each site sought ethical approval as per institutional and national guidance. No identifiable patient data were exchanged or collected. Raw data were unavailable to the funder. The East Midlands Central Ethics Committee advised that no NHS

ethical approval or individual consenting was necessary for the United Kingdom. Given that no individual patient consent was deemed necessary by any of the included sites, as per their local regulations, the study was not prospectively registered. The ethical approval reference number was 2021-799-f-S for German sites and ONZ-2022-0511 for Belgian sites. The study was funded by Boston Scientific (no grant reference available), who had no input in design or analyses.

Definitions and reporting

Diagnoses and clinical events were defined as per the American Heart Association guidance[14] and the reporting standards of the Society for Vascular Surgery for PAD.[15] Technical success was defined as completion of the TLR procedure as planned with no additional intra-procedure intervention, with at least one artery patent to the foot. Pre-, intra-, and post-procedure information was collected using a purpose built data collection form, to identify costs associated with the TLR procedure between the time of admission and hospital discharge. This included hospital care related costs (ward, intensive care unit [ICU], operating theatre or angiography or cardiology suite, and equipment and devices used). The procedures were categorised into groups based on the type of TLR. Exact costs related to each patient's care were collected without estimates or assumptions in any case. For the TLR procedure, the number of healthcare staff present was documented and their salary or payment (including superannuation and all other payments) per minute was costed. The exact amount of indirect costs, estate costs, laboratory, and technician costs for the TLR and throughout each inpatient stay was documented, based on receipts produced by the host institution to healthcare payers. For equipment, tools, and devices used, the exact cost charged to the healthcare payer, based on receipts and each hospital's records, was collected. The Tosaka classification was used to quantify in stent disease: Tosaka 1, in stent re-stenosis $\leq$ 5 cm; Tosaka 2, in stent re-stenosis $>$ 5cm in length; Tosaka 3, in stent occlusion. Indirect costs were collected per institution (as reported by each hospital) and included general administration, health recordkeeping, information technology, physical plant and maintenance costs, human resources, and capital expenses.

Statistical analysis and sample size

Health economic and statistical support was formally provided by the NIHR Leicester BRC by the in house Bioinformatics Hub; this support was independently funded via the NIHR, including the lead author's contributions. A minimum TLR procedure cost of €3 000 per case with a standard deviation (SD) of €500 was assumed. To be able to precisely report the true cost with 90% power within a 95% confidence interval, a minimum of 263 patients needed to be included. A pre-drawn statistical analysis plan was used, following consultation with an independent health economist and a qualified statistician via the University of Leicester Biomedical Research Hub. The funder had no input in analyses. All analyses were performed using SPSS version 24.0 (IBM, Armonk, New York, USA) and the R package version 4.2.3 (Windows). Normality of distributions was assessed using histograms, skewness, and kurtosis.

Results were reported as mean and standard deviation for normally distributed variables and median with range for non-normally distributed values. Absolute values and proportions (%) were reported for categorical variables. Due to heterogeneity in terms of costs reported (based on assessment via skewness and kurtosis of the dataset) per unit or site, costs were reported as median and range. Associations between pre-selected variables of interest (age, sex, urgent operation, nature of TLR procedure [i.e., open *vs.* hybrid *vs.* endovascular]; duration of TLR procedure in hours; duration of hospital stay in days post-TLR procedure; duration of ICU admission in days post-TLR procedure) and subsequent TLR costs in euros (as a continuous variable) were assessed using linear regression. The variables were selected based on previous reports assessing costs of PAD revascularisation[16,17] and discussion and agreement amongst the authors. The site or hospital where each TLR took place was forced in the model, given potential differences between centres and healthcare settings.

Outcomes

The primary outcome of interest was the overall cost of the TLR procedure from the time of presentation to hospital until the time of discharge, reported in euros, from a healthcare payer's perspective. Secondary outcomes of interest included: clinical and anatomical characteristics of patients when presenting for TLR, details of the original femoropopliteal procedure, details of the TLR procedure, and 30 day peri-procedure outcomes after the TLR (death, re-intervention, re-admission, major lower limb amputation). The costs of the TLR per constituent (hospital or ICU stay, operating time, cost of equipment) were also collected and reported.

RESULTS

This study identified 482 TLR procedures performed in patients with symptomatic ISR, occlusion, or stent thrombosis involving the SFA and or PA between January 2017 — December 2021 across 13 participating sites in six European countries (Supplementary Table S1), as per the study's inclusion criteria.

Amongst the included patients, 56% were female and the mean age was 75 $\pm$ 2 years. Baseline demographics and clinical characteristics are shown in Table 1. Of note, 61% were classified as Rutherford class 5 or 6 when they presented for TLR, 39% had diabetes, 71% had established coronary heart disease, and 24% had chronic kidney disease. Twenty-three patients had presented for TLR with acute symptoms (5%) (i.e., symptomatology $<$ 2 weeks in duration); however, 37% were treated as urgent (i.e., within 1 day of presentation due to rest pain and or extent of tissue loss). Table 1 summarises the demographics and clinical characteristics. Anatomical characteristics regarding the site of stenotic or occlusive PAD when the patients

Table 1. Characteristics of 482 participants at baseline, when presenting for a target lesion revascularisation procedure

Characteristic	Participants (n = 482)
Mean age ± SD − years	75 ± 2
Female sex	272 (56)
Acute ischaemia, on 2nd presentation*	23 (5)
Diabetes	189 (39)
CHD	341 (71)
ESRD	72 (15)
CKD	118 (24)
Hypertension	378 (78)
Hyperlipidaemia	339 (70)
Previous stroke	79 (16)
Previous malignancy	12 (2)
Current smoker	212 (44)
Ex-smoker	119 (25)
Aspirin use	241 (50)
Clopidogrel use	299 (62)
Anticoagulant use	192 (40)
Statin use	388 (80)
Rutherford class 2 or 3	11 (2)
Rutherford class 4	179 (37)
Rutherford class 5	278 (58)
Rutherford class 6	14 (3)
Bilateral CLTI	6 (1)
Previous amputation, major†	11 (2)

Data are shown as n (%) unless stated otherwise. SD = standard deviation; CHD = chronic heart disease; ESRD = end stage renal disease; CKD = chronic kidney disease; CLTI = chronic limb threatening ischaemia.
* Symptoms of < 48 hours in duration.
† None had an ipsilateral previous major lower limb amputation.

presented for TLR are listed in Table 2. Tosaka class 3 disease was observed in 67% of the femoropopliteal stents, 62% had proximal SFA involvement, 65% mid-SFA, 63% distal SFA involvement, and 94% had distal PA involvement. Overall, 41% had at least one below the knee artery occluded. A total of 10% had common femoral artery and 6% iliac artery involvement (stenoses ≥ 50%; all symptomatic). No common femoral artery occlusions were noted.

The original treatments (prior to the TLR) are listed in Table 3; most had plain balloon angioplasty (91%) followed by self expandable bare metal stent deployment. Details of the TLR procedures are listed in Table 4, where most procedures involved an open and endovascular component (52% hybrid procedures). General anaesthesia was used in 304 procedures. Technical success was 70%, the 30 day mortality rate was 1%, and 30 day major amputation rate 4%. Outcomes are detailed in Table 5. Notably, 3% of endovascular procedures had to be converted to open surgery. A total 205 patients (43%) were admitted to an ICU after the TLR for a median stay of two days (1 − 17), 30 (6%) needed a further endovascular intervention within 30 days, and 12 a surgical re-intervention (2%). Wound infection (10%) and pseudoaneurysm (4%) were the most common complications within 30 days of TLR.

The costs of endovascular devices are reported in Supplementary Table S2. The costs of peri-operative care are

Table 2. Characteristics of arterial involvement (stenosis ≥ 50% or occlusion) at the time of re-intervention of 482 femoropopliteal target lesion revascularisations (TLR)

Location or disease characteristic	TLR (n = 482)
Iliac	31 (6)
CFA	47 (10)
Proximal SFA	301 (62)
Mid-SFA	311 (65)
Distal SFA	303 (63)
Popliteal, any part	398 (83)
P1	401 (83)
P2	401 (83)
P3	221 (46)
BTK	347 (72)
> 1 BTK arteries involved	198 (41)
> 1 BTK occlusion	209 (43)
Pedal arch disease	107 (22)
Tosaka* class 1	71 (15)
Tosaka class 2	89 (18)
Tosaka class 3	322 (67)

Data are shown as n (%). CFA = common femoral artery; SFA = superficial femoral artery; P = popliteal; BTK = below the knee.
* Tosaka class refers to the femoropopliteal stent. Tosaka 1 = in stent re-stenosis ≤ 5cm; Tosaka 2 = in stent re-stenosis > 5 cm in length; Tosaka 3 = in stent occlusion.

reported in Supplementary Tables S3 and S4. Of interest, most endovascular device related costs (mean of €952 per instance) were secondary to wires and sheaths used during the TLR procedure. No previous research reporting actuarial costs of femoropopliteal TLR from a healthcare payer's perspective was identified, and all actuarial costs incurred in this series are listed in Supplementary Tables S2 — S4, with a median and range value.

Most of the costs were incurred were due to the time spent operating during the TLR (i.e., theatre or suite costs, salaries of staff present during the TLR [including doctors and all associated healthcare professionals], indirect and estate costs, and all salary incurring costs included), with a mean of: €21 917 ± €2

Table 3. Characteristics of the initial or index femoropopliteal stenting treatment for 482 target lesion revascularisations (TLR)

Characteristics	TLR (n = 482)
*Stenting strategy**	
Bare metal stent	299 (62)
Drug eluting stent	61 (13)
Covered stent	58 (12)
Biomimetic stent	79 (16)
Other endovascular modality used alongside stenting	
Atherectomy	31 (6)
Plain balloon angioplasty	441 (91)
Drug coated balloon angioplasty	137 (28)
Inflow and outflow procedures	
Common femoral endarterectomy	61 (13)
Iliac stenting	129 (27)
BTK angioplasty	88 (18)

Data are shown as n (%). BTK = below the knee.
* Combinations of different stents were used in 15 cases.

Table 4. Details of the re-intervention strategy when participants underwent target lesion revascularisation

Treatment strategy and details	TLR (n = 482)
Duration of procedure − minutes	79 (57)
Urgent procedure	179 (37)
Percutaneous procedure	202 (42)
Open surgery only	31 (6)
Hybrid procedure, open and endovascular component	249 (52)
Details of open surgical component	
Bypass, venous conduit	19 (4)
Bypass, prosthetic	10 (2)
Bypass, composite	2 (–)
Common femoral endarterectomy, with patch	193 (40)
Thrombectomy, open	71 (15)
Details of endovascular component	
Plain balloon angioplasty	239 (50)
New stent	138 (28)
Drug coated balloon	119 (25)
Atherectomy	118 (24)
Embolic protection filter use	17 (4)
Thrombolysis used intra-operatively	9 (2)
Combination of endovascular treatments	341 (71)
Use of specialty endovascular wires, chronic total occlusion wire or other	198 (41)
Type of anaesthesia	
Local	77 (16)
Regional or loco-regional	101 (21)
General	304 (63)
Staff details	
Consultant led operator	480 (99)
Interventional radiologist led	282 (59)
Vascular surgery led	200 (41)
Cardiology led	0 (0)
Location of procedure	
Hybrid operating theatre	370 (77)
Open surgical theatre	11 (2)
Radiology or interventional suite	101 (21)

Data are shown as n (%).

Table 5. Procedure and 30 day outcomes following 482 target lesion revascularisations

Outcomes	TLR (n = 482)
Technical success	339 (70)
Peripheral embolisation during TLR	32 (7)
Conversion to open surgery	14 (3)
ICU admission post-operatively	205 (43)
Median stay for those admitted to ICU*	2 (1–17)
30 day death	7 (1)
30 day endovascular re-intervention	30 (6)
30 day open surgical re-intervention	12 (2)
30 day major amputation	17 (4)
30 day re-admission	59 (12)
Wound infection	47 (10)
Access site pseudoaneurysm	17 (4)
Days spent in hospital after re-intervention	1 (0–77)

Data are shown as n (%) or median (range). TLR = target lesion revascularisation; ICU = intensive care unit.
* 93 patients admitted to ICU.

110 for all procedures; €23 337 ± €8 920 for open procedures; €12 903 ± €3 108 for endovascular procedures; and €22 806 ± €3 977 for hybrid procedures. In a regression analysis model (Supplementary Table S5), procedure duration of TLR was the main parameter associated with higher overall TLR costs (coefficient, 2.77; standard error, 0.88; $p < .001$); country or hospital where the procedure took place did not seem to considerably impact cost based on this model. The mean cost per operating minute of TLR (indirect, estate costs, all salaried staff present included) was €177; the mean cost per night stay in hospital (outside ICU) was €356.; and the mean cost per overnight ICU stay (minimum of 8 hours per night) was €1 193.

DISCUSSION

A major limitation of the current cost-analyses relating to PAD treatments is the lack of information regarding the actual costs of future interventions of the treated artery. This was noted both in the European guidance for asymptomatic PAD and claudication published in 2023, as well as international guidance on the management of diabetic foot disease.[12,13] Both documents highlight the importance of research and high quality data relating to the cost of interventions for PAD. This study aimed to evaluate the expense(s) associated with surgical, endovascular, and hybrid treatment for femoropopliteal TLR from the healthcare payer perspective. The main finding was the particularly high intra- and peri-operative care costs, which were mainly driven by procedure time.

It is complex to accrue a specific cost for a procedure (from a healthcare payer's perspective) since costs vary across countries, institutions, and different healthcare policies. Cost effectiveness studies may therefore lack external validity and what may hold true in one study may not translate to other contexts. This study included 13 different centres and institutions across Europe, which may have helped to increase external validity, at least in the European context. These countries all routinely offer contemporary endovascular therapies to patients with PAD and have similar treatment protocols. Further, PAD interventions across all sites were delivered by teams with both surgical and endovascular expertise.

Treating patients with PAD represents a significant financial burden to societies; these costs are expected to increase with the increase in the prevalence of PAD.[1,2,16,18] Only an in depth understanding of the costs involved in treating these patients will enable informed and responsible healthcare policies. One issue regarding the available PAD data is that most of the clinical trials may not reflect routine care practices in terms of PAD technologies used and subsequent costs incurred. The external validity of seven trials of paclitaxel based PAD devices was assessed in the RANDOM-STOP study,[11] with 81.7% of patients seen in routine care across Europe being ineligible for inclusion in any of the seven trials. In the current study, 2% of patients presented with claudication and most had multilevel disease with multiple comorbidities, which reflects routine care in a pragmatic way.[11,19]

The economic burden of treating PAD goes well beyond the cost of TLR and is a complex issue; the following should also be accounted for: medication,[20,21] follow up appointments, wound care, community costs, psychological

support, and social impact.[22] However, the success of the revascularisation procedure and its durability have a significant impact on overall costs; this report and series reported TLR associated costs from a healthcare payer's perspective and showed that these costs are particularly high. Stoner *et al.* previously analysed revascularisation costs using a model of cost per day of patency.[23] In this study, although index endovascular procedures were associated with lower cost, subsequent TLR led to a loss of these index savings.[23] In the current study, TLR was associated with significant costs for the healthcare payer. This highlights the importance of aiming for durable index procedures and not considering re-interventions as benign; this is also supported by the fact that $>$ 40% of patients in this pragmatic series required an ICU stay during their TLR, which often required procedures like bypass or hybrid multilevel revascularisations(s). Adherence to best medical therapy and exercise are paramount in this population.[1,20,21,24] Further, the high costs associated with TLR in the current study are by far not reflected in the reimbursement systems in Europe, which is an issue that needs urgent consideration.

Regarding endovascular costs, it is interesting to observe that the costliest materials were wires and sheaths. This might be related to the complexity of some procedures, requiring multiple wires for navigating and recanalising in the context of TLR. Another important factor relating to costs was the length of hospital and ICU stays. Costs increased by a mean of €356 per night spent in the hospital and €1 193 for an ICU overnight stay. This is especially relevant when considering patients who present with complex wounds, foot infection, and sepsis requiring a more prolonged stay (e.g., for wound care). Additionally, PAD patients are usually at a significant risk of post-operative complications prolonging hospital stay. Malone *et al.*[16] found that the presence of diabetes significantly increased the economic burden of PAD care. Additionally, need for bypass, amputation, chronic kidney disease stage 5, infection, and an emergency or urgent admission were associated with increased costs in the same study.[16] The duration of TLR seemed to be the key parameter leading to subsequently higher costs in the current study, alongside the need for an open surgical procedure.

Post-operative complications are also an important factor to consider when assessing the economic burden of treating PAD. Flu *et al.* showed that complications significantly increased the overall costs of PAD treatments, being responsible for approximately 33% of all costs.[25] The TLR procedures in themselves are a complication of the initial procedure; however, as per Table 5 of this report, due to the complexity of these TLR interventions, they may also lead to several additional post-operative complications. The most common complications in the current cohort were technical failures, peripheral embolisation, re-admission, and wound infection(s).

Finally, it should be noted that although the procedure time was the main factor influencing the in hospital expense(s) of a TLR, this was not considered from the current reimbursement policies in several European countries, like the commonly used Diagnosis Related Group (DRG) system in Germany or the UK healthcare providers (NHS). A reimbursement system based on procedure complexity and or time taken to revascularise seems more suitable for patients with PAD. A more thorough analysis of the overall costs of all PAD patients is required in order to understand the limitations of these reimbursement strategies and ensure that all institutions are receiving appropriate compensation for their expenses when addressing PAD.

Limitations

This study had several limitations. The retrospective nature of this analysis increased the risk of reporting and or recollection bias; however, all missing data were queried with sites, and 100% data completion for the dataset was eventually achieved relating to the primary outcome of interest (costs of TLR from a healthcare payer's perspective). Furthermore, differences in procedure costs and policies across centres may have led to some clinical heterogeneity in the report and analysis and since patient distribution was unequal among centres, this may have led to additional reporting bias. This analysis could not be reported per site or country (as some countries only included one site) due to regulatory issues. The ethical approvals did not cover reporting per site or patient reporting, and hospitals did not agree to openly publish the per unit cost of all devices used due to contractual obligations. The sites that reported per country cannot obviously represent the whole healthcare system in that country; it is fully acknowledged that there may have been considerable heterogeneity in how costs were collected and reported, as well as how contracts were negotiated at each institution. At the same time, a regression and sensitivity analysis was provided to address this important limitation, and a median and range for each cost incurred in these procedures was provided. Another limitation was related to the design of the study and the inclusion of previously stented femoropopliteal arteries in isolation. Applying these findings to other anatomical beds or multilevel procedures (without prior stenting or using other adjuncts) may risk exaggerating TLR costs, as these procedures are well known to be challenging (and hence may consume more resources) than TLR undertaken in patients who have not originally had a femoropopliteal stent.

By only considering the costs of the TLR procedure from a healthcare payer's perspective, the total economic burden of the whole PAD treatment context could not be analysed, as this was outside the scope of this work. The reported regression model based on pre-selected variables, which showed a fairly poor goodness of fit, could definitely have been biased or inaccurate, due to the number of patients included, as well as heterogeneity of data; an in depth economic model or analysis was beyond the scope of this report and would require a formal health economic analysis with prospectively collected targeted data collection, including quality of life measures. This was not a randomised study, societal or individual patients' costs were not collected, and quality adjusted life years were not reported,

and any type of other complex modelling was not performed. Further studies considering all aspects of PAD treatment in the context of patient related outcomes are needed to better inform decision makers and healthcare policies, with regards to cost effectiveness, which could not be assessed using the design of the current study.

Conclusions

In this analysis of 482 TLR procedures for femoropopliteal ISR across several European centres, procedure time was the main driver of the very considerable peri-procedure costs associated with TLR. It seems that the costs of repeat revascularisations are important, and the initial strategy should aim to achieve better patency, as the expenses of a secondary procedure are particularly high. An in depth analysis of all PAD treatment costs in routine practice is needed in order to improve current reimbursement policies.

CONFLICTS OF INTEREST

K.S. — consulting for Phillips, Shockwave, Terumo, Boston Scientific, received honoraria from Medtronic, Abbott, Cook, Bentley, and Biotronic; research grants from Boston Scientific. A.S. — honoraria and lecture fees/consulting for Shockwave, Abbott, Cook; educational grant support from Cook; research funding from Shockwave, Abbott, Boston Scientific, Angiodroid. G.B.T. — research funding and speaker honoraria from Boston Scientific, WL Gore, Cook, and Medtronic. G.F.T. — research funding from WL Gore and speaker honoraria from Penumbra. I.V.H. — honoraria and lecture fees/consulting for Medtronic. H.Z. — speaker/proctor/consultant for Abbott Medical, Boston Scientific, Bentley, Cook Medical, Gore Medical, Limflow, and Cordis. Institutional research grants from Abbott Medical.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2024.02.001.

REFERENCES

1 Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia. *Eur J Vasc Endovasc Surg* 2019;**58**:S1—109.
2 Horvath L, Nemeth N, Feher G, Kives Z, Endrei D, Boncz I. Epidemiology of peripheral artery disease: narrative review. *Life (Basel)* 2022;**12**:1041.
3 Katsanos K, Geisler BP, Garner AM, Zayed H, Cleveland T, Pietzsch JB. Economic analysis of endovascular drug-eluting treatments for femoropopliteal artery disease in the UK. *BMJ Open* 2016;**6**:e011245.
4 Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, et al. Multicentre randomised controlled trial of the clinical and cost-effectiveness of a bypass-surgery-first versus a balloon-angioplasty-first revascularisation strategy for severe limb ischaemia due to infrainguinal disease. The Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial. *Health Technol Assess* 2010;**14**:1—210.
5 Forbes JF, Adam DJ, Bell J, Fowkes FG, Gillespie I, Raab GM, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL) trial: health-related quality of life outcomes, resource utilization, and cost-effectiveness analysis. *J Vasc Surg* 2010;**51**:43—51S.
6 Popplewell MA, Andronis L, Davies HOB, Meecham L, Kelly L, Bate G, et al. Procedural and 12-month in-hospital costs of primary infra-popliteal bypass surgery, infrapopliteal best endovascular treatment, and major lower limb amputation for chronic limb threatening ischemia. *J Vasc Surg* 2022;**75**:195—204.
7 Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005;**366**:1925—34.
8 Shan LL, Wang J, Westcott MJ, Tew M, Davies AH, Choong PF. A systematic review of cost-utility analyses in chronic limb-threatening ischemia. *Ann Vasc Surg* 2022;**85**:9—21.
9 Meecham L, Popplewell M, Bate G, Patel S, Bradbury AW. Comparison of femoropopliteal plain balloon angioplasty for chronic limb-threatening ischemia in the BASIL trial and in a UK contemporary series. *J Vasc Surg* 2021;**74**:1948—55.
10 Menard MT, Rosenfield K, Farber A. The BEST-CLI trial: implications of the primary results. *Eur J Vasc Endovasc Surg* 2023;**65**:317—9.
11 Stavroulakis K, Katsogridakis E, Torsello G, Zayed H, van Herzeele I, Coscas R, et al, RANDOM-STOP group. Editor's Choice — RANDOMisation Screening for Drug coated or Drug Eluting Device Randomised Trials Among Patients Undergoing Endovascular FemorOPopliteal Procedures (RANDOM-STOP study). *Eur J Vasc Endovasc Surg* 2023;**66**:362—8.
12 Nordanstig J, Behrendt CA, Baumgartner I, Belch J, Back M, Fitridge R, et al. European Society for Vascular Surgery (ESVS) 2024 clinical practice guidelines on the management of asymptomatic lower limb peripheral arterial disease and intermittent claudication. *Eur J Vasc Endovasc Surg* 2024;**67**:9—96.
13 Fitridge R, Chuter V, Mills J, Hinchliffe R, Azuma N, Behrendt CA, et al. The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in people with diabetes mellitus and a foot ulcer. *Eur J Vasc Endovasc Surg* 2023;**66**:454—83.
14 Hicks KA, Tcheng JE, Bozkurt B, Chaitman BR, Cutlip DE, Farb A, et al. 2014 ACC/AHA key data elements and definitions for cardiovascular endpoint events in clinical trials: a report of the American College of Cardiology/American Heart Association task force on clinical data standards (writing committee to develop cardiovascular endpoints data standards). *Circulation* 2015;**132**:302—61.
15 Stoner MC, Calligaro KD, Chaer RA, Dietzek AM, Farber A, Guzman RJ, et al, Society for Vascular Surgery. Reporting standards of the Society for Vascular Surgery for endovascular treatment of chronic lower extremity peripheral artery disease. *J Vasc Surg* 2016;**64**:e1—21.
16 Malone M, Lau NS, White J, Novak A, Xuan W, Iliopoulos J, et al. The effect of diabetes mellitus on costs and length of stay in patients with peripheral arterial disease undergoing vascular surgery. *Eur J Vasc Endovasc Surg* 2014;**48**:447—51.
17 Tang L, Paravastu SCV, Thomas SD, Tan E, Farmer E, Varcoe RL. Cost analysis of initial treatment with endovascular revascularization, open surgery, or primary major amputation in patients with peripheral artery disease. *J Endovasc Ther* 2018;**25**:504—11.
18 Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res* 2015;**116**:1509—26.
19 Le Boutillier C, Saratzis A, Saha P, Benson R, Bridgwood B, Watson E, et al. Factors that influence the feasibility and implementation of a complex intervention to improve the treatment of peripheral arterial disease in primary and secondary care: a qualitative exploration of patient and provider perspectives. *BMJ Open* 2023;**13**:e066883.
20 Twine CP, Kakkos SK, Aboyans V, Baumgartner I, Behrendt CA, Bellmunt-Montoya S, et al. Editor's Choice - European Society for

Vascular Surgery (ESVS) 2023 clinical practice guidelines on antithrombotic therapy for vascular diseases. *Eur J Vasc Endovasc Surg* 2023;**65**:627–89.
21 Saratzis A, Jaspers NEM, Gwilym B, Thomas O, Tsui A, Lefroy R, et al, Vascular and Endovascular Research Network (VERN) Collaborators. Observational study of the medical management of patients with peripheral artery disease. *Br J Surg* 2019;**106**:1168–77.
22 Wonderling D, Sawyer L, Fenu E, Lovibond K, Laramee P. National Clinical Guideline Centre cost-effectiveness assessment for the National Institute for Health and Clinical Excellence. *Ann Intern Med* 2011;**154**:758–65.
23 Stoner MC, Defreitas DJ, Manwaring MM, Carter JJ, Parker FM, Powell CS. Cost per day of patency: understanding the impact of patency and reintervention in a sustainable model of healthcare. *J Vasc Surg* 2008;**48**:1489–96.
24 Saratzis A, Paraskevopoulos I, Patel S, Donati T, Biasi L, Diamantopoulos A, et al. Supervised exercise therapy and revascularization for intermittent claudication: network meta-analysis of randomized controlled trials. *JACC Cardiovasc Interv* 2019;**12**:1125–36.
25 Flu H, van der Hage JH, Knippenberg B, Merkus JW, Hamming JF, Lardenoye JW. Treatment for peripheral arterial obstructive disease: an appraisal of the economic outcome of complications. *J Vasc Surg* 2008;**48**:368–76.

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COUP D'OEIL

Left Lower Limb Arteriovenous Fistula Secondary to Post-Thrombotic Syndrome

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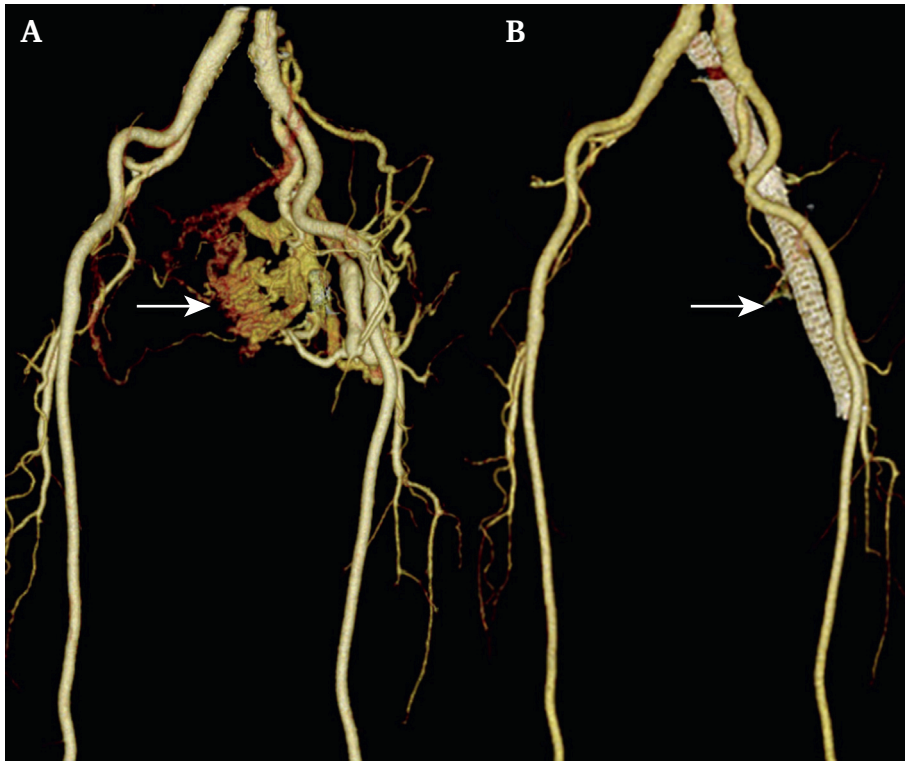

A 72 year old woman, diagnosed with left iliac vein thrombosis four years earlier, was treated with rivaroxaban. Computed tomography angiography (CTA) was performed because of persistent left lower limb swelling, which showed an occluded left iliac vein with multiple arteriovenous fistulae at the level of the left external iliac vein (A, arrow). Two Venovo stents measuring 12 × 100 mm and 12 × 60 mm (Bard, Murray Hill, NJ, USA) were implanted antegradely via the popliteal vein into the left iliofemoral vein. Six weeks later, follow up CTA confirmed stent patency and resolved arteriovenous fistulae (B, arrow), with reduced swelling. Rivaroxaban was continued.

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