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Optimization of Long Superficial Femoral Artery Percutaneous Transluminal Angioplasty by Intraoperative Doppler Ultrasound

Giuseppe Vadalà [1,2,*], Giuseppe Roscitano [3], Vittorio Virga [4], Fausto Castriota [5], Vincenzo Pernice [6], Alfredo Ruggero Galassi [1,2] and Antonio Micari [4]

[1] Division of Cardiology, Universitary Hospital "Policlinico P. Giaccone", 90127 Palermo, Italy; alfredo.galassi@unipa.it
[2] Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (ProMISE), University of Palermo, 90133 Palermo, Italy
[3] Department of General Surgery and Medical Specialities, University of Catania, 95124 Catania, Italy; giuseppe.roscitano@virgilio.it
[4] Interventional Cardiology Department, University Hospital G. Martino, University of Messina, 98122 Messina, Italy; vittorio.virga@policlinico.me.it (V.V.); antonio.micari@unime.it (A.M.)
[5] Cardio-Vascular Department, Maria Cecilia Hospital, GVM Care and Research, 48022 Ravenna, Italy; fcastriota@gvm-vmc.it
[6] Cardio-Vascular Department, Maria Eleonora Hospital, GVM Care and Research, 90124 Palermo, Italy; vpernice@gvm-meh.it
* Correspondence: vpeppe80@gmail.com or giuseppe.vadala@unipa.it; Tel.: +39-3391091678; Fax: +39-0916554530

Abstract: Background: Residual stenosis and dissections occurring after femoro-popliteal percutaneous transluminal angioplasty (PTA) can compromise vessel patency and should therefore be properly dealt with at the time of the index procedure. Sometimes, the decision to optimize the PTA result may be challenging because it is based on evidence from angiography which, as a bi-dimensional imaging technique, has well-known limitations. Objectives: The objective of this study was to evaluate whether an intraoperative Doppler ultrasound (DUS) assessment of femoro-popliteal lesions that have undergone PTA allows for a more accurate definition of technical success compared to angiography. This was assessed through the identification of those lesions that, despite fulfilling angiographic criteria for technical success, have a functional relevance at DUS. Methods: In this cross-sectional study, data from 62 patients who had undergone femoro-popliteal PTA and intraoperative DUS were retrieved. The procedures were performed at two referral hospitals for peripheral interventions between 2018 and 2019. The selected patients had 48 residual stenoses in the range of 40–50% and 14 grade-C dissections. Results: The mean lesion length was 211 ± 85.2. Angiography-based and DUS-based technical success matched 41 lesions (66%). The remaining 21 lesions, which had abnormal DUS, were successfully optimized by post-dilatation or stenting in 19 cases. Finally, after PTA optimization, DUS-based and angiography-based technical success matched 95% of cases. Conclusions: An intraoperative DUS assessment of intermediate residual stenosis or grade C dissections occurring after PTA of long femoro-popliteal arteries allowed for a more accurate definition of technical success than angiography and guided a further PTA optimization in one-third of the cases.

Keywords: PTA of long femoro-popliteal artery; DUS assessment of femoro-popliteal artery stenosis; outcomes after femoro-popliteal artery PTA; multi-imaging modality in peripheral interventions; Doppler ultrasound; multi-imaging modality; long femoro-popliteal PTA; femoro-popliteal PTA outcomes; drug-coated balloons

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Condensed Abstract

Residual stenosis and dissections occurring after femoro-popliteal percutaneous transluminal angioplasty (PTA) can compromise PTA patency and should therefore be fixed at the time of the index procedure. However, the decision to optimize the PTA may be challenging since it is based on angiography, which has well-known limitations. We investigated whether the assessment of residual stenosis and dissections by intraoperative Doppler ultrasound (DUS) allows for a more accurate definition of technical success after long femoro-popliteal PTA compared to angiography. One-third of the lesions assessed by DUS showed abnormal PSVR and were optimized by post-dilatation or stenting. Following this, the integrated technical success, fulfilling both angiographic and DUS-based criteria, increased from 66% to 95%. In conclusion, compared to angiography, an intraoperative DUS assessment of intermediate residual stenosis or grade C dissections allowed for an accurate definition of technical success and guided PTA optimization in 33% of cases.

Clinical Perspective

What is known? A suboptimal result percutaneous transluminal angioplasty might compromise vessel patency and should therefore be properly optimized at the time of the index procedure. However, in the case of borderline residual stenosis or long dissections, the identification of those lesions that would benefit from further optimization may be very challenging since identification is based on angiography, which has well-known limitations.

What is new? An intraoperative DUS assessment, complementary to the angiography, allowed for the identification of a significant proportion of residual stenoses or long dissections that, despite fulfilling the angiographic criteria for technical success, underwent PTA optimization based on their abnormal DUS.

What is next? The next step is to assess whether this approach, characterized by a DUS-guided optimization of long SFA PTA, can improve the long-term primary patency as compared to the standard of care in larger prospective studies.

1. Introduction

Percutaneous transluminal angioplasty (PTA) of femoro-popliteal artery stenosis has become a routine treatment option for symptomatic patients requiring revascularization, especially when their clinical characteristics or surgical risk do not favor bypass surgery [1]. Moreover, tremendous technological advancements such as the widespread adoption of drug-eluting devices have addressed one of the main issues of such a procedure, i.e., PTA durability [2,3]. Indeed, even in settings characterized by a high atherosclerotic burden (long and calcified stenosis, chronic total occlusions, and multilevel disease), the one-year primary patency rates reported are the most satisfactory, being in the range of 80–90% across different studies and different devices used (drug-coated balloons, drug-eluting stents, biodegradable stents, covered stents, etc.) [4–7].

However, the degree of residual stenosis and the presence of dissections occurring after angioplasty are two procedural factors that may affect the long-term result of PTA regardless of the device used and of the recanalization technique adopted [8,9]. Therefore, every relevant residual stenosis or dissection should be properly fixed at the time of the index procedure to reduce the risk of target lesion failure at follow-up. However, in the case of residual "near 50%" stenoses and/or long dissections, the decision of whether or not to optimize the PTA result might be more challenging. This is because the decision is based on angiography, which as a bi-dimensional imaging technique that does not provide any functional information [10,11].

To overcome these issues, new and more sophisticated imaging modalities such as optical coherence tomography (OCT), intravascular ultrasound (IVUS), or CO_2 angiography imaging have been used in small cohorts of patients [12]. Compared to such advanced and expensive techniques, the intra operative assessment of femoro-popliteal artery PTA by Doppler ultrasound (DUS) may represent a cheaper and more widely available alternative imaging modality. To the best of our knowledge, DUS has not been systematically adopted for such a purpose before now.

The aim of this study was to evaluate whether an intraoperative Doppler ultrasound (DUS) assessment of femoro-popliteal lesions that have undergone PTA allows for a more accurate definition of technical success compared to angiography.

2. Methods

In this retrospective cross-sectional study, data from 62 patients who had undergone percutaneous transluminal angioplasty (PTA) of long femoro-popliteal arteries lesions and intraoperative Doppler ultrasound (DUS) were retrieved. The procedures were performed by highly skilled operators, at two referral hospitals for peripheral interventions, in 2018 and 2019. All patients signed an informed consent form for the procedure. The study diagram and patients' eligibility criteria are described in Figure 1.

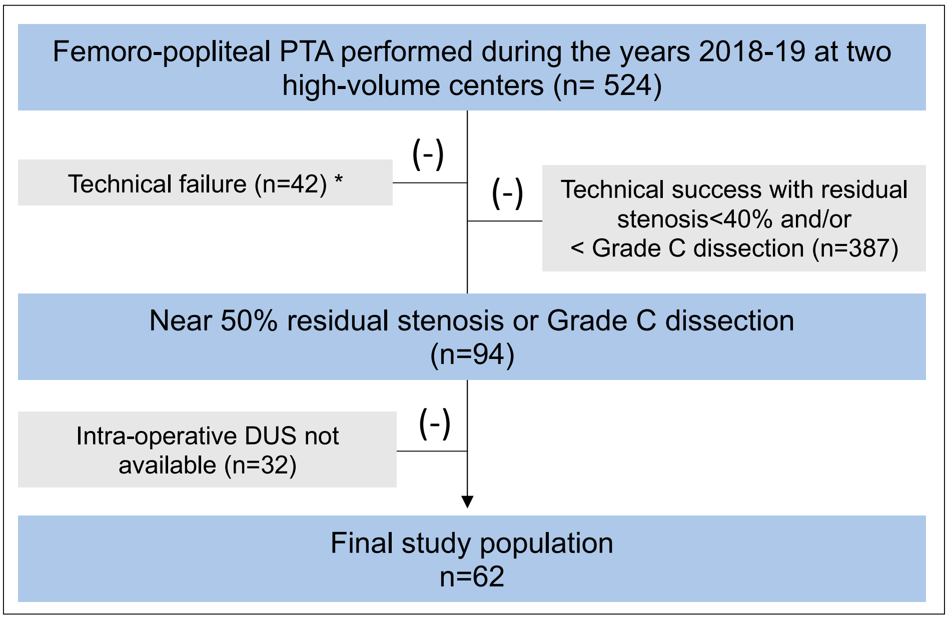

Figure 1. A study flow diagram illustrating patients' eligibility criteria and how the study population was selected. DUS = Doppler ultrasound. PTA = percutaneous transluminal angioplasty. (*) residual stenosis of the treated lesion by visual estimate >50% and/or presence of flow-limiting dissection.

The aim of this study was to evaluate whether an intraoperative DUS assessment allows for a more accurate definition of technical success compared to angiography. This was assessed through the identification of intermediate residual stenosis or grade C dissections that, despite fulfilling the angiographic criteria for technical success, have a functional relevance at DUS assessment and therefore might benefit from further treatment, such as balloon post-dilatation or stenting. The decision to optimize the PTA result by single or multiple post-dilatations or stenting, and also the balloon size and inflation pressure, were entirely left to the operator's discretion. In all cases, a DUS was also performed at the end of the procedure to assess any changes in PSVR or any spectral Doppler abnormality within or distally to the treated segment, respectively.

Out of the 62 patients enrolled, 51 (82%) completed a 1-year clinical follow-up, which also included a DUS evaluation to assess any target lesion restenosis.

The patients' data were anonymized and managed according to the data safety protocols of the two centers. This study was approved by the institutional review board of each center and performed in accordance with the Declaration of Helsinki.

Intraoperative Doppler ultrasound procedure. DUS examination was performed using a 7.5 MHz linear transducer. The treated segment was visualized using B-mode and color-Doppler ultrasound images. The Doppler signal was acquired at an angle of ≤60 degrees. Peak systolic velocity (PSV) proximal within and distal to the residual stenosis were evaluated, respectively. PSVR was calculated using the ratio between the highest PSV within TL and PSV at the level of a normal proximal segment. Consistent with previous studies, residual stenosis was judged as significant in case of PSVR > 2.4 m/s (Figure 2). Similarly, any lumen reduction within the dissection responsible for a PSV > 2.4 m/s or any abnormal spectral flow distally to the dissection were judged as a sub-optimal result [5,13] (Figure 3).

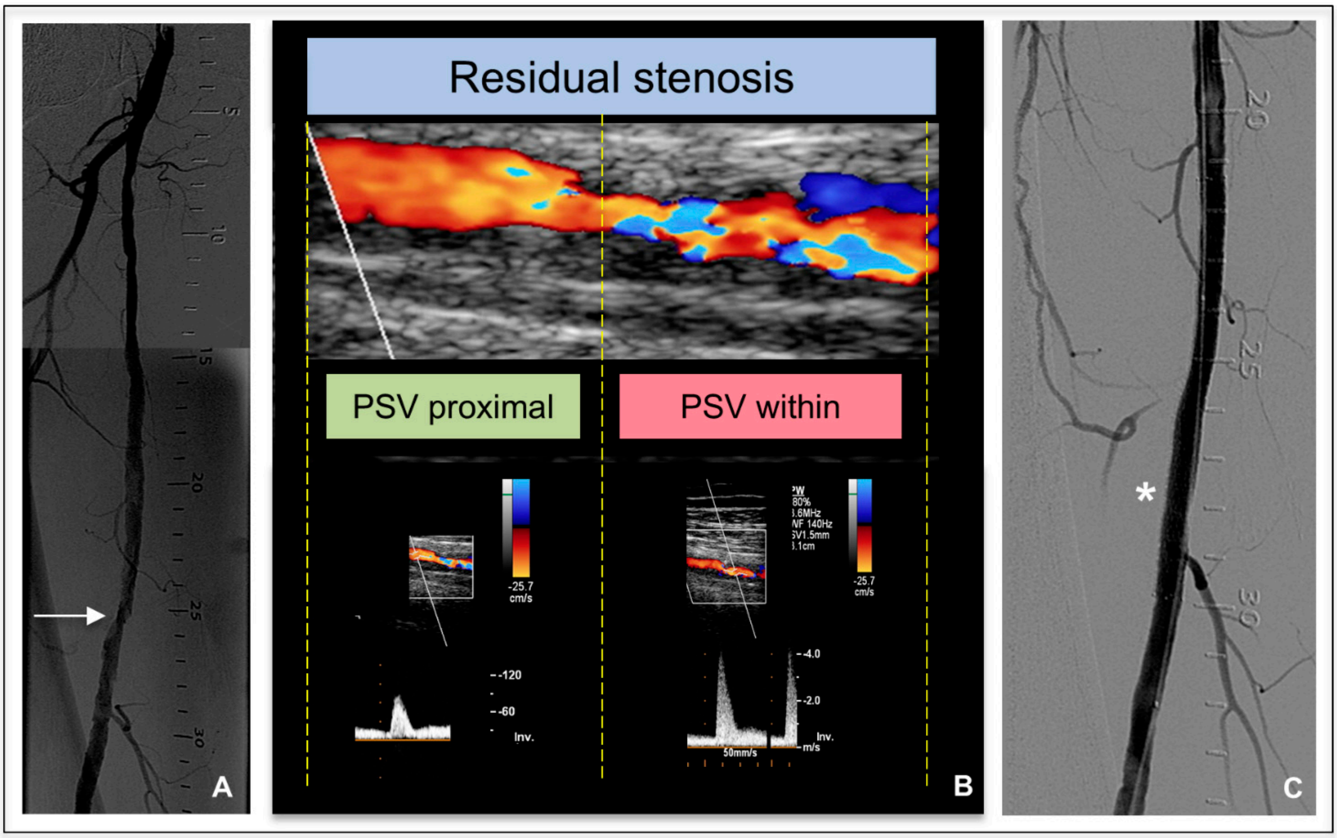

Figure 2. Example of intraoperative DUS assessment of residual stenosis that occurred after PTA of calcified stenosis. (**A**). Digital subtraction angiography showed intermediate residual stenosis < 50% (white arrow). (**B**) Intraoperative DUS showed abnormal PSVR within treated segment. (**C**) Result after bailout stenting that was necessary to fix persistent lesion recoil despite multiple post-dilatation (white asterisk). DUS = Doppler ultrasound. PSV = peak systolic velocity. PTA = percutaneous transluminal angioplasty.

Furthermore, a DUS assessment of residual dissections also included a bi-dimensional color-coded evaluation in both the long- and short-axis views, respectively.

Definitions. Technical success was defined as the completion of the endovascular procedure with <50% residual stenosis of the treated lesion by visual estimate and the absence of flow-limiting dissection. DUS-integrated technical success was defined as the completion of endovascular procedure with angiographic technical success plus a PSVR < 2.4 within the treated segment. Primary patency was defined as freedom from the combined endpoints of clinically driven target lesion revascularization (TLR), occlusion, and >50% restenosis in the treated lesion as assessed by DUS (PSVR > 2.4); clinically driven TLR was defined as any re-intervention within the target lesion due to symptoms and PSVR > 2.4, as assessed by DUS. Secondary endpoints were major adverse events at follow-up (the composite of death of any cause, major target limb amputation, thrombosis at the target lesion site, or non–target lesion target vessel revascularization).

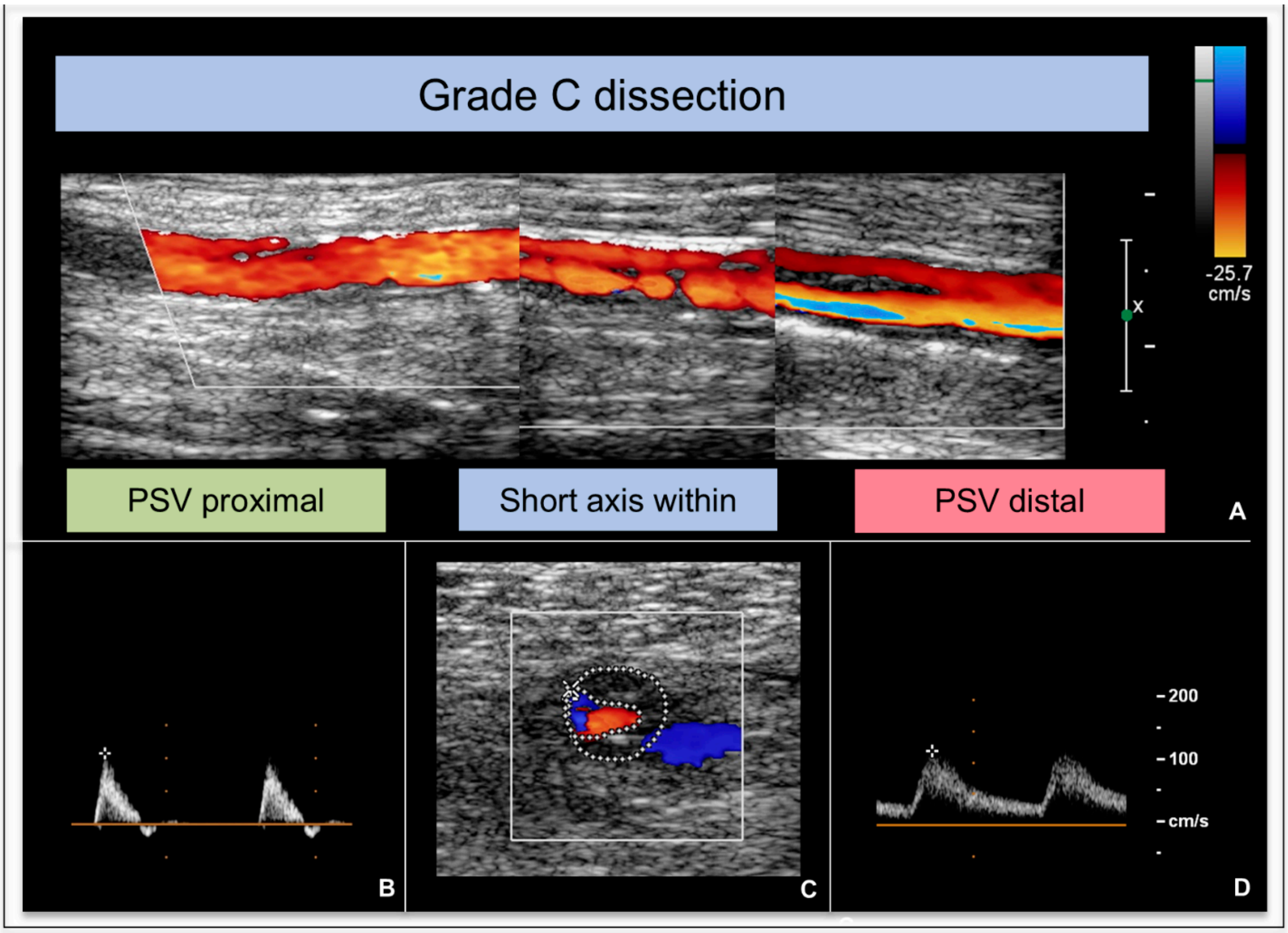

Figure 3. Example of intraoperative DUS assessment of grade C dissection that occurred after PTA. (**A**,**C**) Bi-dimensional images of dissection captured by DUS in long- and short-axis views, respectively. (**B**) Normal spectral Doppler proximal to dissection. (**D**) Abnormal spectral Doppler distal to dissection. After DUS assessment, it was deemed necessary to optimize PTA result. DUS = Doppler ultrasound. PSV = peak systolic velocity. PTA = percutaneous transluminal angioplasty.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation. Categorical variables are presented as counts (%) and were compared using Chi-square test or Fisher's exact test. For all analyses, a two-sided $p < 0.05$ was considered significant. Analyses were performed with the R software 4.1 (R Foundation, Wien, Austria).

3. Results

3.1. Clinical Characteristics

The patients' baseline characteristics are shown in Table 1. The mean age was 69 ± 8.1 years; 74.2% of the patients were male. A total of 37 percent had a previous history of coronary artery disease, and 40% had undergone previous peripheral revascularization. Most of the patients complained of intermittent claudication (88.7%), while the remaining 11.3% had critical limb ischemia characterized by rest pain or minor tissue loss (Rutherford 4 and 5).

Table 1. Baseline clinical characteristics.

Population: N = 62		
Age		69 ± 8.1
Men		46 (74.2)
Hypertension		48 (77.4)
Hyperlipemia		50 (80.6)
Diabetes mellitus		32 (51.6)
Current smoking		37 (59.6)
Renal failure		8 (12.9)
Coronary artery disease		23 (37.1)
Previous peripheral revascularization		25 (40.3)
Rutherford Classification		
Category	Grade	
0	0	0
	1	0
I	2	10 (16.1)
	3	45 (72.6)
II	4	5 (8.1)
III	5	2 (3.2)
	6	0

Values are shown as mean ± SD or (n) %.

3.2. Lesion and Procedural Characteristics

Lesion characteristics are listed in Table 2. The mean lesion length was 211 ± 85.2. Out of the 62 lesions, 50 (80.6%) were de novo, whereas the remaining 12 (19.4%) comprised the following: 10 (16.2%) were restenosis of the native vessel, and 2 (3.2%) were in-stent restenosis. Half of the lesions had chronic total occlusion; furthermore, 54.8% of the lesions had a calcification degree of at least moderate. In four patients, a significant in-flow disease of the iliac artery, ipsilateral to the target limb, was treated successfully before approaching the femoro-popliteal target lesion at the time of the index procedure. All target lesions (TLs) underwent balloon pre-dilatation by a balloon 0.5–1 mm undersized compared to the reference vessel diameter (RVD). Drug-coated balloons (DCBs) were used in 60 cases (96.8%), while primary stenting was used in 2 cases.

Table 3 depicts the differences between the group of patients with lesions who underwent PTA optimization and those who did not. The TL optimization group showed a greater lesion length (244 ± 62.2 vs. 194 ± 73.1; $p < 0.01$), a higher proportion of total occlusion (71% vs. 39%; $p < 0.01$), and a higher proportion of TASC C lesions (81% vs. 61%; $p < 0.01$); conversely, TLs that did not require optimization were less likely non-calcific (29% vs. 51%; $p < 0.01$).

Table 2. Lesions and procedural characteristics.

Lesions	62
Length (mm)	211 ± 85.2
Diameter stenosis (%)	93.1 ± 7.3
Reference vessel diameter (mm)	5.3 ± 0.8
De novo	50 (80.6)
Native vessel restenosis	10 (16)
In stent restenosis	2 (3.2)
Total occlusion	31 (50)
TASC classification	
Type A	0
Type B	11 (18)
Type C	43 (69)
Type D	9 (13)
Calcification degree	
None or slight	27 (44)
Moderate	25 (40)
Severe	10 (16)
Inflow disease	4 (6.4)
Outflow disease	8 (12.9)
Procedural details	
Lesion pre-dilatation	62 (100)
Lesion post-dilatation	37 (59.6)
DEB	60 (96.8)
Primary stenting	2 (3.2)
Intraoperative duplex scan assessment	62
Intermediate residual stenosis	48 (77.4)
Grade C dissection	14 (22.6)
Functional assessment of residual stenosis	
PSVR > 2.4 m/s	16 (25.8)
PSVR < 2.4 m/s	32 (51.6)
Functional assessment of dissection	
Abnormal spectral flow within and distal to dissection	5 (6.4)
Normal spectral flow within and distal to dissection	9 (14.5)
Lesions requiring optimization	21 (33.9)
Treatment for optimization	
Stenting	9 (14.5)
Post-dilatation	12 (19.4)
Residual diameter stenosis (<30%)	59 (95.2)
Integrated technical success	59 (95.2)
Bailout stenting	14 (22.6)
For flow-limiting dissection	6 (9.7)
For persistent residual stenosis	8 (12.9)

Values are shown as mean ± SD or (n)/%. DEB = drug-eluting balloon; PSVR = peak systolic velocity ratio; TASC = TransAtlantic Inter-Society Consensus.

Table 3. Comparison between lesions requiring and not requiring optimization.

	Overall	Optimization	No Optimization	p-Value
Lesions	62	21	41	
Length (mm)	211 ± 85.2	244 ± 62.2	194 ± 73.1	$p = 0.041$
Diameter stenosis (%)	93.1 ± 7.3	95.1 ± 7.3	96.1 ± 4.8	NS
Reference vessel diameter (mm)	5.3 ± 0.8	5.7 ± 0.3	5.5 ± 0.6	NS
De novo	50 (80.6)	14 (80)	31 (76%)	NS
Native vessel restenosis	10 (16)	4 (19%)	4 (10%)	NS
In stent restenosis	2 (3.2)	1 (0.5)	1 (0.2)	NS
Total occlusion	31 (50)	17 (71%)	16 (39%)	$p < 0.01$
TASC classification				
Type A	0	0	0	-
Type B	11 (18)	0	11 (27)	$p < 0.01$
Type C	43 (69)	17 (81)	25 (61)	$p = 0.03$
Type D	9 (13)	4 (19)	5 (12)	NS
Calcification degree				
None or slight	27 (44)	6 (29)	21 (51)	$p < 0.01$
Moderate	25 (40)	11 (52)	14 (34)	$p = 0.047$
Severe	10 (16)	4 (19)	6 (15)	NS
Inflow disease	4 (6.4)	1 (5)	3 (7)	NS
Outflow disease	8 (12.9)	2 (10)	6 (14)	NS
Procedural details				
Lesion pre-dilatation	62 (100)	21 (100)	41 (100)	NS
Lesion post-dilatation	37 (59.6)	21 (100)	16 (40)	$p < 0.01$
DEB	60 (96.8)	21 (100)	39 (95)	NS
Primary stenting	2 (3.2)	0	2	-

Values are shown as mean ± SD or (n)/%. DEB = drug-eluting balloon; PSVR = peak systolic velocity ratio; TASC = TransAtlantic Inter-Society Consensus.

3.3. Intraoperative DUS

Intraoperative DUS was performed to assess 48 RS in the range of 40–50% and 14 grade C dissections. (Central illustration) Out of the 48 intermediate residual stenoses, 16 (33.3%) showed a PSVR > 2.4, whereas the remaining 32 (77.7%) showed a PSVR < 2.4. Out of the 14 "grade C" dissections assessed, 5 (35.8%) showed an abnormal spectral Doppler within and distally to the dissection, whereas the remaining 9 (64.2%) showed a PSVR < 2.4 within the dissection and a normal spectral Doppler distally to the dissection. Among the five grade C dissections with an abnormal spectral Doppler, a lumen narrowing with a PSVR > 2.4 was documented in four cases; the remaining dissection showed an abnormal spectral Doppler distal to the dissection with a PSVR < 2.4 within.

In conclusion, an intraoperative DUS assessment showed an abnormal PSVR within or distally to the treated segment in 21 (34%) procedures.

3.4. DUS-Guided PTA Optimization

All 16 RSs with a PSVR > 2.4 underwent a prolonged balloon post-dilatation that was 1 mm oversized compared to the vessel diameter. This approach resulted in a PSVR < 2.4 in nine cases, while in the remaining five cases, bailout stenting was deemed sufficient to scaffold four persistent residual stenoses and to seal one grade D dissection which occurred after prolonged post-dilatation. In the remaining two cases, a DUS assessment showed a persistent PSVR > 2.4 despite multiple post-dilatations, but no further treatments were performed because of the high amount of calcium.

All five grade C dissections first underwent 1-1 sized prolonged balloon post-dilatation at low pressures. After that, bailout stenting was required to seal persistent residual dissection in three cases and to scaffold a significant lumen narrowing within the dissected segment in one case. In one case, despite multiple post-dilatations, a DUS assessment showed a persistent PSVR > 2.4 within the dissection located at the level of the popliteal artery (segment P2-P3); no further treatments were performed.

In conclusion, after DUS-guided PTA optimization, integrated technical success was achieved in 14 out of 16 residual stenoses and in four out of five grade C dissections, being as high as 95% overall (59/62) (Table 2).

3.5. Clinical Follow-Up

Fifty-one patients (82%) underwent a clinical visit and DUS assessment, while the remaining patients were lost in the follow-up. MAEs occurred in five patients (9.8%) and involved one myocardial infarction and four repeated revascularizations, respectively (Table 4), The one-year primary patency was 82%, and the freedom from clinically driven TLR was 92%. Furthermore, the one-year primary patency was similar between the group of patients with TLs who underwent PTA optimization and those who did not (93% vs. 89%; $p = 0.08$) (Figure 4).

Table 4. Outcomes at 1-year follow-up.

Patients at follow-up	51
MAE	5 (9.8)
Death for any cause	0
Myocardial Infarction	1 (2)
Non-TL	1 (2)
TLR	3 (6)
DUS assessment	51
Primary patency *	45 (82)
Freedom from clinically driven TLR	47 (92)
Freedom from >50% stenosis	43 (84)

Values are shown as mean ± SD or (n)/%. DEB = drug-eluting balloon; MAEs = major adverse events; NTL TLR = target lesion revascularization. PSVR = peak systolic velocity ratio; TLR = target lesion revascularization. * Freedom from combined endpoint of clinically driven TLR and restenosis >50% at DUS, as defined by PSVR > 2.4.

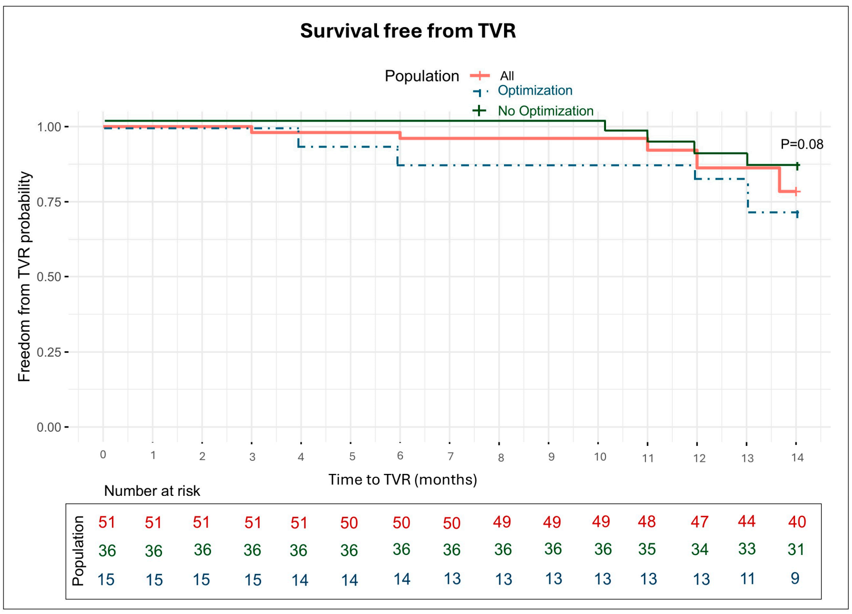

Figure 4. Kaplan Mayer curve for target lesion revascularization (TVR) at follow-up. Analysis was stratified by lesions requiring optimization (blue dotted line) and lesions not requiring optimization (green line). Red line: overall population.

4. Discussion

This study's main findings are as follows: (1) one-third of "near 50%" residual stenoses and long grade C dissection cases occurring after the endovascular treatment of long femoro-popliteal lesions showed an abnormal PSVR at the intraoperative DUS assessment; (2) the PTA optimization of the treated lesions guided by DUS led to an integrated technical success rate of 95.2%.

4.1. Intraoperative DUS Assessment for Definition of Technical Success

In the majority of the studies reported in the literature, technical success is defined by angiography as the completion of the endovascular procedure with <50% residual stenosis of the treated lesion by visual estimate and the absence of flow-limiting dissection [2,3]. The accurate definition of technical success has relevant consequences since the degree of residual stenosis and the presence of long and/or flow-limiting dissections at the index procedure may affect the long-term patency of femoro-popliteal artery angioplasty [8,9,14]. However, this type of evaluation has two main issues: first, the angiographic bi-dimensional evaluation of a complex tri-dimensional environment such as a dissection or an eccentric stenosis can be challenging; second, angiography does not provide any functional evaluation of the PTA, which may help the healthcare professional to discriminate more effectively between the success and failure of PTA, especially in ambiguous cases of stenosis with a lumen reduction very close to 50% or in the case of a long dissection. Indeed, the functional relevance of stenosis can be indirectly supposed with angiography by means of an observation of a slow flow downstream of a dissection; furthermore, it is supposed that stenosis > 50% is producing a trans-stenotic gradient according to the physical laws of fluid hemodynamics. However, the slow flow itself might also have different causes such as the distal embolization of debris. Another important issue is that the current classifications of dissections have many caveats, and even the recent DISFORM (diameter reduction, spiral shape, flow impairment, or adverse morphology) classification system for peripheral vessel dissections, using the Delphi consensus methodology, has the inherent limitations of being based on experts' suggestions and not being directly supported by any clinical or functional data [9,13].

We found that one-third (5/14) of the grade C dissections had functional relevance at the DUS assessment despite no clear signs of flow impairment at angiography. Similarly, we demonstrated that one-third of residual intermediate stenoses <50% had functional relevance at the DUS assessment and should therefore be considered as a sub-optimal result in a multi-imaging evaluation perspective. In conclusion, in the present cohort of patients, characterized by long and calcific femoro-popliteal lesions, one-third of angiography-based successes should be reclassified as failures after an intraoperative DUS assessment.

4.2. DUS-Guided Procedural Optimization

In the present study, the intraoperative DUS assessment guided further treatment such as post-dilatation or stenting that eventually produced an integrated technical success rate of 95%. Of note, following our purposed optimization algorithm, the final stent rate increased significantly from 8% (5/62) to 23% (14/62) since in nine cases, balloon post-dilatation only failed to fix residual stenosis or seal flow-limiting dissections properly. In fact, in our study, the reported stent rate (23%) was higher than those reported in the LONG SFA study (10.5%) or in the reports of the ILLUMINATE Global Study (17.3%) [15,16]. In this regard, it is important to underline that despite the bail-out stenting of the superficial femoral artery being generally accepted, it might also result in restenosis due to neointimal hyperplasia secondary to the mechanical damage of the arterial wall produced by the stent itself. However, the stenting of heavily calcified lesions, such those in our study population, often results in persistent residual stenosis and should therefore be avoided unless anticipating adequate lesion preparation using calcific plaque modification devices (CMPDs). Indeed, devices like intravascular lithotripsy (IVL) or debulking systems like atherectomy were shown to be safe and effective for the treatment of heavy calcific plaque at different vascular districts, including lower limb arteries [17–19]. In our study, CPMDs had never been employed, but in consideration of the fact that the proportion of moderate to severely calcified lesions was very high (56%), it would have been possible to lower the stent rate if a proper lesion preparation by CPMD had been performed systematically in cases of persistent residual stenosis despite many conventional balloon dilatations.

Compared to other more expensive intravascular imaging modalities, such as IVUS or OCT, intraoperative DUS has the advantage to minimize the impact on procedural costs, and it is also available in most Cath-labs where peripheral interventions are performed. Furthermore, in patients with severe chronic kidney disease (CKD), intraoperative DUS may reduce the total procedural load of contrast if used instead of angiography to assess the results after lesion pre-dilatation, after DEB angioplasty, post-dilatation, or after stenting. This strategy might represent a valid and cheaper alternative to CO_2 angiography to reduce the incidence of contrast-induced nephropathy among patients with CKD undergoing peripheral angioplasty.

4.3. Long-Term Outcomes

Although the impact of a perioperative DUS assessment on long-term outcomes was not the main subject of this study, it would seem to be relevant to make some comparisons among the long-term outcomes of different studies considering the following issues: (1) the population enrolled in our study consisted entirely of patients with declared angiographic technical success but with a higher degree of residual stenosis or long grade C dissection; (2) the mean lesion length and the number of severely calcified lesions were very high.

For example, Phair et al. reported a cumulative one-year primary patency of 80% with DES versus 49% with DCB in a small retrospective cohort of 84 patients, with long femoro-popliteal lesions of a mean length of 110 mm (interquartile range [IQR] of 100–150, absolute range of 100–260), which is definitively lower compared to the primary patency reported in our study. However, this difference might be a result of the fact that to detect stenosis >50%, Phair et al. adopted a PSVR > 2.0, which is lower than the PSVR > 2.4 adopted in our study. Conversely, in the SFA-LONG study in which 105 patients with femoropopliteal lesions >15 cm underwent PTA by DEB, Micari et al. reported 1-year primary patency and clinically driven TLR rates of 83.2% and 96%, respectively. The primary patency and clinically driven revascularization reported in our study are consistent with those reported in the SFA-LONG study despite a higher rate of severe calcified lesions (16 vs. 13.3%), but a lower mean length of the lesion was attempted (211 $\pm$ 85.2 mm vs. 251.71 $\pm$ 78.9 mm) [16].

Interestingly, the one-year primary patency of the sub-group of patients with lesions who underwent PTA optimization was similar to that of patients with lesions that did not require any PTA optimization, although the first group included longer and more complex lesions, as demonstrated by a higher proportion of TASC C and D lesions, and a higher proportion of calcific and total occlusion lesions.

Whether this "functional-guided" optimization algorithm might positively impact long-term outcomes should be investigated in dedicated prospective trials. In this regard, it is reassuring that very recently, for the first time, the systematic use of IVUS to optimize femoro-popliteal angioplasty was associated with better primary patency and freedom from clinically driven target lesion revascularization at 12 months compared with the conventional angiography guidance [20]. Therefore, we believe that there is room to implement a more extensive multi-imaging modality approach for the treatment of long femoro-popliteal atherosclerotic disease.

4.4. Study Limitations

First, the present study is subject to the limitations of observational studies. Second, the data presented in this manuscript reflect the practice of two high-volume referral hospitals for peripheral interventions, where highly skilled operators performed the procedures; therefore, these data may not be wholly generalizable. Third, this study does not have core laboratory assessments of the patients' angiograms, CTO lesion characteristics, and a final procedural approach. Furthermore, there is no independent angiographic and clinical event adjudication, which might lead to an overestimation of technical success and, conversely, an underestimation of procedural complications. In addition, **the variation in lesion length represents a potential bias in the analysis of the outcome; moreover,** the selection of guidewires and equipment was left to the operator's discretion, and its impacts on success and complication rates were not assessed. Moreover, although the use of CPMD would be desirable for the treatment of severely calcific lesions, it was never used in our cohort of patients. **Furthermore, the small sample size remains a concern, reducing the power of the statistical analysis and limiting the generalizability of the data.** In addition, a one-year follow-up with DUS was available in only 82% patients; however, this was not the main object of the study. Finally, our results should be considered as hypothesis-generating and validated in larger studies.

5. Conclusions

An intraoperative DUS assessment of intermediate residual stenosis or grade C dissections occurring after PTA of long and calcified femoro-popliteal artery stenosis allowed for a more accurate definition of technical success than angiography and guided further PTA optimization in one-third of cases.

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Conflicts of Interest: A. Micari reports consulting/speaker honoraria from Medtronic and Philips, though not in relation to the present study. F. Castriota reports consulting/speaker/proctoring honoraria from Boston Scientific and Medtronic, though not in relation to the present study. The other authors do not report any conflicts of interest.

Abbreviations

CMPDs	calcific plaque modification devices
DUS	Doppler ultrasound
IVL	intravascular lithotripsy
IVUS	intravascular ultrasound

PTA	percutaneous transluminal angioplasty
MAE	major adverse event
MI	myocardial infarction
OCT	optical coherence tomography
PSVR	peak systolic velocity ratio
SFA	superficial femoral artery
TLR	target lesion revascularization
TVL	target vessel revascularization

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