Outcomes of endovascular treatment of superficial femoral artery in-stent stenosis and/or occlusion

Maher Abdelmoneim, Hussien M. Khairy, Ahmed A.H. Ghanem, Amr A. Rahim, Samy Khalefa, Ahmed A. Shaker

Department of Vascular and Endovascular Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence to Ahmed A. Shaker, MD, Department of Vascular and Endovascular Surgery, Faculty of Medicine, Cairo University, Cairo, 11562, Egypt Tel: +20 106 353 9447; fax: 202 23644383; e-mail: ahmed.alaaeldin@kasralainy.edu.eg

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Introduction
In-spite the development of novel therapies for femoropopliteal disease treatment, nitinol stents remain the mainstay of therapy following balloon angioplasty popliteal artery (POPA). femoropopliteal in-stent restenosis remains an important clinical dilemma.
Materials and methods
A randomized controlled study, including 40 patients undergoing elective endovascular treatment for superficial femoral artery in stent restenosis (SFA ISR), was conducted to clarify the technical feasibility and the outcomes of the endovascular intervention.
Results
In total, 55% of cases were females (n=22), 70% were diabetics (n=28), 32.5% had a history of tobacco abuse (n=13), 57.5% were hypertensive (n=23), and 27.5% with past history of open revascularization (n=11). Median age and per-procedural ankle brachial indices was 62 and 0.4, respectively. Procedural and clinical success was achieved in 32 limbs (80%). Failure of engagement occurred in eight patients with total occlusion of the stent (class III). The results for POPA alone versus combined drug-coated balloons and plain old balloon angioplasty (POBA) in relation to primary and secondary outcomes in successful cases at 3, 6, and 12 months of follow-up were usage of combined drug-coated balloons and POBA associated with increasing percentage of targeted outcomes (21.9, 30.4, and 54.5%, respectively) with significant P value. Deployment of bare-metal nitinol stent was associated with improvement in primary and secondary outcomes at 3 and 6 months of follow-up (59.4 and 65.2%, respectively), but the percentage reduced at 12 months of follow-up into 54.5% (significant P values 0.004, 0.009, and $<$0.001, respectively).
Conclusion
Endovascular treatment of in-stent occlusion is associated with high success rates and higher primary and secondary patency rates.

Keywords:
stenosis, stent, superficial femoral artery

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Introduction

Posterior tibial artery (PTA) of the superficial femoral artery has three-year primary patency rate of 30–61% according to lesion length and clinical stage. The poor patency after PTA has led toward different techniques for new lesions of the femoral segment [1].

The biology of ISR differs from balloon angioplasty. Stents are used in general if unsatisfactory balloon angioplasty is achieved or if there is immediate recoil, dissection, or residual stenosis more than 30% [2].

After PTA, intimal hyperplasia, elastic recoil, and negative remodeling occurs. In contrast, after stent placement, neither elastic recoil nor negative remodeling happens, but thrombus formation and then intimal hyperplasia are the main reasons of in-stent restenosis [3].

Drug-eluting stents with Sirolimus-, paclitaxel-, and ABT-578 (polymer coating needed for their delivery) had marked reduction in restenosis through decreasing smooth muscle cell proliferation [4].

The main success of DEBs is the no-metal-left-behind concept and polymer barriers that disrupt or delay vascular healing, However, treated vessels with this technology show delayed vascular healing characterized by dose-dependent increases in fibrin deposition, delayed re-endothelialization, lower number of neointimal cells, and increased medial vascular smooth muscle cell (VSMC) loss [4].

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Materials and methods

Study design

This was a randomized controlled prospective study conducted at Kasr Al Ainy hospitals. The ethical committee approved our work and gave full permission.

All participants provided oral informed consent to participate in this study.

Study population

In total, 40 patients (a number suggested by the statisticians) undergoing elective endovascular treatment for SFA ISR were collected to clarify the technical feasibility and the outcomes of the endovascular intervention.

Inclusion criteria

(1) People who are presented with SFA ISR with good runoff.
(2) SFA ISR with patent popliteal artery with at least one patent tibial vessel as runoff.

Exclusion criteria

(1) People with complete total occlusion of all tibial vessels (isolated popliteal segment)
(2) People who need primary amputation:
    (a) Demographics, clinical history, procedural characteristics, in-hospital stay, and 3, 6-, and 12-month outcomes were analyzed

The data included clinical characteristics, for example, ankle brachial indices and Rutherford classification; angiographic characteristics, for example, runoff and pattern of ISR and treatment techniques.

Definitions

A classification system in which ISR lesions are assigned to one of three categories based on angiographic features [5]:

(1) Class I (focal ISR): includes lesions less than or equal to 50 mm in length that are positioned in the stent body, at the stent edge, or both
(2) Class II (diffuse ISR): includes stent-body lesions and stent-edge lesions greater than 50 mm in length
(3) Class III: totally occluded ISR

Procedural success was defined as less than 30% angiographic stenosis and normal antegrade flow in the treated vessel after intervention. Clinical success was defined as improvement in baseline symptoms by at least one Rutherford class.

Indications for the treatment of ISR included duplex ultrasound evidence of restenosis with or without associated clinical symptoms of intermittent claudication or critical limb ischemia. In asymptomatic patients, the duplex ultrasound was performed as part of noninvasive surveillance of previously stented vessels.

After repeat treatment, patients underwent surveillance duplex ultrasound studies at 3, 6, and 12 months or when clinically indicated.

Primary outcomes are clinically improved with reduction in Rutherford classification, while secondary outcomes include limb salvage and arterial patencies.

Statistical analysis

(1) Microsoft Excel 2013 was used for data entry and the Statistical Package for Social Science (SPSS version 21) (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp USA) was used for data analysis. All collected data were revised for competencies and logical consistency.
(2) Simple descriptive statistics (arithmetic mean and standard deviation) used for summary of normal quantitative data and frequencies used for qualitative data.
(3) Bivariate relationship was displayed in cross-tabulations and Comparison of proportions was performed using the χ^2 and Fisher's exact tests where appropriate.
(4) Independent *t*-test was used to compare normally distributed quantitative data.
(5) The level of significance was set at probability (*P*) value less than 0.05.

Results

Demographic data

Endovascular treatment for ISR was performed on 40 limbs in 40 patients. About 55% of cases were females (n=22), 70% were diabetics (n=28), 32.5% had a history of tobacco abuse (n=13), and 57.5% were hypertensive (n=23) . The median age and preprocedural ankle brachial indices was 62 and 0.4, respectively.

Rutherford classification

Cases presented according to Rutherford classification by the following categories: 3 (n=1), 4 (n=15), 5 (n=20), and 6 (n= 4), with percentages 2.5%,

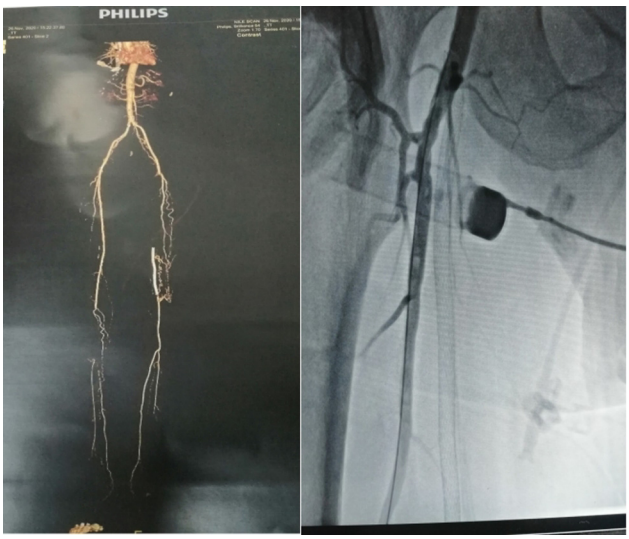
37.5%, 50%, and 10%, respectively, with the majority of cases (55%) having class III pattern of ISR (*n*=22) and 87.5% having peroneal artery (may be alone or with any other tibial vessel) as a runoff vessel (*n*=35). Total leukocytic count (TLC) was normal in 55% of cases (*n*=22) (Table 1, Fig. 1).

Table 1 Clinical characteristics of patients undergoing endovascular treatment for SFA ISR

	Count	%
Rutherford classification		
Grade 3	1	2.5
Grade 4	15	37.5
Grade 5	20	50.0
Grade 6	4	10.0
Total	40	100.0
TLC		
Normal	22	55.0
High	18	45.0
Total	40	100.0
Pattern of ISR		
Class I	5	12.5
Class II	13	32.5
Class III	22	55.0
Total	40	100.0
Runoff – PA		
No	5	12.5
Yes	35	87.5
Total	40	100.0
Runoff – ATA		
No	20	50.0
Yes	20	50.0
Total	40	100.0
Runoff – PTA		
No	17	42.5
Yes	23	57.5
Total	40	100.0

ATA, anterior tibial artery; PTA, posterior tibial artery; TLC, total leukocytic count.

Figure 1



Type III SFA ISA.

Access

Retrograde femoral puncture was the most used access in 28 cases (70%).

Procedural data

Drug-coated balloons (DCBs) and restenting with a bare-nitinol stent were used in 17.5% and 47.5% of cases, respectively (*n*=7 and 19, respectively). Adjunctive balloon angioplasty was performed following stenting, Thus, primary or adjunctive balloon angioplasty was performed in 100% of successful cases (Table 2).

Table 2 Angiographic and procedural characteristics of patients undergoing endovascular treatment for in-stent restenosis

	Count	%
Total	40	100.0
Access – antegrade femoral		
No	32	80.0
Yes	8	20.0
Total	40	100.0
Access – retrograde femoral		
No	12	30.0
Yes	28	70.0
Total	40	100.0
Access – transbrachial		
No	36	90.0
Yes	4	10.0
Total	40	100.0
Access – retrograde popliteal		
No	31	77.5
Yes	9	22.5
Total	40	100.0
Access – retrograde pedal		
No	39	97.5
Yes	1	2.5
Total	40	100.0
Balloons – DCB		
No	33	82.5
Yes	7	17.5
Total	40	100.0
Balloons – POBA		
No	8	20.0
Yes	32	80.0
Total	40	100.0
Stents		
No	21	52.5
Yes	19	47.5
Total	40	100.0
Procedural success		
No	8	20.0
Yes	32	80.0
Total	40	100.0

DCB, drug-coated balloon; POBA, plain old balloon angioplasty.

Procedural success

Procedural and clinical success was achieved in 32 limbs (80%). Failure of engagement occurred in eight patients who had completely occluded a previously stented segment (class III).

Procedural was significantly higher in nonsmokers (P=0.037), those with normal renal function (P<0.001), diabetics (P<0.001), chronic kidney disease (87.5%), and male gender (P=0.054).

Patients with procedural success showed a significantly lower Rutherford grade (P=0.019) and normal TLC (P=0.001). On the other hand, unsuccessful cases showed higher Rutherford grade and TLC with a statistically significant P value.

Technical success in relation to class of ISR I, II, and III was 100% (n=5), 92% (n=12), and 68% (n=15), respectively, with a statistically insignificant P value (Fig. 2).

At 3, 6, and 12 months of follow-up, peroneal artery as a runoff vessel compared with the anterior or posterior tibial arteries was associated with higher clinical improvement with reduction in Rutherford classification and limb salvage and arterial patencies (87.5, 87, and 81.8%, respectively) with a statistically insignificant P value.

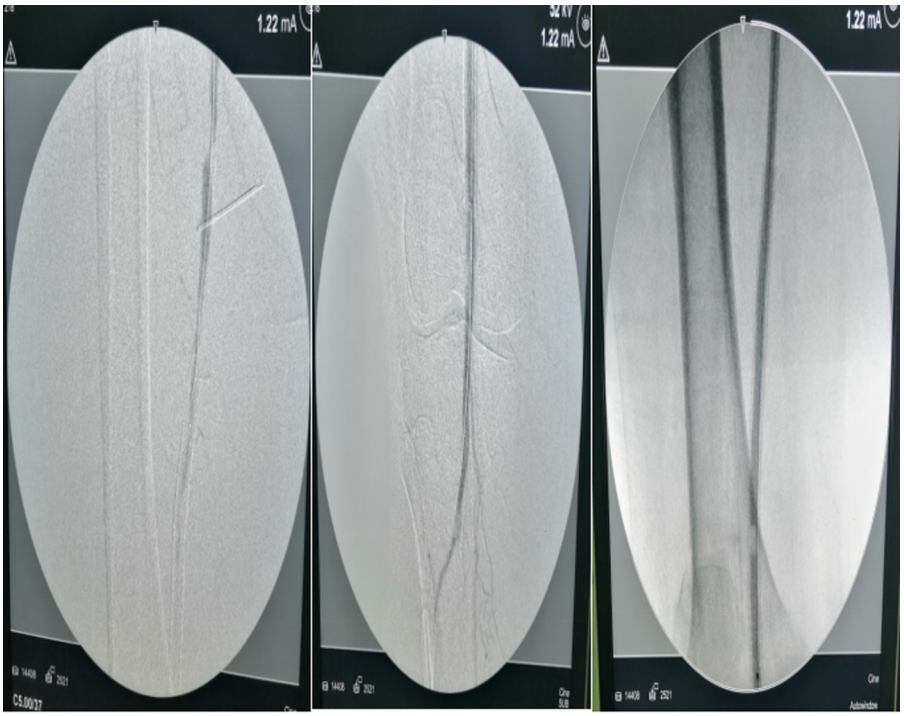
The results for DCBs in relation to primary (clinical improvement with reduction in Rutherford classification) and secondary (limb salvage and patency) outcomes at 3, 6, and 12 months of follow-up were (21.9, 30.4, and 54.5%, respectively), all with a significant P value. While in plain old balloon angioplasty (POBA) patients, we had very good outcomes at 3, 6, and 12 months with a significant P value (Table 3).

The results of bare-metal nitinol stent were associated with improvement in primary and secondary outcomes at 3 and 6 months of follow-up (59.4 and 65.2%, respectively), but the percentage reduced at 12 months of follow-up into 54.5%, all with significant P values (0.004, 0.009, and <0.001, respectively) (Table 3).

People who presented with Rutherford classification grade 4 were associated with decreasing percentage in primary and secondary outcomes at 3, 6, and 12 months (46.9, 34.8, and 27.3%, respectively), all with a significant P value (Table 4).

People who presented with Rutherford classification grade 6 were associated with increasing percentage in primary and secondary outcomes at 3, 6, and 12 months (12.5, 17.4, and 36.4%, respectively), all with a significant P value (Table 4).

Figure 2



PTA for distal SFA type III ISR.

Table 3 Primary outcomes (clinical improvement with reduction in Rutherford classification)and secondary outcomes (limb salvage and patency) of follow-up in relation to runoff vessel, balloons, and stents

	Primary and secondary outcomes at 3 m Yes [*n* (%)]	*P* value	Primary and secondary outcomes at 6 m Yes [*n* (%)]	*P* value	Primary and secondary outcomes at 12 m Yes [*n* (%)]	*P* value
Runoff – PA						
No	4 (12.5)	1.000	3 (13.0)	1.000	2 (18.2)	0.603
Yes	28 (87.5)		20 (87.0)		9 (81.8)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	
Runoff – ATA						
No	12 (37.5)	0.309	11 (47.8)	0.749	4 (36.4)	0.288
Yes	20 (62.5)		12 (52.2)		7 (63.6)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	
Runoff – PTA						
No	13 (40.6)	0.702	9 (39.1)	0.616	4 (36.4)	0.730
Yes	19 (59.4)		14 (60.9)		7 (63.6)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	
Balloons – DCB						
No	25 (78.1)	0.003	16 (69.6)	0.014	5 (45.5)	0.001
Yes	7 (21.9)		7 (30.4)		6 (54.5)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	
Balloons – POBA						
No	0	<0.001	0	<0.001	0	0.003
Yes	32 (100.0)		23 (100.0)		11 (100.0)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	
Stents						
No	13 (40.6)	0.004	8 (34.8)	0.009	5 (45.5)	<0.001
Yes	19 (59.4)		15 (65.2)		6 (54.5)	
Total	32 (100.0)		23 (100.0)		11 (100.0)	

DCB, drug-coated balloon; POBA, plain old balloon angioplasty; PTA, posterior tibial artery.

Table 4 Primary outcomes (clinical improvement with reduction in Rutherford classification) and secondary outcomes (limb salvage and patency) of follow-up in relation to clinical data

	Primary and secondary outcomes at 3 m			Primary and secondary outcomes at 6 m			Primary and secondary outcomes at 12 m		
	No [*n* (%)]	Yes [*n* (%)]	*P* value	No [*n* (%)]	Yes [*n* (%)]	*P* value	No [*n* (%)]	Yes [*n* (%)]	*P* value
Rutherford classification									
Grade 3	0	1 (3.1)	0.019	1 (5.9)	0	0.026	1 (3.4)	0	0.008
Grade 4	0	15 (46.9)		7 (41.2)	8 (34.8)		12 (41.4)	3 (27.3)	
Grade 5	8 (100.0)	12 (37.5)		9 (52.9)	11 (47.8)		16 (55.2)	4 (36.4)	
Grade 6	0	4 (12.5)		0	4 (17.4)		0	4 (36.4)	
Total	8 (100.0)	32 (100.0)		17 (100.0)	23 (100.0)		29 (100.0)	11 (100.0)	
TLC									
Normal	0	22 (68.8)	0.001	8 (47.1)	14 (60.9)	0.001	19 (65.5)	3 (27.3)	0.030
High	8 (100.0)	10 (31.3)		9 (52.9)	9 (39.1)		10 (34.5)	8 (72.7)	
Total	8 (100.0)	32 (100.0)		17 (100.0)	23 (100.0)		29 (100.0)	11 (100.0)	

TLC, total leukocytic count.

Presentation with high TLC versus normal TLC is associated with better primary and secondary outcomes at 3, 6, and 12 months of follow-up (31.3, 52.9, and 72.7%, respectively), all with a significant *P* value.

Discussion

The endovascular treatment of the FP segment has been encountered by high rates of restenosis. Stenting has surpassed PTA as the preferred treatment for FP disease, and with this, there has been a significant increase in the number of cases of FP-ISR.

Our study provides relevant data on the technical feasibility and outcomes of endovascular treatment of SFA ISR.

We reported that the mean age was 62 years, 70% were diabetics, 32.5% had a history of tobacco abuse, and 57.5% were hypertensive .

Zhao *et al.* [6] in a study comparing DCB versus bare-nitinol stent in the femoropopliteal artery reported that the mean age was 63 years in the DCB group and 66 years in the stent group (P=0.186).

Zhao *et al.* [6] also reported that more than 50% of patients had diabetes; roughly two-thirds of the patients had hypertension and were current smokers.

Our data suggested female gender as the independent risk factor of restenosis (55% of cases).

The DEBATE-ISR trial [7] and Schmidt *et al.* [8] reported similar results that indicated female sex as an independent predictor of restenosis, as well as the PACIFIER trial [9].

A recent meta-analysis also reported that male patients treated with DCBs performed significantly better than female patients [10].

This finding could be either due to a smaller vessel diameter seen in female patients or due to processes inherent to metabolic or hormonal changes related to female gender that promote intimal hyperplasia and restenosis that merit further investigation [8].

We achieved procedural and clinical success in 32 limbs (80%). Failure of engagement occurred in eight patients with class III ISR.

Zhao and colleagues reported that device success, procedure success, and clinical success were achieved in all patients of the DCB group, while few patients in the stent group failed. About 25.5% of the DCB patients were with the provisional stent; these patients were classified as the DCB group rather than the stent group and regraded as procedure success according to the definition mentioned above [6].

Ho *et al.* [11] reported that recurrent ISR at 2 years after angioplasty was higher in patients with class III lesions (84.9%) than in those with class I or class II lesions (about 50%).

Recurrent occlusion at 2 years was 64.6% in class III compared with the other two classes (<20%). These results highlight that diffuse, occlusive ISR is a difficult problem [11].

This may explain that all failed cases in our study were all type III ISR with failure of engagement.

We reported that DCBs are associated with increasing percentage of targeted primary and secondary outcomes of follow-up at 3, 6, and 12 months (21.9, 30.4, and 54.5%, respectively), all with a significant P value.

We also reported that deployment of bare-metal nitinol stent was associated with improvement in primary and secondary outcomes at 3 and 6 months of follow-up, but the percentage reduced at 12 months of follow-up.

Zhao *et al.* [6] reported that the DCB provided superior outcomes at 12 months compared with bare-nitinol stent for FP-ISR with 1-year primary patency rate of 74.5% in the DCB group.

The DRASTICO study, which compared DCB without bailout nitinol BMS stenting versus systematic drug-eluting stent in a real-world scenario and included 96 DCB participants with 119 lesions, reported a primary patency rate of 77.5% at 12 months [12].

Schmidt reported a patency rate of 79.2 and 53.7% at 1 and 2 years, respectively [8].

Furthermore, our outcomes confirmed the results of the AcoArt I Trial (primary patency, 76.1%) using the same DCB for treatment of lesions [13].

Similarly, DCB angioplasty appears to be significantly superior to PTA [10].

In our study, presentation with normal TLC is associated with higher percentage of procedural success. In contrast, presentation with high TLC is associated with better primary and secondary outcomes at 3, 6, and 12 months of follow-up .

This may be explained as individuals presented with high inflammatory markers (including high TLC), gain drainage, and debridement of septic focus after endovascular revascularization, consequently, the TLC returns to normal during follow-up visits giving improvement in the primary and secondary outcomes at 3, 6, and 12 months of follow-up.

Araújo and colleagues in a study to evaluate the inflammatory markers in in-stent restenosis after femoral PTA revealed that restenosis was observed in 38.5% patients who underwent PTA and stenting. There was no statistical difference in inflammatory marker

levels when comparing restenosis and no-restenosis groups [14].

Conclusion

It was concluded that SFA ISR is more common in diabetics, hypertensives, nonsmokers, and females.

Endovascular treatment is technically feasible with a success rate of 80%.

Combined DCBs and POBA are associated with increasing the percentage of targeted primary and secondary outcomes of follow-up at 3, 6, and 12 months .

Deployment of bare-metal nitinol stent was associated with improvement in primary and secondary outcomes at 3 and 6 months of follow-up, but the percentage reduced at 12 months of follow-up.

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Conflicts of interest

There are no conflicts of interest.

References

1 Yeo KK, Malik U, Laird JR. Outcomes following treatment of femoropopliteal in-stent restenosis: a single center experience. Catheter Cardiovasc Interv 2011; 78:604–608.

2 Buszman PP, Tellez A, Afari ME, Peppas A, Conditt GB, Rousselle SD, Granada JF. Tissue uptake, distribution, and healing response after delivery of paclitaxel via second-generation iopromide-based balloon coating: a comparison with the first-generation technology in the iliofemoral porcine model. JACC Cardiovasc Interv 2013; 6:883–890.

3 El Sayed H, Kerensky R, Stecher M, Mohanty P, Davies M. A randomized phase II study of Xilonix, a targeted therapy against interleukin 1α, for the prevention of superficial femoral artery restenosis after percutaneous revascularization. J Vasc Surg 2016; 63:133–141.

4 Krankenberg H, Tübler T, Ingwersen M, Schlüter M, Scheinert D, Blessing E, Zeller T. Drug-coated balloon versus standard balloon for superficial femoral artery in-stent restenosis: the randomized Femoral Artery In-Stent Restenosis (FAIR) trial. Circulation 2015; 132:2230–2236.

5 Tosaka A, Soga Y, Iida O, Ishihara T, Hirano K, Suzuki K, Nobuyoshi M. Classification and clinical impact of restenosis after femoropopliteal stenting. J Am Coll Cardiol 2012; 59:16–23.

6 Zhao H, Ma B, Chen J, Zheng L, Sun CR, Sun MS, Ye ZD. Drug-coated balloon versus bare nitinol stent in femoropopliteal artery: 12 months outcome from a Single Center in China. Ann Vasc Surg 2021; 5:5096.

7 Grotti S, Liistro F, Angioli P, Ducci K, Falsini G, Porto I, Bolognese L. Paclitaxel-eluting balloon vs standard angioplasty to reduce restenosis in diabetic patients with in-stent restenosis of the superficial femoral and proximal popliteal arteries: three-year results of the DEBATE-ISR study. J Endovasc Ther 2016; 23:52–57.

8 Schmidt A, Piorkowski M, Görner H, Steiner S, Bausback Y, Scheinert S, Scheinert D. Drug-coated balloons for complex femoropopliteal lesions: 2-year results of a real-world registry. JACC Cardiovasc Interv 2016; 9:715–724.

9 Werk M, Albrecht T, Meyer DR, Ahmed MN, Behne A, Dietz U, Hänninen EL. Paclitaxel-coated balloons reduce restenosis after femoro-popliteal angioplasty: evidence from the randomized PACIFIER trial. Circulation 2012; 5:831–840.

10 Caradu C, Lakhlifi E, Colacchio EC, Midy D, Bérard X, Poirier M, Ducasse E. Systematic review and updated meta-analysis of the use of drug-coated balloon angioplasty versus plain old balloon angioplasty for femoropopliteal arterial disease. J Vasc Surg 2019; 70:981–995.

11 Ho KJ, Owens CD. Diagnosis, classification, and treatment of femoropopliteal artery in-stent restenosis. J Vasc Surg 2017; 65:545–557.

12 Liistro F, Angioli P, Porto I, Ducci K, Falsini G, Ventoruzzo G, Bolognese L. Drug-eluting balloon versus drug-eluting stent for complex femoropopliteal arterial lesions: the DRASTICO study. J Am Coll Cardiol 2019; 74:205–215.

13 Jia X, Zhang J, Zhuang B, Fu W, Wu D, Wang F, Guo W. Acotec drug-coated balloon catheter: randomized, multicenter, controlled clinical study in femoropopliteal arteries: evidence from the AcoArt I trial. JACC Cardiovasc Interv 2016; 9:1941–1949.

14 Araújo PV, Ribeiro MS, Dalio MB, Rocha LA, Viaro F, Joviliano RD, Joviliano EE. Interleukins and inflammatory markers in in-stent restenosis after femoral percutaneous transluminal angioplasty. Ann Vasc Surg 2015; 29:731–737.