Plain uncoated balloon versus drug-coated balloon in the management of in-stent restenosis of femoropopliteal lesions: a comparative study of the effect of lesion length on the outcome

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Aim
To compare the effectiveness of plain balloon and drug-coated balloon (DCB) in the management of in-stent restenosis (ISR) of femoropopliteal lesions regarding reocclusion rate and target lesion revascularization (TLR).
Patients and methods
A retrospective study was carried out on 31 patents complaining of critical limb ischemia, Rutherford categories 4 or 5, due to femoropopliteal ISR during the period from June 2018 to June 2020 at Sohag University Hospitals and 6 October Insurance Hospital, Cairo. Patients were managed by one of two different modalities: group A, where patients were managed by DCB, and group B, where patients were managed by plain balloon. In each group, according to the lesion length of the ISR, patients were classified into long lesions (>10 cm) and short lesions (<10 cm). Recurrent occlusion and TLR were evaluated and compared between the two groups.
Results
Group A consisted of 19 patients, with 11 long lesions and eight short lesions, whereas group B consisted of 12 patients, with five long lesions and seven short lesions. In short lesions, reocclusion was recorded in 12.5% (1/8 patients) of the DCB group compared with 57.1% (4/7 patients) in the plain balloon group ($P \leq 0.001$), whereas in long lesions, the reocclusion was recorded in 36.4% (4/11 patients) of the DCB group compared with 60% (3/5 patients) ($P=0.65$). TLR was recorded in two patients of plain balloon group, whereas no cases were reported in the DCB group in short lesions, whereas in long lesions, four cases developed TLR [two (18.2%) cases of DCB group and two (40%) cases of plain balloon group). Regarding TLR results, the performance of DCB in ISR differs significantly in short lesions compared with long lesions ($P \leq 0.05$).
Conclusion
DCB angioplasty offers an effective outcome in the management of femoropopliteal ISR, especially in short lesions. However, in long lesions, it yields higher but insignificant results compared with plain balloon angioplasty. Long-term results of management of ISR in long lesions are awaited irrespective of the technology used.

Keywords:
drug-coated balloon, femoropopliteal, in-stent restenosis, plain balloon

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Introduction

Peripheral arterial disease is a progressive pathology affecting the quality of life of more than 200 million people worldwide [1]. Advances in the endovascular tools have allowed longer and more complex lesions to be treated with endovascular intervention. Management of these lesions are challenging as long-term outcomes are not satisfactory because of its increased prevalence of restenosis, particularly in TASC II C and D lesions [2,3].

In-stent restenosis (ISR) is defined as luminal narrowing within the cylinder of the stent and/or 5-mm margin proximal or distal to the stent. Its incidence has increased over years and will keep on increasing in the future. Several endovascular technologies have been evaluated separately or in combination with each other for its management. They include balloon angioplasty [plain balloon, drug-coated balloon (DCB), and cutting balloon], stent in stent (nitinol stent, covered stent, and drug-eluting stent (DES)], atherectomy (laser atherectomy, directional atherectomy, and rotational atherectomy), bypass surgery, and others [2]. Although

all of these modalities achieve acceptable short-term success rates, long-term results are not satisfactory. Therefore, there was little consensus regarding the best treatment algorithm [4].

Neointimal hyperplasia has multiple factors that contribute in its formation, for example, stent type, lesion length, and site of stent implantation in superficial femoral artery [5]. Tosaka *et al.* [6] had classified ISR according to visual assessment on angiography into three classes: class I, focal lesion (<5 cm length); class II, diffuse lesion (>5 cm length) in either stent body or stent edge; and class III, total occlusion of the stent. They also had concluded that ISR long lesions respond less properly than short lesions, and stent fracture was associated with high recurrent rates. Regarding stent type, it was reported that braided stents, that is, Supera stents, are more resistant to fracture and also are more resistant to dilation than bare metal stents (BMS).

DCB offers combining balloon dilatation with local administration of an antiproliferative drug, a proof of evidence in decreasing the incidence of restenosis with acceptable patency rate and freedom from target lesion revascularization (TLR) [7]. Although DCBs maintain their effectiveness in primary lesions for long periods, recent data indicate less impressive performance when treating ISR [8]. The direction of current trials is blowing toward the DCBs and excimer-laser atherectomy, which may be considered the preferred modalities of treatment in the near future [7].

Therefore, the aim of this series was to compare the effectiveness of plain balloon and DCB in the management of femoropopliteal ISR regarding reocclusion rate and TLR.

Patients and methods

This retrospective study was carried out from June 2018 to June 2020 at Sohag University Hospitals and 6 October Insurance Hospital, Cairo, on patients with the following inclusion criteria:

(1) Patients with femoropopliteal ISR, Rutherford categories 4 or 5.
(2) No proximal hemodynamically significant occlusion.
(3) At least one patent distal run-off vessel.

Exclusion criteria were as follows:

(1) Patients with untreated proximal occlusions above the implanted stent.
(2) Stent occlusion that could not be crossed by wire.
(3) Presence of stent fracture grades 3–5.
(4) Patients with nonsalvageable limb or those with life-threatening infection.

This series was approval by the hospital's ethical committee. Patients were assessed clinically and through investigation. The entire clinical data were analyzed carefully, especially the level of occlusion, Rutherford category, ankle brachial index (ABI), details of the previous intervention, as well as risk factor assessment. Duplex ultrasound reports and computed tomography angiography (CTA) were reviewed in all cases for confirmation of the diagnosis, identification of the lesion's characteristics, and recognition of the distal run-off vessels. All of patients had comprehensive laboratory testing, focused on renal function and coagulation profile.

Procedure details

Dual antiplatelet treatment in the form of salicylates 75 mg and clopidogrel 300 mg as a loading dose were used as pre-procedural drugs. Depending on the anatomical features and location of the lesion, the procedure was carried out via ipsilateral or contralateral femoral access. After sheath placement, 70–100 U/kg unfractionated heparin was administered intra-arterially. Length of the stent, degree of ISR according to Tosaka classification [6], and patency of the distal run-off vessels were all assessed by pre-intervention angiography. A 0.035 Terumo hydrophilic guidewire (Radifocus, Terumo, Japan) combined with 4 Fr vertebral catheter were used to cross the lesion. When the antegrade approach failed, retrograde popliteal access, tibial access, or direct stent puncture were tried to cross the lesion. ISR lesions were managed by one of two different modalities of balloon angioplasty according to the discretion of the operator: group A, where patients were managed by DCB, and group B, where patients were managed by plain balloon.

Plain balloon group

After bridging the lesion with a wire, it was dilated for 1–2 min using a low-profile standard balloon at its nominal pressure. Balloon length was determined by a ruler placed over the patient thigh or by angiographic measurements. Repeated balloon dilatation for 2 min was attempted in cases of flow-limiting dissection. To assess the degree of technical success, completion angiography was performed. In conditions of residual stenosis of more than 30% or persistence of the flow-limiting dissection at the stent edge, bail-out stents were used.

Drug-coated balloon group

After crossing the wire, lesions were dilated for 1–2 min with a low-profile standard balloon to

reduce friction between the DCB surface and the diseased section. This was followed by inflation of DCB (IN. PACT balloon, Medtronic, Minneapolis, USA) for 3 min. The dosage of paclitaxel in the balloon was 3.5 μg/mm^2. In lesions that required more than one DCB balloon, 5-mm balloon overlap was permitted to achieve a homogenous drug elution. As advised by Schmidt *et al.* [9], repeated dilatation up to 5 min was tried in conditions of flow-limiting dissection. Completion angiography was performed to determine the technical success of the procedure. In situations of residual stenosis of more than 30% or persistence of the flow-limiting dissection, bail-out stents were used.

After achieving a technically successful procedure of the ISR revascularization, recanalization of any associated infrapopliteal arterial occlusions was tried in all patients of the study group to maximize the foot perfusion as possible.

Daily follow-up was done during the admission period and then at 1, 3, 6, 9, and 12 months in vascular surgery outpatient clinic. Daily maintenance dosage of 75-mg clopidogrel was continued postoperatively for at least 3 months. Patients with ischemic foot ulcers or gangrene underwent wound management, debridement, and/or minor amputation within their hospital stay. During follow-up visits, assessments were made for regaining pulse, measuring the ABI, getting rid of rest pain, progress of wound healing, arterial patency assessment by duplex ultrasound, and recording any procedure-related consequences. Follow-up CTA was required in cases of worsened patients' manifestations or if restenosis was more than 50% as assessed by duplex ultrasound (US).

Definitions

Technical success was defined as patency of the targeted vessel with residual stenosis less than 30%.

Clinical success was defined as foot ulcer healing, increase in ABI, and improvement in clinical Rutherford category after the procedure.

Vessel patency was defined as absence of hemodynamically significant stenosis assessed by duplex ultrasound and peak systolic velocity (PSV) ratio less than 2.4.

Reocclusion was defined as more than 50% diameter stenosis on duplex US or angiography.

TLR was defined as requirement for re-intervention within the targeted lesion because of return of the ischemic manifestations or decreased ABI measurements by more than 20% as reported by Zeller *et al.* [10].

The study outcome was the 1-year recurrent occlusion and TLR.

Statistical analysis

Continuous variables are expressed as mean±SD. Categorical variables were expressed as numbers and percentage. χ^2 test and Fisher exact test were used. Reocclusion rate and TLR were described using Kaplan–Meier analysis and log-rank test to compare groups over time on relevant outcome measures. Statistical significance was defined by P value less than 0.05.

Results

Data collected and reviewed from patients' records revealed that 43 patients presented with femoropopliteal ISR during the period between June 2018 and June 2020. Of them, eight patients were manifested by intermittent claudication and were treated medically and four patients were critical limb ischemia (CLI), Rutherford category '6' with extensive nonsalvageable foot infections. Therefore, those patients were managed by limb amputation and excluded from the study. The remaining 31 patients were CLI, Rutherford category '4' and '5' and fulfilled the inclusion criteria and were subjected to two different modalities of treatment: 19 patients were managed by DCB angioplasty (group A) and 12 patients were managed by plain balloon (group B). In each group, according to the lesion length, patients were classified into long lesions (>10 cm) and short lesions (<10 cm). Group A had 11 long lesions and eight short lesions, whereas group B had five long lesions and seven short lesions. Clinical presentation, operative details, and follow-up results were analyzed retrospectively in this study.

The commonest risk factors were diabetes mellitus and smoking in both groups (63.2 and 57.9%, respectively, in group A and 66.7 and 50%, respectively, in group B). In group A, the mean age was 56 (47–68) years, whereas in group B, the mean age was 59 (52–69) years. Baseline characteristics and risk factors are shown in Table 1. Tosaka classifications of ISR lesions were 15.8, 47.4, 36.8%, and 8.3, 58.3, and 33.3% in class I, II, and III of groups A and B, respectively. The mean length of the stent was 15 ± 5 and 12 ± 3 cm in groups A and B, respectively. The commonest sites of stent implantation were proximal superficial femoral artery and the segment related to the adductor canal, (P1) popliteal artery. Among the study groups, most of

Table 1 Demographic data and risk factors

	Group A (DCB group) (*N*=19) [*n* (%)]	Group B (plain balloon group) (*N*=12) [*n* (%)]
Age (years)	56 (47–68)	59 (52–69)
Males/females	11 (57.9)/8 (42.1)	7 (58.3)/5 (41.7)
Risk factors		
DM	12 (63.2)	8 (66.7)
Smoking	11 (57.9)	6 (50)
Hypertension	9 (47.4)	9 (52.9)
Ischemic heart disease	10 (52.6)	5 (41.7)
Stroke	2 (10.5)	1 (8.3)
Renal impairment	3 (15.8)	2 (16.7)

DCB, drug-coated balloon; DM, diabetes mellitus.

ISR lesions (25 patients, 80.6%) were crossed through the antegrade approach either ipsilateral or crossover contralateral access, two (6.5%) cases through popliteal access, three (9.7%) cases through retrograde tibial access, and one (3.2%) patient by direct stent puncture. There were no significant differences in patient baseline criteria between the two groups (Table 2). In DCB group, only one DCB balloon was used for each patient, with either short or long lesions, except six patients with long lesions, who were treated by double 5-mm overlapped DCB balloons because of the extended length of their lesions.

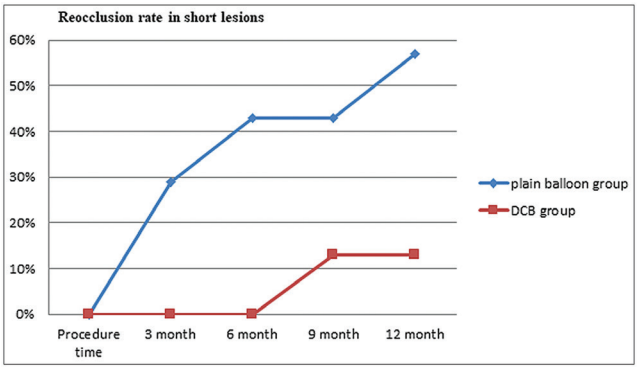
In short lesions (ISRË,10 cm), reocclusion rate was recorded in 12.5% (1/8 patients) of DCB group compared with 57.1% (4/7 patients) of plain balloon group, *P* value less than or equal to 0.001, whereas in long lesions, reocclusion was recorded in 36.4% (4/11 patients) of DCB group compared with 60% (3/5 patients) in plain balloon group (*P*=0.65) (Figs 1 and 2). It was recorded that in short lesions, the peak of reocclusion was noticed earlier in patients treated with plain balloon (3th-6th month) than those treated with DCB balloon (9th-12th month), whereas in long lesions, reocclusions were recorded from the third month in both groups and increased by time. Reocclusion was more common in the stent length of 15 and 20 cm and in those who had overlapped double stents. Analysis of these results revealed that the patency rate after DCB angioplasty was favorable in short-lesion ISR, with highly significant difference. In long lesions, reocclusions occurred earlier in both groups with better performance of DCB group patients. However, the difference was statistically insignificant. In group A, five patients (one short lesion and four long lesions) developed recurrent occlusion; three patients were claudicants and treated medically, and two patients worsened clinically by reappearance of rest pain and/or ulceration or gangrene. Duplex US detected significant stenosis, which was confirmed by CTA findings. Those patients were subjected to reintervention as follows:

Table 2 Lesion criteria and intraoperative data

	Group A (DCB group) (*N*=19) [*n* (%)]	Group B (plain balloon group) (*N*=12) [*n* (%)]
Rutherford classification		
Rutherford category 4	5 (26.3)	3 (25)
Rutherford category 5	14 (73.7)	9 (75)
Approach		
Crossover contralateral access	12 (63.2)	7 (58.3)
Ipsilateral antegrade access	3 (15.8)	3 (25)
Retrograde popliteal access	1 (5.3)	1 (8.3)
Retrograde tibial access	2 (10.5)	1 (8.3)
Stent puncture	1 (5.3)	0
Lesion length		
Short lesions Ë,10 cm	8(42.1)	7 (58.3)
Long lesions Ë*f*10 cm	11 (57.9)	5 (41.7)
Tosaka classification		
Class I	3 (15.8)	1 (8.3)
Class II	9 (47.4)	7 (58.3)
Class III	7 (36.8)	4 (33.3)
Run-off vessels		
One vessel	4 (21.1)	3 (25)
Two vessels	12 (63.2)	8 (66.7)
Three vessels	3 (15.8)	1 (8.3)

DCB, drug-coated balloon.

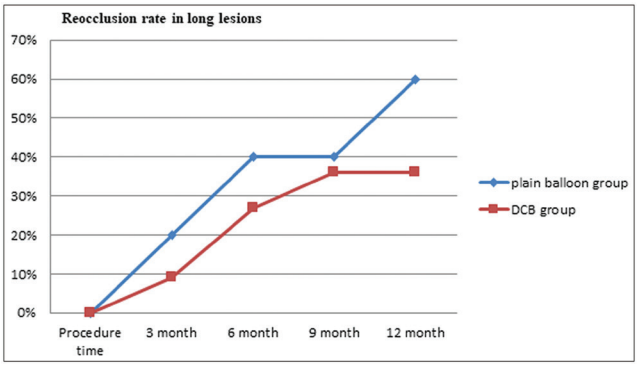
Figure 1



In short-lesion ISR, DCB achieves highly significant difference in the reocclusion rate compared with plain balloon, *P* value less than 0.001. DCB, drug-coated balloon; ISR, in-stent restenosis.

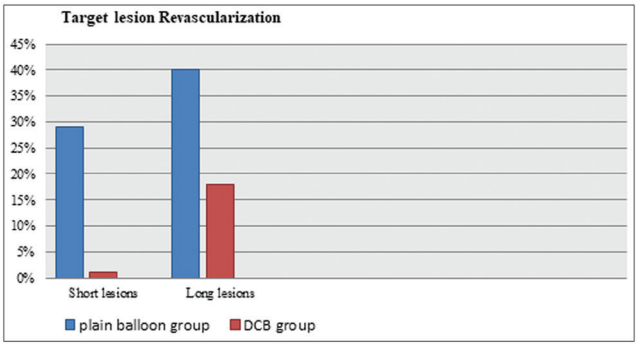
one patient was treated by nitinol stent-in-stent implantation owing to occurrence of flow-limiting dissection adjacent to stent edge, whereas the other was treated by femoropopliteal bypass owing to failure of lesion crossing by wire. In group B, seven patients (four short lesion and three long lesions) developed recurrent occlusion: three patients were claudicants and treated medically. The other four patients had CLI and were treated as follows: one patient was treated by femoropopliteal bypass surgery, one patient was treated by nitinol stent-in-stent implantation owing to the presence of significant residual stenosis, and two patients

Figure 2



In long lesions, DCB had statistically insignificant results compared with plain balloon (*P*=0.65). DCB, drug-coated balloon.

Figure 3



TLR, DCB achieves highly significant performance in short-lesion compared with long-lesion ISR (*P*Ë,0.05). DCB, drug-coated balloon; ISR, in-stent restenosis; TLR, target lesion revascularization.

were treated by amputation owing to the absence of distal run-off vessels and associated extensive gangrene in one patient and flaring infection in the other.

In short lesions, TLR was recorded in two patients of plain balloon group, whereas no cases were reported in the DCB group. In long lesions, four cases developed TLR [two (18.2%) cases of DCB group and two (40%) cases of plain balloon group). Reliant on the TLR results, it was noted that the performance of DCB in the management of short lesions was significantly wide ranging when compared with long lesions (*P*Ë,0.05) (Fig. 3).

Regarding procedure-related complications, among all of the study patients, four (12.9%) patients developed groin hematoma that resolved spontaneously, and five (16.1%) patients developed flow-limiting dissection at stent edge during balloon dilatation (four were treated by repeating the balloon dilatation, whereas the other was managed by bail-out stent-in-stent implantation). Two (6.5%) patients developed acute thrombosis during the procedure and were treated by thrombolytic therapy. Distal embolization was recorded in two (6.5%) patients and managed conservatively. There was no procedure-related mortality in both groups.

Discussion

Endovascular treatment is an acceptable strategy for treating longer and challenging femoropopliteal lesions. Because stent implantation is more common in such lesions, ISR is also more common [11]. Laird *et al.* [12] reported that the greater the length of the stented lesion, the increased the risk of restenosis.

Guidelines of the society for vascular surgery [13] did not endorse prophylactic intervention for ISR with absence of clinical manifestations. This was matched with the aforementioned series, where all cases in this study were symptomatic patients, that is, Rutherford category '4' and '5.'

Duplex US was the preliminary diagnostic tool in diagnosis of ISR in this series. ISR was defined by either absolute cutoff of PSV (e.g. >200 cm/s) or PSV ratio more than 2.4 between the proximal reference artery and the highest PSV within the stent. Therefore, it is considered as a reliable indicator of hemodynamically significant stenosis [14].

Tosaka *et al.* [6] had classified ISR according to visual assessment on angiography into three classes: class I, focal lesion (<5 cm length); class II, diffuse lesion (>5 cm length) in either stent body or stent edge; and class III, total occlusion of the stent. In this study, Tosaka classes I, II, and III were 15.8, 47.4, and 36.8%, respectively, in DCB group patients, whereas 8.3, 58.3, and 33.3%, respectively, in plain balloon group.

Effectiveness of DCB is also justified by the dose of the drug coat. Milewski *et al.* [15] showed that DCB coated with paclitaxel dose 3 μg/mm^2 is more effective when compared with DCBs coated with paclitaxel dose 1 μg/mm^2. Their study highlighted the dose-dependent effect of DCB. They also assumed that during balloon inflation for 1 min, only 6% of the drug will be diffused into the vessel wall, 4% is retained on the surface of the balloon, and 90% of the drug is lost in the bloodstream.

In short lesions (ISRË,10 cm), reocclusion was recorded in 12.5% (1/8 patients) of the DCB group compared with 57.1% (4/7 patients) of the plain balloon group (*P*≤0.001), whereas in long lesions, reocclusion was recorded in 36.4% (4/11 patients) of the DCB group compared with 60% (3/5 patients) of the plain balloon group (*P*=0.65). These results highlighted the efficacy of DCB over plain balloon in short lesions, with highly significant difference. On the contrary, in long lesions,

the performance of DCB was much better than plain balloon, but the statistical differences were not large enough to be significant. These results matched with FAIR trial [16] and Liao *et al.* [17] who performed their series on short lesions with mean lesion lengths of 8.2 and 7.9 cm, respectively, and recorded reocclusion rates of 15.4 and 12.1% in DCB group and 44.7 and 48.4% of plain balloon group, respectively. Regarding the long lesion results, it was found that ISAR-PEBIS trial [18] worked on mean lesion length of 14 cm and reported reocclusion rate of 30% in DCB angioplasty. Schmidt *et al.* [9] performed their study on a 24-cm mean lesion length and recorded 1-year reocclusion rate of 23.4%. Regarding the results of plain balloon, the PACUBA trial [19] recorded 86.6% reocclusion rate of plain balloon angioplasty in the mean long lesion of 18.4 cm. Variation in these percentages can be attributed to the small number of patients in this series as well as the type of DCB balloon and its dose of paclitaxel covering. The DEBATE-ISR study [20] had confirmed that there are certain predictors that contribute in the rate of reocclusion, for example, Tosaka classification, lesion length, as well as the dose of paclitaxel drug.

Long-term follow-up of more than 1 year remains essential to establish DCB effectiveness. The ISAR-PEBIS trial [18] documented a high patency rate up to 2 years, although the LEVANT '1' trial [21] had reported that there was no significant difference at 2 years between the DCB group and plain balloon group regarding TLR (36 vs. 49%; *P*=0.23). Cassese *et al.* [22] denied the DCB value in certain circumstances, for example, uncontrolled diabetes, long calcified lesions, and completely occluded vessels. Unfortunately, 2017 European guidelines [23] have recently assigned a weak recommendation (class IIb) for DCB angioplasty in patients with femoropopliteal ISR.

Regarding the correlation of reocclusion with Tosaka classification, it was noticed that reocclusion is more common in class III than in other groups (00, 20, and 80% in classes I, II, and III, respectively, in DCB group, whereas in the plain balloon group, it was 14.3, 14.3, and 71.4% in classes I, II, and III, respectively. Liistro *et al.* [20] had confirmed that in Tosaka class III, DCB treatment was independently associated with recurrent ISR, and therefore, class III lesions treated with DCBs only without adjuvant modalities are exposed to four-times higher risk of reocclusion and therefore, they preferred its use in combination with atherectomy devices.

In short lesions, TLR was recorded in two (28.6%) patients of the plain balloon group, whereas in the DCB group, no cases were reported. In long lesions, four cases developed TLR [two (18.2%) cases of DCB group and two (40%) cases of plain balloon group]. Analysis of these data revealed that DCB was highly efficient in short lesions compared with long lesions (*P*Ë,0.05). These results were matched with the DEBATE-ISR study [20] on long lesions, which reported TLR incidence of 13.6% in the DCB group compared with 31.0% in the plain balloon group, with insignificant statistical value (*P*=0.045).

The concept of stent-in-stent technique achieves an immediate success rate in spite of several drawbacks. Deployment of noncovered stent followed by balloon angioplasty will lead to compression of the neointimal tissue and redistributes it again along the stent struts and, therefore, stimulates a new process of intimal growth. Yang *et al.* [24] had reported that additional stenting in a stent failure will add nothing, rather it increases the risk of stent fracture and thrombosis. In this series, stent-in-stent implantation was not preferable as it would leave more metal behind. Therefore, it was performed in only two cases as a bail-out procedure because of occurrence of flow-limiting dissection in one patient and significant residual stenosis in the other. Kim and Choi [4] agreed with this concept but they preferred DES instead of self-expandable stents. On the contrary, Katsanos *et al.* [25] stated that DES results are not preferable as they are not of great variance.

Covered stent grafts are considered a valuable option in ISR and have several advantages over BMS, such as highly flexible, withstand the forces applied by the previous deployed stent, and prevent the risk of neointimal growth and the risk of in-stent thrombosis [26]. The Reline study [27] had evaluated the Viabahn stent graft in long lesions and reported high 1-year patency rate (74.8%). Regarding the long-term results, the VIBRANT trial [28] evaluated 3-year follow-up and reported no significant difference in TLR between Viabahn stent and BMS. No covered stents were used in this study. One step back to bypass surgery which is the traditional treatment option of femoropopliteal occlusive disease. Comparing bypass surgery to DCB angioplasty in ISR showed that recurrent stenosis occurs too frequently with DCB, and this is not a 'one and done' therapy like the successful bypass surgery [5]. Unfortunately, surgical intervention does not provide favorable results. Nolan *et al.* [29] had reported that bypass surgery for ISR has a poor outcome because repeated endovascular re-interventions will lead to decreased distal run-off vessels. Moreover, the BASIL trial [30] demonstrated that patients who underwent bypass surgery after failed angioplasty had a lower

limb salvage rate compared with those who underwent bypass surgery first.

Treatment options for management of ISR are numerous but there is no ideal strategy for its treatment allowing the operators to make their best decision [5]. Currently available algorithms for management are unclear. Virga *et al.* [32] preferred the DCB in complex lesions and diabetic patients, but the need of long-term results remains fundamental. Others [33] suggest that DCB angioplasty provides nothing, especially to patients with occlusive lesions. Finally, Ho and Christopher [2] appreciated DCB angioplasty for focal ISR (class I) and covered stent for diffuse or long ISR lesions (class II) and debulking strategies with DES for occlusive lesions (class III).

Conclusion

DCB angioplasty offers an effective outcome in the management of femoropopliteal ISR, especially in short lesions. However, in long lesions, it yields higher but insignificant results compared with plain balloon angioplasty. Long-term results of management of ISR in long lesions are awaited irrespective of the technology used.

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Conflicts of interest

Nothing to declare.

References

1 Fowkes FG, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet 2013; 382:1329.

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

3 Cao S, He T, Xie J, *et al*. Drug-coated balloon angioplasty versus balloon angioplasty for treating patients with in-stent restenosis in the femoropopliteal artery: a meta-analysis. Medicine (Baltimore) 2021; 100:e25599.

4 Kim W, Choi D. Treatment of femoropopliteal artery in-stent restenosis. Korean Circ J 2018; 48:191–197.

5 Gray BH, Buchan JA. The treatment of superficial femoral artery in-stent restenosis. The jury is still out. JACC Cardiovasc Interv 2016; 9:1393–1396.

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

7 Micari A, Cioppa A, Vadalà G, Castriota F, Liso A, Marchese A. 2-year results of paclitaxel-eluting balloons for femoropopliteal artery disease: evidence from a multicenter registry. JACC Cardiovasc Interv 2013; 6:282–289.

8 Herten M, Torsello GB, Schonefeld E, Imm B, Osada N, Stahlhoff S. Drug-eluting balloons for femoropopliteal lesions show better performance in de novo stenosis or occlusion than in restenosis. J Vasc Surg 2015; 61:394–399.

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

10 Zeller T, Dake MD, Tepe G, Brechtel K, Noory E, Beschorner U. Treatment of femoropopliteal in-stent restenosis with paclitaxel-eluting stents. JACC Cardiovasc Interv 2013; 6:274–281.

11 Tepe G, Schroeder H, Albrecht T, Reimer P, Diehm N, Baeriswyl J. Paclitaxel-coated balloon vs uncoated balloon angioplasty for treatment of in-stent restenosis in the superficial femoral and popliteal arteries: the COPA CABANA trial. J Endovasc Ther 2020; 27:276–286.

12 Laird JR, Katzen BT, Scheinert D, Johannes Lammer J, Carpenter J, Buchbinder M. Nitinol stent implantation versus balloon angioplasty for lesions in the superficial femoral artery and proximal popliteal artery: twelve-month results from the RESILIENT randomized trial. Circ Cardiovasc Interv 2010; 3:267–276.

13 Conte MS, Pomposelli FB, Clair DG, Geraghty PJ, McKinsey JF, Mills JL. Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: management of asymptomatic disease and claudication. J Vasc Surg 2015; 61:1S.

14 Gerhard-Herman M, Gardin JM, Jaff M, *et al*. Guidelines for noninvasive vascular laboratory testing: a report from the American Society of Echocardiography and the Society of Vascular Medicine and Biology. J Am Soc Echocardiogr 2006; 19:955–972.

15 Milewski K, Afari ME, Tellez A, Aboodi MS, Kim JS, Cheng Y. Evaluation of efficacy and dose response of different paclitaxel-coated balloon formulations in a novel swine model of iliofemoral in-stent restenosis. JACC Cardiovasc Interv 2012; 5:1081–1088.

16 Krankenberg H, Tubler T, Ingwersen M, Schlüter M, Scheinert D, Blessing E. 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.

17 Liao CJ, Song SH, Li T, Zhang Y, Zhang W. Randomized controlled trial of orchid drug-coated balloon versus standard percutaneous transluminal angioplasty for treatment of femoropopliteal artery in-stent restenosis. Int Angiol 2019; 38:365–371.

18 Ott I, Cassese S, Groha P, Steppich B, Voll F, Hadamitzky M. ISAR-PEBIS (paclitaxel-eluting balloon versus conventional balloon angioplasty for in-stent restenosis of superficial femoral artery): a randomized trial. J Am Heart Assoc 2017; 6:e006321.

19 Kinstner CM, Lammer J, Willfort-Ehringer A, Matzek W, Gschwandtner M, Javor D. Paclitaxel-eluting balloon versus standard balloon angioplasty in in-stent restenosis of the superficial femoral and proximal popliteal artery: 1-year results of the PACUBA trial. JACC Cardiovasc Interv 2016; 9:1386–1392.

20 Liistro F, Angioli P, Porto I, Ricci L, Ducci K, Grotti S. Paclitaxel-eluting balloon vs. standard angioplasty to reduce recurrent restenosis in diabetic patients with in-stent restenosis of the superficial femoral and proximal popliteal arteries: the DEBATE-ISR study. J Endovasc Ther 2014; 21:1–8.

21 Scheinert D, Duda S, Zeller T, Krankenberg H, Ricke J, Bosiers M. The LEVANT I (Lutonix paclitaxel-coated balloon for the prevention of femoropopliteal restenosis) trial for femoropopliteal revascularization: first-inhuman randomized trial of low-dose drug-coated balloon versus uncoated balloon angioplasty. JACC Cardiovasc Interv 2014; 7:10–19.

22 Cassese S, Wolf F, Ingwersen M, Kinstner CM, Fusaro M, Ndrepepa G. Drug-coated balloon angioplasty for femoropopliteal in-stent restenosis. Circ Cardiovasc Interv 2018; 11:e007055.

23 Aboyans V, Ricco JB, Bartelink MLEL, Björck M, Brodmann M, Cohnert T. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2018; 39: 763–816.

24 Yang X, Lu X, Li W, Huang Y, Huang X, Lu M. Endovascular treatment for symptomatic stent failures in long-segment chronic total occlusion of femoropopliteal arteries. J Vasc Surg 2014; 60:362–368.

25 Katsanos K, Spiliopoulos S, Karunanithy N, Krokidis M, Sabharwal T, Taylor P. Bayesian network meta-analysis of nitinol stents, covered stents, drug-eluting stents, and drug-coated balloons in the femoropopliteal artery. J Vasc Surg 2014; 59:1123–1133.

26 Monahan TS, Vartanian S, Schneider DB. Effective treatment of femoropopliteal in-stent restenosis with stent grafts. J Vasc Surg 2011; 54:917–918.

27 Bosiers M, Deloose K, Callaert J, Verbist J, Hendriks J, Lauwers P. Superiority of stentgrafts for in-stent restenosis in the superficial femoral artery: twelve-month results from a multicenter randomized trial. J Endovasc Ther 2015; 22:1–10.

28 Geraghty PJ, Mewissen MW, Jaff MR, Ansel GM, Investigators V. Three-year results of the VIBRANT trial of VIABAHN endoprosthesis versus bare nitinol stent implantation for complex superficial femoral artery occlusive disease. J Vasc Surg 2013; 58:386–395.

29 Nolan BW, De Martino RR, Stone DH, Schanzer A, Goodney PP, Walsh DW. Prior failed ipsilateral percutaneous endovascular intervention in patients with critical limb ischemia predicts poor outcome after lower extremity bypass. J Vasc Surg 2011; 54:730–735.

30 Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: analysis of amputation free and overall survival by treatment received. J Vasc Surg. 2010; 51:18S–31S.

31 Grotti S, Liistro F, Angioli P, Ducci K, Falsini G, Porto I, *et al*. 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.

32 Virga V, Stabile E, Biamino G, Salemme L, Cioppa A, Giugliano G. Drug eluting balloons for the treatment of the superficial femoral artery in-stent restenosis: 2-year follow-up. JACC Cardiovasc Interv 2014; 7:411–415.