Scoring - Plus Drug Coated Balloon in Femoro-Popliteal Lesions - 6 Months Results of the DCB-Trak-Registry

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Abstract: *Background*: Recent trials demonstrated favorable results with drug-coated-balloons (DCB) in femoro-popliteal lesions. Additional vessel preparation with a scoring-balloon prior to DCB-angioplasty might reduce rates of flow-limiting dissections and subsequent need for bail-out stenting due to a controlled laceration of the intimal layer. However, clinical data for this combined procedure are lacking.

Methods: In a single center registry, 20 consecutive patients with femoro-popliteal lesions were treated with a scoring-balloon (VascuTrak®) and a DCB subsequently. The primary endpoint was the clinically driven target lesion revascularization (TLR). Secondary endpoints were clinically driven target vessel revascularization (TVR), binary restenosis (PSV>2.4), change in rutherford classification and ABI. Safety endpoints were major cardiovascular events (cardiovascular death, MI, stroke, death) and need for amputation.

Results: The procedure was successful in 17 patients, 1 patient was lost to follow-up. Therefore 16 patients (4 female) were analyzed at the 6 months follow-up visit. There were no clinically driven TLR or TVR after 6 months. Rutherford classification improved from 3.5±0.97 to 0.88±0.72 ($p<0.01$) after 6 months. ABI increased from 0.85±0.26 to 1.02±0.19 ($p=0.01$) after the procedure with no further change at 6 months (1.01±0.15, $p=0.83$). Duplex ultrasound was performed in 9 patients at 6 months, with one binary restenosis (11%). There were neither major cardiovascular events nor amputations at 6 months follow-up.

Conclusions: Vessel preparation with a scoring-balloon prior to DCB-angioplasty in femoro-popliteal lesions is suggested to improve clinical outcome of patients without any safety concerns. Further trials with more patients are needed for validation of the results of our registry.

Keywords: Scoring-balloon, drug-coated balloon, femoro-popliteal lesion, peripheral artery disease, vessel preparation.

INTRODUCTION

Endovascular techniques for treatment of symptomatic peripheral artery disease (PAD) developed enormously within recent years. In femoro-popliteal lesions, percutaneous transluminal angioplasty (PTA) with optional or provisional stenting improved short- and midterm results and might be suggested as a standard treatment in most vascular centers [1]. However, clinically driven target lesion revascularization (TLR) due to in stent re-stenosis within the first months remains a major problem with this concept. Anti-proliferative drug coating on peripheral stents may reduce the risk of re-stenosis, nevertheless the risk of stent fractures with an increased risk of re-stenosis remains [2]. The use of drug-coated balloons (DCB) in femoro-popliteal lesions demonstrated favorable results in several clinical trials [3-6]. This concept provides a homogenous delivery of the anti-proliferative drug paclitaxel to the vessel wall avoiding an implanted metallic scaffold [3]. However, the DCB-alone technique might be limited by significant recoil of the target lesion or by a flow-limiting dissection with consecutive need for bail-out stenting, especially in heavily calcified lesions or in total occlusions, which are very common in the femoro-popliteal region. In complex lesions, reported rates of bail-out stenting in real world settings are suggested to exceed 20% in several trials [7, 8]. Moreover, calcified lesions might limit the beneficial effects of the antiproliferative drug.

Scoring-balloon angioplasty (SBA) provides a controlled and local laceration of the intimal layer and the atherosclerotic plaque, with a decreased arterial wall trauma [9]. This is suggested to result in a decreased inflammatory response in the treated lesion with less formation of neo-intima [9]. Recent trials demonstrated higher patency rates of femoro-popliteal lesions treated with SBA compared to conventional PTA.

Thus, the combination of vessel-preparation with a scoring-balloon and subsequent drug-coated-balloon angioplasty might be beneficial in patients with peripheral artery disease. The objective of the current DCB-Trak registry was to evaluate for the first time the effects of vessel preparation with a SBA and subsequent DCB-angioplasty on clinical outcome in patients with femoro-popliteal lesions.

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METHODS

Study Population

20 consecutive patients with a symptomatic PAD (Rutherford classification 2-6) due to a femoro-popliteal lesion (>70% diameter stenosis or occlusion, reference vessel diameter 4-6mm) were included in the single-center, non-blinded, prospective DCB-Trak-registry. Patients with stenosis >70% proximal to the target lesion were excluded. Informed consent was obtained from all patients, the study protocol of the DCB-Trak registry was approved by the local ethics committee. The registry was registered at clinical-trials.gov: NCT02198105.

Procedure

The target lesion was first dilated with the scoring-balloon (VascuTrak®, 5mm diameter, BARD GmbH, Karlsruhe, Germany) for 60-120 seconds. Subsequently, DCB-PTA was performed with an inflation time of 60 seconds. Any recoil >50% of the reference vessel diameter or flow limiting dissection >type B were treated with bail-out-stenting. Those patients were excluded from further analysis and follow-up. Spot stenting <1/3 of the initial target lesion length was accepted by the protocol. After the procedure, a dual-antiplatelet treatment with aspirin (100mg) and clopidgorel (75mg) was recommended for 4 weeks following life-long treatment with either aspirin or clopidogrel.

Study Endpoints

Follow-up was conducted after 6 months. The primary endpoint was the clinically driven TLR. Secondary endpoints were clinically driven TVR, binary restenosis (PSV>2.4), change in ankle-brachial-index (ABI) and rutherford-classification.

Ankle-brachial-index was determined with a mercury sphygmomanometer (WelchAllyn, Hechingen, Germany) and a portable doppler-ultrasound (handydop, ELCAT, Wolfratshausen, Germany) after the patient had rested in a supine position for at least five minutes. ABI was measured as the ratio of the ankle systolic blood pressure divided by the brachial systolic blood pressure. The higher of the two ABI-values at the ankle, as well as the higher brachial value was used for analysis. In patients with an ABI higher than 1.30, analysis was performed with 1.30.

Safety endpoints were major cardiovascular events (myocardial infarction, stroke, death, cardiovascular death) and freedom from amputation.

Statistical Analysis

All data are expressed as mean±standard deviation (SD). Statistical significance was assumed at a p-level <0.05. Data were tested for normal distribution, further analysis was performed with the paired-students´ t-test or one-way ANOVA were applicable. PSPP® for Mac-OS was used for statistical analysis.

RESULTS

20 consecutive patients (4 female) were enrolled in the DCB-Trak registry. Baseline characteristics were demonstrated in Table **1**, lesion- and procedural characteristics in Table **2**. The procedure was successful in 17 patients (85%), bail-out-stenting was performed in three patients (one patient with recoil >50%, one patient with type-c-dissection, one patient with both). Spot stenting <1/3 of lesion length was necessary in three patients (15%). Lesion length was significantly longer in those patients with bail-out-stenting ($p<0.05$, Table **2**). One patient was lost of follow-up. Thus, 16 patients (80%) were followed after 6 months.

Table 1:

Patient Characteristics	N (% of total)
Male Gender	16 (80%)
Age (yrs)	69 (52-81)
HLP	19 (95%)
Diabetes	10 (50%)
Hypertension	19 (95%)
Current Smoking	14 (70%)
Rutherford classification	3.5±0.9 (3-6)
3	15 (75%)
4	1 (5%)
5	3 (15%)
6	1 (5%)
ABI	0.84±0.25 (0.4-1.3)

Patient characteristics at baseline. (HLP – hyperlipoproteinaemia, ABI – ankle brachial index).

The primary and secondary study endpoints, the clinically driven TLR and TVR, were not achieved by any patient. Duplex-ultrasound was performed in 9 patients at 6 months with one binary-restenosis (11%, PSV 2.48, Table **3**). Rutherford classification and ankle

brachial index improved significantly after 6 months (Figures **1** and **2**).

Table 2:

Lesion Characteristics	N ± SD (Range)
Vessel diameter (mm)	5.6±0.56 (4.5-6.6)
Lesion length (mm)	
Total (mm, n=20)	62±59 (12-260)
Technical success (mm, n=17)	49±35 (12-120)*
Technical failure (mm, n=3)	134±118 (26-260)*
Grade of stenosis (%)	80±12 (55-100)
Total occlusion	3 (15%)
Peri-Procedural dissection	
none	9 (45%)
Type A	2 (10%)
Type B	7 (35%)
> Type B	2 (10%)
Spot stenting <1/3 lesion length	3 (15%)

*p<0.05.

Table 3:

Primary Endpoint	N (%)
Clinically driven TLR	0 (0%)
Secondary Endpoints	**N (%)**
Clinically driven TVR	0 (0%)
Binary restenosis (PSV >2.4)	1 (11%)
MACE	0 (0%)
Any amputation	0 (0%)

Primary and secondary endpoints at 6 months follow-up. TLR – target lesion revascularization, TVR – target vessel revascularization, PSV - peak systolic velocity, MACE - major adverse cardiovascular events – myocardial infarction, stroke, death, cardiovascular death. Change in Rutherford classification and change in ABI were demonstrated in Figures **1** and **2**.

There were neither major cardiovascular events nor amputations at 6 months follow-up (Table **3**).

DISCUSSION

Treatment of femoro-popliteal lesions with scoring-balloon- and subsequent drug-coated balloon angioplasty was safe and demonstrated favorable results in the current study.

Within the last decade, patency rates after endovascular treatment of femoro-popliteal lesions increased due to improvement of endovascular techniques using optional or provisional stenting with or without a drug coating. Recently, drug-coated balloons

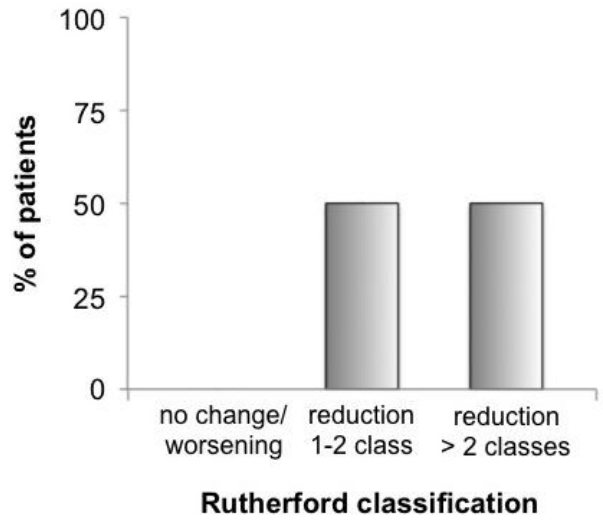

Figure 1: Change of Rutherford-classification

Change of Rutherford-Classification – 6 months follow-up versus pre-procedural baseline data.

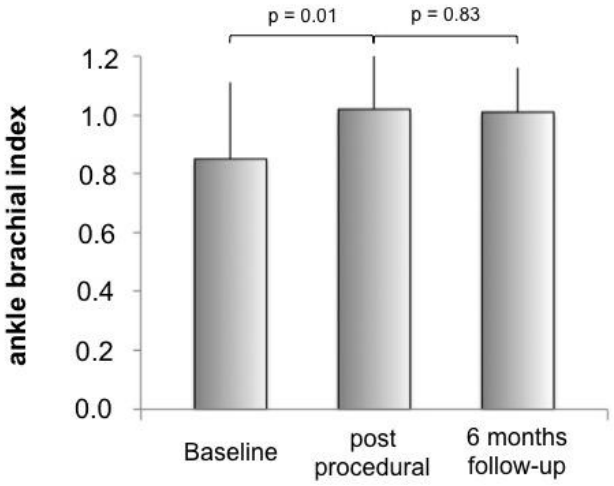

Figure 2: Change of ankle brachial index

Change of ankle brachial index – 6 months follow-up versus pre- and post-procedural baseline data (± SD, paired t-test).

with a homogeneous delivery of the anti-proliferative drug paclitaxel were demonstrated to further reduce rates of re-stenosis and need for revascularization avoiding an implanted scaffold [3-6]. This is particularly important in distal femoro-popliteal lesions with an increased risk of stent-fracture and subsequent in-stent re-stenosis due to a high mechanical stress [10]. Thus, avoidance of stent implantation preserves all future treatment options in those patients [4].

However, significant recoil of the treated lesion or a flow-limiting dissection might limit the strategy of using a drug-coated balloon only. Rates of provisional stenting vary from about 10-50% in recent trials [2, 11, 12]. Furthermore, the grade of calcification might

influence the effects of anti-proliferative treatment using a drug-coated-balloon. In a small trial in patients with circumferential calcifications, patency rates of DCB-treated femoral lesions at 12 months were 50% only, likely due to a decreased drug-delivery into the vessel wall [13].

Regarding these limitations for the stand-alone usage of a drug-coated-balloon, vessel-preparation prior to DCB-angioplasty might result in further improvement of patency rates. One reasonable option for vessel preparation in femoro-popliteal lesions is the directional atherectomy. A small trial with 30 patients demonstrated promising result in heavy calcified femoro-popliteal lesions using the TurboHawk-System® with additional DCB-angioplasty [14]. These results were confirmed in the multi-center DEFINITIVE AR-trial. At 12 months, primary patency rates for long lesions (>10cm) were 96.8% in patients treated with atherectomy + DCB-angioplasty compared to 85.9% in patients treated with DCB-angioplasty alone [15]. It remains speculative, whether these beneficial effects are related to enhanced vascular effects of the paclitaxel itself or just due to a decreased plaque burden. One might suppose the latter option, because there was no difference in paclitaxel levels in the vessel wall after DCB-angioplasty with or even without prior atherectomy in an animal study [16]. However, vessel preparation is suggested to further improve patency rates in combination with DCB-angioplasty.

Another technique for vessel preparation is the scoring-balloon (SB) angioplasty. The controlled and precise laceration of the atherosclerotic plaque is suggested to be less traumatic and might therefore be associated with a less inflammatory response and neo-intimal growth [9, 17]. This might further reduce rates of re-stenosis. Recent results of SB-angioplasty in several small trials in femoro-popliteal lesions were rather promising [17-23]. Especially in short lesions, SB-angioplasty was superior to PTA alone [21].

The current study combined both favorable treatment options for the first time. Vessel preparation with the VascuTrak®-balloon and subsequent DCB-angioplasty resulted in a significant clinical improvement of patients after the procedure, which remained at 6-months follow-up. There were no clinically driven target lesion or target vessel revascularizations despite a high rate of peri-procedural dissections. In duplex-ultrasound guided follow-up, we found one binary restenosis, which was clinically not apparent. Moreover, the procedure was safe, with no adverse events during follow-up.

Overall, the technical success of the procedure was high. However, bail-out-stenting was necessary particularly in long lesions. Future trials have to evaluate, whether the promising results of our study are reproducible in long and even heavy calcified lesions. Our pilot-trial was not powered to answer these remaining questions.

LIMITATIONS

The limitation of our trial is the small sample size and the lack of a control group. The main intention of our study was to prove the concept of the combination of vessel-preparation with a scoring-balloon and additional DCB-angioplasty. The results might serve for the design of a future multi-center trial in femoro-popliteal lesions.

CONCLUSION

Vessel preparation with a scoring-balloon prior to DCB-angioplasty in femoro-popliteal lesions is suggested to further improve clinical outcome of patients with peripheral artery disease without any safety concerns. Further trials with more patients were needed for validation of the results of our registry.

CONFLICTS OF INTEREST

There are no conflicts of interest of all authors regarding the submission. The manuscript is not under consideration elsewhere.

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