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Peripheral Arterial Occlusive Disease – PAOD

Chronic Femoropopliteal Occlusions: Comparison of Drug-Eluting Balloon Angioplasty with or without Prior Rotational Thrombectomy

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Background: The aim of this study was to compare drug eluting balloon (DEB) angioplasty with and without mechanical thrombectomy system in patients with chronic (> 6 months) femoropopliteal occlusions.

Method: We retrospectively identified patients from May 2012 to September 2014 at our clinic with severely diseased femoropopliteal arteries treated by endovascular approach with or without adjunctive thrombectomy system. All patients had ankle-brachial index (ABI) measured before and after the intervention, and regular clinical follow-up with Doppler ultrasonography performed at 1 month, 6 months and 1 year. Patients underwent peripheral angiography if needed.

Results: Mechanical thrombectomy system (MTS + DEB) was used in 33 patients (31 enrolled 2 patients were lost to follow-up, mean lesion length 149.7mm ± 82.69). The remaining 33 patients were treated without MTS (31 enrolled 2 patients were lost to follow-up DEB N = 31 mean lesion length 157.3 mm ± 92.90). There were 5 restenosis in the MTS + DEB group (83.3% patency rate) and 5 restenosis in the DEB group (82.8% patency rate) at 1 year. The technical success rate was 93.5% in both groups. A statistically significant increase in the ABI (MTS + DEB before 0.47 ± 0.11 vs. after 0.92 ± 0.11 $p < 0.01$ DEB before 0.47 ± 0.11 vs. after 0.90 ± 0.14 $p < 0.01$) and improvement in Rutherford staging ($p < 0.01$) was noted in both groups following intervention.

Conclusions: DEB angioplasty is effective in the treatment of chronic total femoropopliteal occlusions. Combining DEB angioplasty and thrombectomy system does not appear to improve outcomes for treatment of chronic femoropopliteal occlusions.

Key Words: Thrombectomy • Drug eluting balloon • Peripheral arterial disease • Peripheral intervention

INTRODUCTION

Coronary artery disease and peripheral arterial disease (PAD) are major public health and medical concerns in both developed and developing countries.[1] Obstructive disease due to atherosclerosis of the superficial femoral artery (SFA) is the most common cause of intermittent claudication,[2] and atherosclerotic lesions in the SFA may cause critical limb ischemia leading to serious complications such as tissue loss, amputation and even death. Owing to its clinical feasibility and minimally-invasive nature, percutaneous transluminal angioplasty (PTA) has become increasingly popular, and it is usually the first choice of revascularization for patients with PAD.[3,4] The results of balloon angioplasty for complex femoropopliteal disease have been disappointing.[5,6] Several factors negatively affect the long-term results of percutaneous femoropopliteal angioplasty, including the length of the diseased segment, total occlusion, diabetes mellitus, and poor distal runoff.[7] Advances in technology and therapeutic devices for femoropopliteal occlusive lesions over

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the last decade have led to a dramatic increase in the number of SFA obstructions that are amenable to treatment. Drug-eluting balloons (DEBs) and drug-eluting stents are used to inhibit restenosis,[8] and techniques such as retrograde popliteal access have become successful alternatives after failure of the antegrade femoral approach or in cases where it is not suitable.[9,10] The thrombectomy systems has proved its efficiency in the treatment of acute and subacute occlusions, however few studies have investigated its use for the treatment of chronic femoropopliteal occlusions.[11] The main purpose of this study was to compare DEB angioplasty with and without a mechanical thrombectomy system in patients with chronic femoropopliteal (> 6 months) occlusions.

Patient population

This retrospective, single-center study of 62 patients (66 patients were enrolled and four were lost to follow-up) compared endovascular recanalization with and without Mechanical Atherothrombectomy System (MTS) (Figure 1). Primary indications for interventions included claudication and rest pain. The inclusion criteria were: SFA and/or popliteal occlusion above the knee with a vessel diameter of 4-7 mm, and the presence of symptoms of Rutherford stage 2 (< 200 meters) to 6 persisting for > 6 months despite appropriate medical therapy and exercise regimen. All patients at our institution undergo baseline physical examinations with a focus on detecting manifestations of lower limb ischemia, classified according to Rutherford and Becker scales. Patients requiring immediate revascularization (those with acute ischemia) were excluded. The demographic data were similar between the two groups (Table 1).

Statistical analysis

Number Cruncher Statistical System 2007 software (NCSS, Kaysville, Utah, USA) was used for the statistical analysis. Data were reported as mean, standard deviation, median, frequency and ratio. The Student's t test was used for comparisons of normally distributed parameters, and the Mann Whitney U test was used for comparisons of non-normally distributed parameters. Fisher's exact test and Yates' continuity correction test were used for comparisons of qualitative data, and the Wilcoxon signed ranks test was used to test differences between preop and postop values. The log rank test was used to compare patency rate between groups. The results were evaluated using 95% confidence intervals and at a significance level of $p < 0.05$.

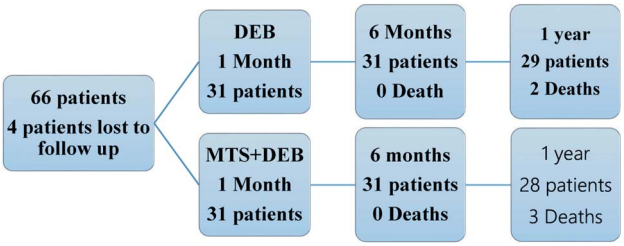


Figure 1. *Study profile.*

METHODS

The study was approved by the Local Ethics Committee. From May 2012 to September 2014, 66 (four patients were lost to follow-up) patients with femoropopliteal chronic total occlusion underwent endovascular recanalization with or without MTS (MTS + DEB N = 31, mean length 149.7 mm; DEB N = 31 mean length 157.3 mm). All of the patients with femoropopliteal chronic total occlusion [patients with either peripheral angiography or ultrasonography (USG) reports showing occlusion > 6 months before our intervention] underwent procedures via an endovascular approach. A retrograde popliteal approach was preferred in 24 patients. Before the proce-

Table 1. Demographics data

Variable	MTS + DEB (n = 31)	DEB (n = 31)	p value
	n (%)	n (%)	
Age (years), mean ± SD	63.23 ± 10.90	59.65 ± 8.72	0.734*
Gender			1.000#
Male	24 (77.4)	23 (74.2)	
Female	7 (22.6)	8 (25.8)	
Diabetes mellitus	24 (77.4)	25 (80.6)	1.000#
Hypertension	25 (80.6)	24 (77.4)	1.000#
Hypercholesterolaemia	18 (58.1)	16 (51.6)	0.799#
Current smoker	29 (93.5)	27 (87.1)	0.671†
Coronary artery disease	20 (64.5)	21 (67.7)	1.000#
End stage renal disease	2 (6.5)	3 (9.7)	1.000#

* Student t Test. # Yates' Continuity Correction Test. † Fisher's Exact Test.

DEB, drug eluting balloon; MTS, mechanical atherothrombectomy system; SD, standard deviation.

dure, all patients underwent preoperative ultrasound evaluations to visualize the extension and morphology of the femoropopliteal lesion. SFA and popliteal artery calcifications were initially evaluated and quantified using Doppler USG, and then with digital subtraction angiography (DSA) before the intervention. The ankle-brachial index was measured before and after the intervention.

The femoral (N = 38) or popliteal (N = 24, MTS + DEB N = 11, DEB N = 13) artery was punctured under ultrasound guidance. After a 6-8F introducer sheath was inserted and diagnostic angiography performed, intravenous heparin (100 μ/kg) was administered. Through a mostly antegrade ipsilateral strategy (61.3%, MTS + DEB N = 20, DEB N = 18), we used a Judkins right catheter (5-6F) with a hydrophilic guide wire to cross the lesions. In the MTS + DEB group, a mechanical thrombectomy system (6F N = 17, 8F N = 14) was used (Figure 2). The standard guide wire in most of the cases was 0.018 inches in diameter. A local injection of contrast agent was given to all patients via an over-the-wire catheter to verify a safe intravascular position. DEB angioplasty was the preferred intervention in both groups. More than one DEB was deployed in long occlusions (> 120 mm), and the ratio of DEB to vessel diameter was planned to be 1:1 (4-7 mm). The overlap zone was at least 5 mm if more than one balloon was used per lesion. The inflation time was three minutes. In cases of flow-limiting dissection or residual stenosis of > 50%, another prolonged dilation of up to three minutes was performed. A self-expandable stent was deployed when the dissection affected the flow or when there was > 50% residual stenosis after DEB angioplasty (Figure 2, 3). A completion angiogram concluded the procedure. Technical success was defined as restoration of direct flow in the target vessel with runoff to the foot and residual stenosis < 50%. Popliteal and femoral access sites were managed with digital pressure. The operative data are summarized in Table 2. The patients with additional below the knee lesions were treated in a different session with DEB angioplasty (MTS N = 3, DEB N = 3) and no bailout stents were needed afterwards. All patients were discharged with three months and were given dual antiplatelet therapy consisting of aspirin (100 mg per day) and clopidogrel (75 mg per day), and then aspirin alone after three months. Appropriate medications for risk factors such as coronary artery disease, hypertension and hyperlipidemia (especially statins) were given after the intervention. Patency during follow-up was evaluated with Doppler USG and angiography when indicated. A peak systolic velocity ratio of 2.5 was the threshold for duplex criteria for binary stenosis. The primary endpoint of this study was restenosis (50% at the narrowest point) or occlusion after one month, six months, and one year.

RESULTS

The median follow-up period in the MTS + DEB group was 14.8 ± 4.4 months including 28 (90.3%) patients with ≥ 12 months of follow-up, compared to 15.1 ± 4.3 months including 29 (93.6%) patients with ≥ 12 months of follow-up in the DEB group. The mean DEB diameter was 5.6 ± 0.88 mm per intervention in the MTS + DEB group (N = 65), compared to 5.6 ± 0.82 mm per inter-

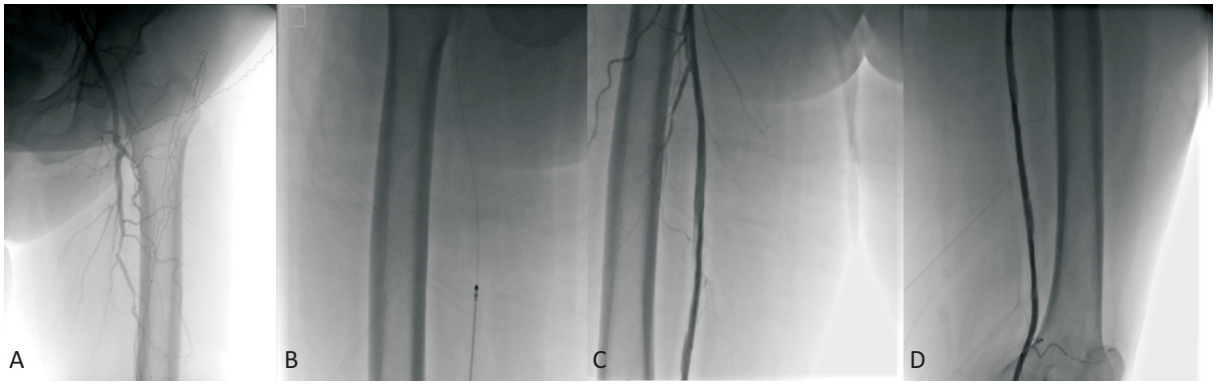


Figure 2. *Pre-interventional angiogram (DSA) of a chronic total occlusion of the SFA (A). Prone Position; Recanalization of the occlusion with a 6F thrombectomy-catheter and angioplasty with a paclitaxel-coated balloon (B). Prone position; Final result after recanalization (C). Peripheral angiography 1 year after (D)*

vention in the DEB group (N = 73). Procedural characteristics, including The Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC) classification of the lesions, are summarized in Table 2. The primary endpoint was restenosis rate at one year. The technical success rate was 93.5% in both groups. Stent implantation was necessary in four patients [two (6.5%) in the MTS + DEB group and two (6.5%) in the DEB group] because of residual stenosis of 50% or dissection affecting flow after DEB angioplasty (Figure 3). After 12 months of follow-up, five patients in the MTS+DEB group (83.3% patency) and five in the DEB group (82.8% patency) had restenosis (Figure 4). These 10 high-grade cases of restenosis were documented by clinical investigations and ultrasound, and repeat angiography was performed in these cases after the diagnosis. All of the patients with restenosis were diabetic except for one, and five continued smoking after the intervention (Table 3). These cases of restenosis were successfully treated by repeat PTA. One pseudoaneurysm was detected in the MTS group (popliteal pseudoaneurysm two months after the intervention detected with USG), and a stent-graft was used to repair it. There were no perforations or amputations. Three cases of access-related hematoma occurred (one in the MTS + DEB group, two in the DEB group), which resolved on digital pressure. There were statistically significant improvements in Rutherford stage (12 months $p < 0.01$) and an-

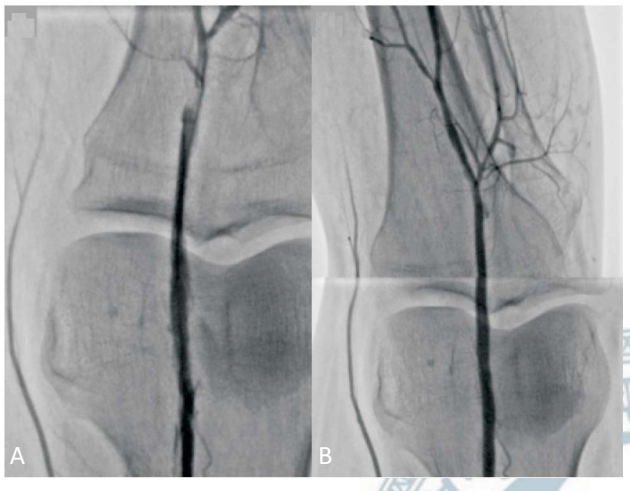


Figure 3. *Dissection affected flow at distal SFA through popliteal artery (A) After self expandable stents deployed dissection treated (B).*

Table 2. Lesion and procedure characteristics

Variable	MTS + DEB (n = 31)	DEB (n = 31)	p value
	n (%)	n (%)	
Mean length (mm), mean ± SD	149.7 ± 82.7	157.3 ± 92.9	0.158*
Total occlusion	31 (100)	31 (100)	-
Stent implantation	2 (6.5)	2 (6.5)	1.000#
Standard balloon performed	2 (6.5)	31 (100)	0.001†
Multiple DEB performed	8 (25.8)	9 (29)	1.000#
Severe calcification	18 (58.1)	16 (51.6)	0.799#
Mean DEB diameter (mm)	5.6 ± 0.82	5.6 ± 0.88	1.000#
Antegrade ipsilateral approach	20 (64.5)	18 (58.0)	0.749#
Retrograde popliteal approach	11 (35.5)	13 (41.9)	0.828#
Subintimal lesion crossing	23 (74.2)	24 (77.4)	1.000#
TASC			1.000#
A	0 (0)	1 (3.2)	
B	6 (19.4)	6 (19.4)	
C	8 (25.8)	7 (22.6)	
D	17 (54.8)	17 (54.8)	
Lesion types			
Denovo	24 (77.4)	25 (80.6)	1.000#
Restenosis	5 (16.1)	4 (12.9)	1.000#
Instent	2 (6.5)	2 (6.5)	1.000#

* Student t Test. # Yates Continuity Correction Test. † Fisher's Exact Test.

DEB, drug eluting balloon; MTS, mechanical atherothrombectomy system; SD, standard deviation; TASC, The Trans-Atlantic Inter-Society Consensus Document.

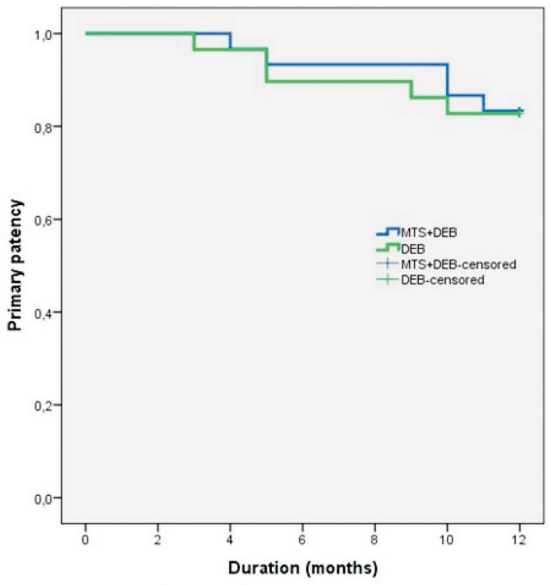
kle-brachial index in both groups (after the intervention before discharge, $p < 0.01$) (Table 4). Overall, five patients died (three in the MTS + DEB group; one due to non-cardiac-related mortality, and two due to acute myocardial infarction, and two in the DEB group; one due to non-cardiac-related mortality, and one due to acute myocardial infarction).

DISCUSSION

The use of DEB and advances in stents and atherectomy have reduced the failure rates of endovascular approaches to femoropopliteal occlusions. Mechanical thrombectomy system is a safe and effective alternative in the treatment of acute or subacute infrainguinal and chronic occlusions (particularly for clinicians with limited experience) of the iliac and femoropopliteal arteries.[11] In this study, we investigated the clinical outcomes of DEB angioplasty in patients with or without prior mechanical thrombectomy system to treat chronic femoropopliteal occlusions.

The aim of the therapeutic approach of current mechanical atherothrombectomy systems is to open a channel, particularly in heavily calcified occlusions, and to remove some of the stenotic material instead of simply using a balloon to compress it against the arterial wall. Atherothrombectomy has the potential to decrease plaque burden, and thus it has been suggested to be suitable for the treatment of heavily calcified plaques. Endovascular atherothrombectomy should be considered as a treatment option for shorter complex calcified lesions in smaller vessels.[12,13] It is not possible to penetrate deep into smaller arteries with the mechanical thrombectomy system, and this may be one of the reasons why the system did not improve the outcomes in the MTS group in the present study.

Primary patency rates with older atherectomy devices have been disappointing, and consequently atherectomy has fallen out of favor.[14] With the advent of newer and better devices that have shown promising mid-term patency rates and low complication rates,



MTS+DEB	n	30	30	30	28	28	28	25
	SE	*0,00*	*0,00*	*0,05*	*0,05*	*0,05*	*0,07*	*0,07*
DEB	n	29	29	28	26	26	25	24
	SE	*0,00*	*0,03*	*0,06*	*0,06*	*0,06*	*0,07*	*0,07*

Figure 4. *Patency rate in both groups. DEB, drug eluting balloon; MTS, mechanical atherothrombectomy system.*

Table 3. Restenosis patients characteristics

Restenosis patients	DM	Continued smoking	Instent restenosis	Lesion length > 150 mm	MTS + DEB	DEB	HT
Patient 1	+	+	-	+	-	+	+
Patient 2	+	-	-	+	-	+	+
Patient 3	+	+	-	+	-	+	-
Patient 4	+	+	-	-	-	+	-
Patient 5	+	-	-	+	+	-	-
Patient 6	+	+	-	+	+	-	+
Patient 7	+	-	-	+	+	-	+
Patient 8	+	-	-	-	-	+	-
Patient 9	-	+	-	-	+	-	-
Patient 10	+	-	-	+	+	-	+

DEB, drug eluting balloon; DM, diabetes mellitus; HT, hypertension; MTS, mechanical atherothrombectomy system.

Table 4. Clinical and hemodynamic improvement

	MTS + DEB	DEB	p value
ABI Index			
Before procedure	0.47 ± 0.11 (0.44)	0.47 ± 0.11 (0.44)	0.641
After procedure	0.92 ± 0.11 (0.93)	0.90 ± 0.14 (0.92)	0.761
	p 0.001**	p 0.001**	
Difference	0.45 ± 0.15 (0.47)	0.43 ± 0.16 (0.43)	0.517
Preop Rutherford Becker Classification			
0,1	0 (0)	0 (0)	
2,3	19 (61.3)	21 (67.7)	
4,6	12 (38.7)	10 (32.3)	
12 months follow up Rutherford Becker Classification	22 (78.6)	22 (75.9)	
0,1			
2,3	6 (21.4)	7 (24.1)	
4,6	0 (0)	0 (0)	
	p 0.001**	p 0.001**	

ABI, ankle-brachial index; DEB, drug eluting balloon; MTS, mechanical atherothrombectomy system.

there has been a resurgence in interest on the use of atherectomy and thrombectomy as a primary modality of treatment for PAD. The one-year patency rate in this study is comparable to other studies with newer atherectomy and thrombectomy devices, however treatment with the thrombectomy system before DEB angioplasty did not appear to improve the outcomes of the treatment of femoropopliteal chronic total occlusions (MTS + DEB group 83.3% patency rate; DEB group 82.8% patency rate).[15,16] However, the studies with other atherectomy and thrombectomy devices were performed before DEBs were used in PAD and did not include a control group. Instead of using an adjunctive thrombectomy system in all patients irrespective of calcification of the lesions in the MTS group, we should have used this system for heavily calcified lesions to examine the benefits in terms of patency rate.[17,18]

Restenosis rates have been reported to range from 18% to 54% after mechanical atherothrombectomy in acute and subacute occlusions of the femoropopliteal artery.[19,20] In addition, a previous study reported a 6-month restenosis rate of 6.9% after the use of the mechanical thrombectomy system and DEBs.[20] Therefore we compared 1-year outcomes of DEB angioplasty for chronic femoropopliteal occlusions in patients with or without prior mechanical thrombectomy system to examine whether the use of atherectomy before DEB angioplasty influences these high patency rates.

The main indications for the retrograde popliteal approach are a short SFA stump, flush occlusion or tandem common femoral artery (CFA) involvement with SFA lesions, and failure of the antegrade approach.[9] Recanalization may be more successful when the occlusion is approached from the distal end, since the thrombus here is less fibrotic and calcified.[21] Because of these advantages and our experience with the retrograde popliteal artery approach, we used this approach in 24 patients (38.7%).

Limitations

The number of patients and 1-year follow-up period were inadequate to allow for statistically significant differences to be detected between the two groups. The bail-out stent deployment rate was the same in both groups (N = 2 in both groups), and no restenosis was noted in any of these patients. Neither intravascular ultrasonography nor axial computed tomography was performed before or during the procedure, and thus quantitative angiographic data and differences in lumen gains with or without debulking were not available.

CONCLUSIONS

DEB angioplasty is effective for the treatment of chronic total femoropopliteal occlusions. Combining DEB angioplasty and mechanical thrombectomy system did not appear to improve outcomes with regards to treatment of chronic femoropopliteal occlusions. Further studies with a longer follow-up time and larger population are needed to evaluate the efficacy, safety

and cost-effectiveness of atherectomy in chronic total femoropopliteal occlusions.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest.

SUPPLEMENTARY MATERIALS

Research materials can be accessed through hospital pax center and archives.

REFERENCES

1. Sung SH, Chen TC, Cheng HM, et al. Comparison of clinical outcomes in patients undergoing coronary intervention with drug-eluting stents or bare-metal stents: a nationwide population study. *Acta Cardiol Sin* 2017;33:10-9.
2. White C. Clinical practice. Intermittent claudication. *N Engl J Med* 2007;356:1241-50.
3. Chen IC, Yu CC, Wu YH, Chao TH. Elevated neutrophil-to-lymphocyte ratio predicts intermediate-term outcomes in patients who have advanced chronic kidney disease with peripheral artery disease receiving percutaneous transluminal angioplasty. *Acta Cardiol Sin* 2016;32:532-41.
4. Norgren L, Hiatt WR, Dormandy JA, et al.; TASC II Working Group. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007;45(Suppl S):S5-67.
5. Dorrucci V. Treatment of superficial femoral artery occlusive disease. *J Cardiovasc Surg (Torino)* 2004;45:193-201.
6. Jeans WD, Armstrong S, Cole SE, et al. Fate of patients undergoing transluminal angioplasty for lower-limb ischemia. *Radiology* 1990;177:559-64.
7. Capek P, McLean GK, Berkowitz HD. Femoropopliteal angioplasty: factors influencing long-term success. *Circulation* 1991; 83(suppl I):I-70-80.
8. Zeller T, Rastan A, Macharzina R, et al. Drug-coated balloons vs. drug-eluting stents for treatment of long femoropopliteal lesions. *J Endovasc Ther* 2014;21:359-68.
9. Brountzos EN, Moulakakis KG, Avgerinos ED, et al. Retrograde transpopliteal approach of iliofemoral lesions. *Vasc Endovascular Surg* 2011;45:646-50.
10. Schmidt A, Bausback Y, Piorkowski M, et al. Retrograde recanalization technique for use after failed antegrade angioplasty in chronic femoral artery occlusions. *J Endovasc Ther* 2012;19:23-9.
11. Freitas B, Steiner S, Bausback Y, et al. Rotarex mechanical debulking in acute and subacute arterial lesions: single-center experience with 525 patients. *Angiology* 2016;68:233-41.
12. Zeller T, Rastan A, Schwarzwälder U, et al. Midterm results after atherectomy-assisted angioplasty of below-knee arteries with use of the Silverhawk device. *J Vasc Interv Radiol* 2004;15: 1391-7.
13. Henry M, Henry I. *Percutaneous Peripheral Atherectomy Using the Rotablator.* In: Richard R Heuser, Michel Henry editor(s). Textbook of Peripheral Vascular Interventions Chapter 16. London and New York: Martin Dunitz Ltd, 2004:107-19.
14. The Collaborative Rotablator Atherectomy Group (CRAG). Peripheral atherectomy with the rotablator: a multicenter report. *J Vasc Surg* 1994;19:509-15.
15. Ramaiah V, Gammon R, Kiesz S, et al.; TALON Registry. Midterm outcomes from the TALON Registry: treating peripherals with SilverHawk: outcomes collection. *J Endovasc Ther* 2006;13:592-602.
16. Zeller T, Krankenberg H, Steinkamp H, et al. One-year outcome of percutaneous rotational atherectomy with aspiration in infrainguinal peripheral arterial occlusive disease: the multicenter pathway PVD trial. *J Endovasc Ther* 2009;16:653-62.
17. Spaargaren GJ, Lee MJ, Reekers JA, et al. Evaluation of a new balloon catheter for difficult calcified lesions in infrainguinal arterialdisease: outcome of a multicenter registry. *Cardiovasc Intervent Radiol* 2009;32:132-5.
18. Minko P, Katoh M, Jaeger S, Buecker A. Atherectomy of heavily calcified femoropopliteal stenotic lesions. *J Vasc Interv Radiol* 2011;22:995-1000.
19. Wissgott C, Kamusella P, Andresen R. Treatment of in-stent reocclusions of femoropopliteal arteries with mechanical rotational catheters. *Fortschr Röntgenstr* 2011;183:939-44.
20. Scheer F, Lüdtke CW, Kamusella P, et al. Combination of rotational atherothrombectomy and paclitaxel-coated angioplasty for femoropopliteal occlusion. *Clin Med Insights Cardiol* 2014;8: 43-8.
21. Fanelli F, Lucatelli P, Allegritti M, et al. Retrograde popliteal access in the supine patient for recanalization of the superficial femoral artery: initial results. *J Endovasc Ther* 2011;18:503-9.