

Original Research Article

Drug-coated balloons versus 1ry stenting for TASC C and D femoropopliteal lesions

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ABSTRACT

Background: To compare the effectiveness and outcome of Drug-Coated Balloon (DCB) versus primary nitinol stenting for the treatment of long femoropopliteal lesions (TASC II C and D).

Methods: This was retrospective study along 3 years included all the cases of femoropopliteal disease TASC C and D that was treated with DEB or primary stenting. The safety endpoint was 30-day free from major limb amputation and mortality. The primary end point was primary patency and freedom from clinically driven target lesion revascularization at 6 and 12 months, patient genders, demographics, co-morbidities, smoking history, indications for intervention were recorded.

Results: PTA and post-dilation with paclitaxel-eluting balloons was done in 32 patients (group I) and 1ry stenting was done in 30 patients (group II) with either stenosis or occlusion. The mean lesion length was 18.43 ± 2 cm in group I and 18.8 ± 2.32 cm in group. The technical success rate was 100% in group II and 93.7% in group I. 6 months and 12-month patency rate for group I and II were 93.3% vs. 93.3% and 83.3% vs. 86.6%, respectively. There were no 30 days related major amputations or mortalities in either group.

Conclusions: DCB for long femoropopliteal lesions showed a comparable result to primary stenting and provide durable results and lower incidence of target revascularization in patients with TASC C and D lesions.

Keywords: DCB, Femoropopliteal lesions, Nitinol stent, Paclitaxel

INTRODUCTION

During the last few years, the treatment of SFA occlusive disease has undergone a shift in management within these paradigms to include more aggressive endoluminal therapy.¹

More than 50% of all Peripheral Artery Disease (PAD) cases affect the SFA and popliteal artery (PA). The unique slow-flow and high resistance environment in the femoropopliteal region creates a milieu that seems to increase the prevalence of de novo disease.² Endovascular intervention has evolved as the primary mode of

revascularization for femoropopliteal peripheral artery disease. Multiple modalities of treatment exist; however, the mainstay is percutaneous transluminal angioplasty (PTA) and implantation of a Bare Metal Stent (BMS). However, angioplasty has been associated with restenosis rate of up to 60% at 12 months.³

Although implantation of a BMS has been shown to reduce this restenosis rate by nearly half.^{3,4} BMSs are associated with inherent problems, including in-stent restenosis, thrombosis, and stent fracture.⁵ Given these challenges, an effective “leave nothing behind” treatment strategy that avoid the use of metallic implants while

preserving future therapeutic options is attractive. To overcome the limitations of standard interventions such as PTA or BMSs, Drug-Coated Balloons (DCBs) were developed in hopes of improved patency over the long term without the disadvantages of a major metal implant such as a stent.⁶

The sustained presence of paclitaxel provides continuous antiproliferative activity that inhibits neointimal hyperplasia, which is a major contributing factor to restenosis after angioplasty.⁷

In recent years, the use of Drug-Coated Balloons (DCB) in femoropopliteal lesions has become widespread. To date, randomized clinical trials have demonstrated superior patency with DCBs compared to PTA.^{8,9} However, these studies were limited to patients with short and intermediate lesions defined as Transatlantic Inter-Society Consensus (TASC) A or B lesions.¹⁰

The aim of this study was to evaluate the long-term safety and effectiveness of endovascular recanalization with a paclitaxel DCB versus self-expanding nitinol stent in patients with TASC C and D femoropopliteal lesions.

METHODS

This was a retrospective study of 2 centers study conducted on 62 patients presenting mainly to the vascular and endovascular department in this hospital along three years. All patients presenting with long femoropopliteal occlusive disease with either stenosis and/or occlusion PTA and post-dilation with paclitaxel-eluting balloons was done for 32 cases and 1ry stenting was done for 30 cases.

Patient gender, demographics, presence of comorbidities, history of smoking, presentation and indication for intervention were recorded. The procedure, possible complications were explained to the patients and an informed consent was obtained.

The methodology done by clinical assessment includes history taking and clinical examination was done for all patients and was classified according to Rutherford classification, pre-procedural investigations include routine laboratory tests such as complete blood picture, kidney and liver function tests, coagulation profile and blood glucose level, lipid profile and also includes ECG, Echocardiography in which arterial imaging was done using either duplex or CT angiography or both.

Patient having incapacitating claudication or critical limb ischemia (rest pain or gangrene) with long femoropopliteal lesions more than 15cm with lesions ranged in complexity from TASC C to D and at least one patent distal run off was included in this study.

Patients with non-atherosclerotic lesions, patients with failure of crossing the lesion and those who need open

surgery, patients with restenosis or occluded graft, lesions less than 15cm TASC A and B, patients with renal impairment and intolerance contrast agents, patients who needed stenting after DCB were excluded from comparison.

All endovascular procedures were done in the angiosuite and hybrid room under local anesthesia. For every patient in each group, the data recorded were location and length of the lesion, size of the balloon and stent used, inflow or outflow angioplasty, quality of distal runoff and complications.

Stent length was selected to cover the lesion and at least 5mm of lesion-free proximal and distal vessel. The overlap zone was at least 10mm if >1 stent was used. Post dilation was done if the stent was under expanded.

Procedural outcome and follow up

Group I: After crossing the lesion with a guidewire, predilatation was done in all cases with POBA (30 lesions) followed with drug coated balloon author used lutonix (2µg/mm², bard, wexford, Ireland), if more than 1 balloon was used the overlap zone was not less than 10mm. The inflation time of the DCBs was 3minutes with nominal pressure to allow full drug delivery. Bailout bare metal stents were used in cases of suboptimal angiographic result with residual stenosis of >50% or flow-limiting dissection after prolonged dilation for 3min.

Group II: Technical success was considered to occur when less than 30% residual stenosis was obtained.

Clinical success was considered to occur with regaining of pulse, revascularization warmth and disappearance of rest pain and good healing of ulcer or minor amputation.

All patients received loading dose of 300mg clopidogrel before the procedure. 5,000units Unfractionated heparin was administered during the procedure. Aspirin was given for life in all patients and clopidogrel was used for 3months. All patient was followed up clinically and CT angio if needed for 12 months at regular visits at 3,6 and 12 months.

The primary end point was the primary patency at 3, 6, and 12 months the target lesion revascularization (CD-TLR) was defined as reinterventions performed for recurrent clinical symptoms after the procedure within 5mm of the target lesion after significant stenosis or occlusion.

RESULTS

Total 62 patients with long femoropopliteal lesions underwent endovascular revascularization with PTA and post-dilation with paclitaxel-eluting balloons was done for 32 patient (group I) with average length lesion 18.43±2cm and 1ry stenting was done for 30 patients

(group II) average length lesion $18.8\text{cm} \pm 2.32\text{cm}$. There was no statistical difference between demographic data and risk factors in both groups (Table 1).

Table 1: Demographic features of the patients.

	Group I	Group II	P value
Age (mean $\pm$ SD)	64 $\pm$ 8.57	65.8 $\pm$ 8.93	0.43
Male	34.3%	23.3%	0.40
Smoking	43.7%	70%	0.19
Diabetes	100%	100%	
Hypertension	50%	56.7%	0.39
Hyperlipidemia	31.5%	43.3%	0.23

In group I, 7 patients presented with incapacitating claudication (21.9%). 12 patients presented by rest pain (37.5%) Rutherford 4, 4 patients presented by non-healing ulcer (12.5%) Rutherford 5 and 9 patients presented by gangrene (28.1%) Rutherford 5.

In group II, 7 patients presented with incapacitating claudication (23.3%). 10 patients presented by rest pain (33.3%) Rutherford 4, 3 patients presented by non-healing ulcer (10%) Rutherford 5 and 10 patients presented by gangrene (33.3%) Rutherford 5 (Table 2).

Table 2: Clinical presentation of the patients.

Rutherford(R) classification	Group I	Group II	P value
R3	22 %	23 %	0.94
R4	35%	33 %	0.94
R5	33 %	35 %	0.95
R6	10%	9%	0.50

The lesions described that lesion characteristics were similar between two groups with no statistical difference between two groups Table 3.

Table 3: Lesion characteristics of the patients.

Lesion characteristics	Group I	Group II	P value
TASC C	59.4%	53.3%	0.41
TASC D	40.6%	46.74%	0.40
Popliteal artery involvement	15.6%	20%	0.50
Lesion length (mean $\pm$ SD)	18.43 $\pm$ 2	18.8 $\pm$ 2.32	0.41
Occlusion	71.9%	63.3%	0.31
Severe calcification	37.5%	23.3%	0.17
Intraluminal passage	62.5%	56.7%	0.4
Subintimal passage	37.5%	43.3%	0.3
Single tibial runoff	12.5%	10%	0.9
two tibial run-offs	59.4%	63.3%	0.4
Three tibial run-offs	28.1%	26.7%	0.3

Bailout stenting was done in two patients in group 1 due to flow limiting dissection and these two patients were removed from 1ry end point and patency rates. The procedural data: Antegrade approach was used in all patients using 6 French (6f) sheath. Crossing the lesion was done using terumo 0.035inch wire and vertebral catheter in all patients.

GROUP I: Ipsilateral in 17/30 (56.7%) and contralateral in: 13/30 (43.3%). Intraluminal passage of the wire was used in 20 cases (62.5%) while subintimal route was used in 12 cases (37.5%). The balloon diameter ranged from 4-7mm and balloon length ranged between 50 and 150mm.

GROUP II: Ipsilateral in 20/30 (66.7%) and contralateral in: 10/30 (33.3%). Intraluminal passage of the wire was used in 17 cases (56.7%) while subintimal route was used in 13 cases (43.3%). 1ry stenting with self-expandable nitinol stent with trial of PTA before decision to stent. 2 stents in 29/30 (96.7%) cases, 3 stents in 1/30 (3.3%) cases. In all patients, diameter was 5mm in 10 patients and 20 patients had 6mm stents and stent length was 40mm in one case, 80mm in 10 case, 100mm in 15 cases and 150mm in 4 cases.

Follow up of the studied patients immediately after 3, 6 and 12months: safety endpoint was defined as 30days free from procedure or device-related mortality or major amputations which was achieved in both group with no mortality or major amputation.

Procedural technical success was achieved in 100% of both groups with 1ry patency, CD TLR and major amputation were reported at 3,6 and 12months follow up (Table 4).

Table 4: 12 months follow up of the patients.

Outcome	Group I	Group II	P value
Primary patency	25 (83.3%)	26 (86.7%)	0.50
TLR	2 (6.7%)	2 (6.7%)	
Major amputation	1 (3.3%)	1 (3.3%)	

The 12months outcomes after DCB group showed that the incidence of restenosis was comparable to stenting groups. The patency rate and freedom from re-intervention and TLR in group I were comparable group II (83.3% vs. 86.6% and 93.3% vs. 93.3%.

Major below knee amputation was done in 1 patient (3.3%) in group I due to extensive infection and 1 patient (3.3%) in group II with poor runoff due to progression of tibial disease at 12months. Relationship between risk factors and 1ry end point: In both groups, no significant correlation was found between sex, risk factors and patency rate and free from TLR (Table 5).

Relationship between Rutherford presentation and 1ry end point. In both groups the 12months strong correlation were found between incidence of restenosis and CDTLR

and patients with critical limb ischemia denoting severity of the disease but this correlation were not statistically significant. Relationship between lesions characteristic and 1ry end point: In both groups, the 12 months strong correlation were found between incidence of restenosis

and CDTLR and patients with total occlusion in the presence of severe calcification, subintimal crossing of the lesion and with low runoff vessels but this correlation were not statistically significant (Table 6).

Table 5: Relationship between risk factors and 12 months primary patency rate (PPR) and target lesion revascularization (TLR).

Risk factors (NO)	Group I		P-value	Group II		P-value
	PPR (%)	TLR (%)		PPR (%)	TLR (%)	
Smoking (14)	85.7	0	0.27	88.9	11.1	0.5
Diabetic (30)	83.3	6.6		86.7	6.6	1
Hyperlipidemic (16)	81.3	6.2	0.72	82.4	5.9	0.6
HTN (10)	80	12.5	0.56	84.6	7.7	0.68

Table 6: Relationship between lesions characteristic and 12 months primary patency rate (PPR) and target lesion revascularization (TLR).

Lesion characteristics	Group I				Group II			
	PPR	P value	TLR	P value	PPR	P value	TLR	P value
TASC C (n=17)	88.2%	0.36	0%	0.17	100%	0.24	0%	0.20
TASC D (n=13)	76.9%	0.36	15.4%	0.17	78.6%	0.24	14.3%	0.20
SFA (n=25)	92%	0.18	4%	0.31	87.5%	0.61	8.3%	0.63
SFA and POP (n=5)	60%	0.18	20%	0.31	83.3%	0.61	0%	0.63
Stenosis (n=9)	88.9%	0.52	0%	0.48	100%	0.14	0%	0.39
Occlusion (n=21)	73.9%	0.52	9.5%	0.48	78.9%	0.14	10.6%	0.39
Intraluminal (n=20)	85%	0.55	0%	0.10	94.1%	0.59	0%	0.17
Subintimal (n=10)	100%	0.55	20%	0.10	77%	0.59	15.4%	0.17
One tibial runoff (n=4)	25%	0.003	50%	0.001	66.7%	0.55	0%	0.70
Two runoff (n=18)	94.4%	0.012	0%	0.010	89.5%	0.62	5.3%	0.66
Three runoff (n=8)	87.5%	0.038	0%	0.008	87.5%	0.54	12.5%	0.41

DISCUSSION

The present study was done on 62 patients. 32 patients were managed PTA and post-dilation with paclitaxel-eluting balloons and 30 patients were managed with 1ry stenting for long femoropopliteal occlusive disease with either stenosis and/or occlusion that fulfilled the selection criteria. According to the Trans-Atlantic Inter-Society Consensus (TASC) classification, all patients (62) were TASC type C and D lesions.

This study was undertaken to determine whether the addition of paclitaxel to PTA of the SFA and popliteal artery was comparable to 1ry nitinol stent in long femoropopliteal occlusive disease and avoid leaving metallic implant behind with increase the potential for restenosis, thrombosis or fracture. So far, no randomized, controlled trials have compared DCBs with stents in long, TASC C and D femoropopliteal lesions. In stent restenosis was determined by neointimal hyperplasia of smooth muscle cells, to reduce neointima formation, it is

necessary to arrest smooth muscle cell proliferation and migration.¹¹ Local delivery of paclitaxel in the arterial wall impairs normal microtubule and cytoskeleton arrangement, prevent neointimal hyperplasia by inhibiting smooth muscle cell migration and proliferation.¹²

Early results using the IN. PACT DCB in 39 femoropopliteal ISR lesions with a mean lesion length of 83mm were favorable with a 12month primary patency rate of 92%. While in this study, 30 (100%) at 3months for DCB 30 (100%) at 3months for stent group, 28 (93.3%) at 6months for DCB 29 (96.7%) at 6months for stent group, 25 (83.3%) at 12months for DCB, 26 (86.7%) at 12months for stent group while the lack of head to-head data makes it difficult to directly compare technologies, the reported patency rates in this study were comparable or superior to published studies of nitinol stents for similar lesion lengths (49% to 55%).¹³⁻¹⁵

In a study by Schmidt A et al, there 1-year primary patency rate was 78.2% in femoropopliteal lesions with a mean lesion length of 24cm while in DCB group patency were more promising (83.3%) and average lesion length was 18.43 ± 2 .¹⁵

Several patient and lesion characteristics were associated with reduced patency rates including diabetes, obesity, heavy calcification, treatment of the popliteal segment, and female sex.¹⁵ Smokers had less restenosis, a phenomenon that has been previously observed after femoropopliteal interventions.¹⁶ This was confirmed that female sex and diabetes and hypertension and hyperlipidemia in both DCB and stent groups had lower patency rates after 12months. Smokers on the other hand had higher patency in the DCB group but lower patency in the stent group. Severe calcification has been postulated before to reduce the anti-restenosis effect of DCB in the femoropopliteal segment, which was evident in this study (63%) compared to stenting (71%) as calcification may interfere with the transfer and deposition of paclitaxel, which was necessary to suppress restenosis.¹⁷

Clinically driven target lesion revascularization rate of 12.7% in recent randomized trial of bare metal tents, despite their inclusion of shorter lesions (average lesion lengths of 7.0) while it was 6.7% in this study which was significantly lower.⁷

CONCLUSION

Overall, the SFA-Long analysis demonstrates that treatment of long atherosclerotic lesions in the femoropopliteal region can be safely and effectively performed with DCBs more than stenting. Further studies incorporating longer follow-up periods will ultimately determine its efficacy.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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