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ORIGINAL RESEARCH

Safety and Efficacy of a Paclitaxel-Coated Balloon for the Treatment of Symptomatic Patients with Long Superficial Femoral Artery Disease

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Background: The clinical performance of drug-coated balloons (DCBs) for the treatment of femoro-popliteal lesions may depend on the specific device used. There is limited evidence on the clinical safety and efficacy of the paclitaxel-coated device Stellarex® for the treatment of long (>180 mm) femoro-popliteal lesions.

Methods: This is a single arm, prospective, open label, observational study including symptomatic patients with long femoro-popliteal lesions undergoing endovascular revascularization with Stellarex® DCB. The primary endpoints were the safety and efficacy of the DCB over time. Secondary endpoints were represented by functional outcomes.

Results: Ninety-five patients (median age 72, lesion length 250 mm) were included. At 6 months after the procedure, 61% of patients were asymptomatic as defined by the Rutherford classification, decreasing over time (57% at 12 months, 56% at 24 months, 44% at 36 months). Walking Impairment Questionnaire showed a remarkable improvement at 6 months, with a decreasing trend over time. When single components were analysed, better performances were observed for distance and climbing scores throughout the study period, while speed returned to baseline levels after 24 months. EQ5D Questionnaire showed a statistically significant improvement throughout the study period (with a decreasing trend over time, as seen for Rutherford classification and Walking Impairment Questionnaire). During the 36-months follow-up, 9% of patients died, with previous limb amputation being an independent predictor of mortality (HR = 7.4, p = 0.013). One-year primary patency was 76.5%, with no significant difference compared to the reference rate of 80% (p = 0.810). Primary patency defined as PSVR ≤2.4 (peak systolic velocity ratio) was maintained over time (median survival time free from PSVR >2.4 was not assessable as it exceeded the 36 months of follow-up).

Conclusion: In our sample, Stellarex showed to be safe and effective and it was associated with an event rate comparable to other devices reported in literature.

Keywords: superficial femoral artery disease, lower extremities artery disease, endovascular revascularization, drug-coated balloon, paclitaxel

Introduction

Peripheral artery disease (PAD) is a prevalent condition affecting a significant portion of the global adult population, with its occurrence rising with age.[1] The prevalence of lower extremity artery disease (LEAD) reaches up to 18% in individuals aged 70–75, with approximately one-third of patients experiencing symptoms.[2] Percutaneous transluminal angioplasty (PTA) has emerged as a widely used, minimally invasive revascularization technique for treating PAD.[3] However, balloon angioplasty alone remains associated with high rates of restenosis and limited long-term effectiveness.[4] Recent advancements, including drug-coated balloons (DCBs) and drug-eluting stents (DESs) utilizing paclitaxel in

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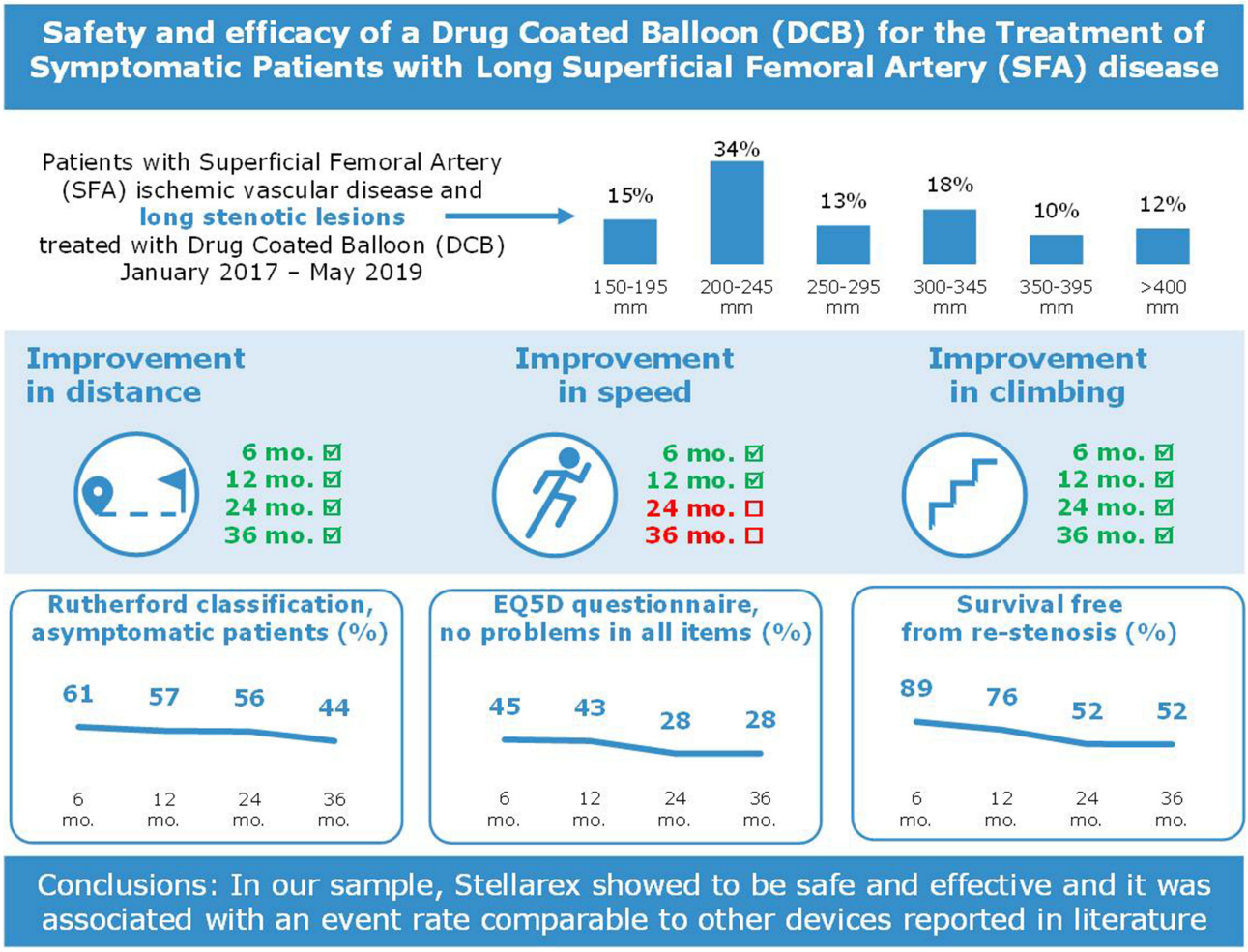
Graphical Abstract



femoro-popliteal arteries (FPAs), have demonstrated significant improvements in reducing restenosis, target lesion revascularization, and late lumen loss.[5,6]

Paclitaxel binds to and stabilizes microtubules, preventing their depolymerization.[7] This disrupts normal cytoskeletal dynamics, which are essential for cell division and migration. By stabilizing microtubules, paclitaxel halts the cell cycle at the G2/M phase, preventing smooth muscle cells (SMCs) from proliferating.[8] SMC proliferation is a major contributor to restenosis. Paclitaxel can trigger apoptosis (programmed cell death) in SMCs, further reducing neointimal thickening. It also has anti-inflammatory properties that help mitigate local vascular inflammation, which plays a role in restenosis development. These combined effects make paclitaxel an effective drug for preventing restenosis in drug-coated balloons (DCBs) and drug-eluting stents (DESs).[9]

Despite the advancements in drug-coated technologies, current clinical gaps include the need for long-term safety data, optimized patient selection criteria, and alternative drug formulations to address concerns regarding paclitaxel-associated mortality and restenosis rates.[10]

Several drug-coated devices are utilized for treating long superficial femoral artery (SFA) lesions, including paclitaxel-based drug-coated balloons (DCBs) and sirolimus-coated devices.

The IN.PACT Admiral DCB, a Paclitaxel-Coated Device, has demonstrated sustained long-term safety and effectiveness in treating long femoropopliteal lesions. Clinical studies have shown that DCB angioplasty is effective in complex

lesions, with freedom from clinically driven target lesion revascularization (CD-TLR) rates of 64.0% in provisional stented subgroups and 81.9% in non-stented subgroups through 36 months.[11]

The Magic Touch PTA, a Sirolimus-Coated Device, is currently under investigation for its safety and efficacy in treating femoropopliteal artery disease. Ongoing trials aim to compare its performance to established paclitaxel-coated balloons.

While direct head-to-head comparisons between Stellarex® DCB and other drug-coated devices in long SFA lesions are limited, the available data suggest that Stellarex® offers favorable outcomes, particularly in complex and calcified lesions. Ongoing studies, such as the SIRONA trial, are comparing sirolimus-coated balloons to established paclitaxel-coated balloons to provide more comprehensive insights into their relative efficacy and safety. In summary, the Stellarex® DCB has demonstrated promising clinical outcomes in treating long SFA lesions, with sustained patency rates and effectiveness in challenging lesion subsets. As research progresses, more data will become available to further elucidate the comparative performance of these drug-coated devices.[12]

Randomized controlled trials (RCTs) have not consistently demonstrated a significant reduction in restenosis with drug-eluting stents (DES) compared to drug-coated balloons (DCBs), making paclitaxel-coated DCBs a common choice in clinical practice.[13] However, a 2018 meta-analysis raised concerns about a potential increase in mortality associated with paclitaxel-coated devices in femoropopliteal arteries, prompting regulatory reviews and further investigations into their long-term safety.[10]

To address this issue, this research adopted two key approaches: (1) an extended follow-up periods to monitor overall survival rates and assess any late adverse effects potentially linked to paclitaxel exposure and (2) specific safety outcomes, including all-cause mortality, cardiovascular-related mortality, and major adverse limb events (MALE), were monitored and analyzed.

The meta analysis finding was not corroborated by subsequent studies, which failed to confirm the link.[14,15] A variety of paclitaxel-based DCBs are available for peripheral artery applications, each differing in drug dosage, excipient composition, and other factors that affect drug release kinetics.[16] These variables, in turn, impact the efficiency of drug delivery to the target tissue, tissue drug levels, and drug loss during the procedure. As a result, the performance of these devices may vary based on their specific characteristics. While the superiority of DCBs over non-drug therapies has been demonstrated across various lesion lengths, including superficial femoral artery (SFA) lesions longer than 100 mm, limited evidence exists for some commercially available devices in this context.[17–19]

The Stellarex® DCB is an over-the-wire dual-lumen catheter featuring a distal semi-compliant balloon coated with a low dose of paclitaxel (2 μg/mm² of the expanded balloon surface). Its unique hybrid formulation, combining both amorphous and crystalline paclitaxel with a polyethylene glycol excipient, ensures coating integrity and optimal drug release.[20] However, the clinical evidence supporting Stellarex DCB in patients with long SFA lesions remains limited. Furthermore, additional device-specific studies are recommended to rule out potential increases in mortality associated with different paclitaxel-coated devices in patients undergoing PTA of the FPA. Against this background, we conducted a single arm, prospective, open-label, observational study to evaluate the clinical safety and efficacy of Stellarex DCB for the treatment of long (>150 mm) SFA lesions.

Methods

The present study is a single arm, prospective, multicentric, open label, observational study. Symptomatic adult patients (aged >18 years) with long femoro-popliteal lesions undergoing endovascular revascularization with DCB from August 2016 to May 2019 were asked to give their written consent to the use of their personal data.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Vast Area of Romagna (CEROM). Protocol code 2984/2016, date of approval May 11, 2016 (Clinical trial registration number: NCT01658540).

Inclusion criteria were: symptomatic arterial disease in the superficial femoral artery and/or popliteal artery (P1-2-3) according to Rutherford Category 2, 3 or 4; target lesion consists of a single solitary or multiple adjacent de novo or re-stenotic lesions (non-in-stent) with diameter stenosis ≥70% by visual estimate and cumulative lesion length ≥15 cm; life expectancy >1 year; written informed consent. Exclusion criteria were: administration of local or systemic thrombolytic

therapy within 48 hours prior to the index procedure; known allergies or sensitivities to heparin, aspirin, other anticoagulant/antiplatelet therapies, and/or paclitaxel; additional planned cardiac or peripheral percutaneous or surgical intervention including CABG within 30 days following the study procedure; ≥15-cm-long inflow lesion (≥50% DS); failure to successfully treat <15-cm-long inflow lesion in the ipsilateral iliac artery. Revascularization was performed as per standard procedure of the sites.

Being part of the same healthcare group, the procedure is common across the centers participating in the study and can be described as follows: Procedure is performed under local or regional anesthesia, with arterial access typically obtained via contralateral retrograde or antegrade common femoral artery puncture. A hydrophilic guidewire is advanced across the lesion under fluoroscopic guidance, with re-entry techniques used if subintimal tracking occurs. Pre-dilation with a low-pressure balloon is performed for resistant or calcified lesions, and atherectomy may be used in severe cases.

The paclitaxel-coated balloon diameter is selected to match the reference vessel diameter, typically between 3 and 7 mm, while the balloon length is chosen to ensure complete lesion coverage and avoid edge stenosis; it is then inflated at nominal pressure, generally between 6 and 10 atm, for 30–60 seconds to optimize drug absorption while minimizing movement to prevent coating loss. Care is taken to minimize balloon movement during inflation to prevent loss of the paclitaxel coating. Post-dilation is avoided unless significant recoil or residual stenosis occurs.

Final assessment with intravascular ultrasound or angiography confirms luminal gain and the absence of complications such as significant dissection or thrombus formation. Hemostasis is achieved with manual compression or closure devices; post-procedural monitoring includes observation for access site complications, distal embolization, or acute vessel closure. This standardized technique ensures optimal drug delivery, vessel preparation, and lesion coverage, improving long-term patency while minimizing restenosis and the need for adjunctive stenting.

After discharge all patients attended clinic visits at 30 days (±14 days), 6 months (±30 days), 12 months (±30 days), 24 and 36 months (±30 days). Angiographic follow-up was performed in symptomatic patients, as clinically indicated.

Statistical Analysis

Continuous variables were reported as median and 1st–3rd quartile; categorical variables were reported as absolute number and frequencies. Incidences were reported with 95% Fisher's exact confidence interval; differences in outcomes at different time points were assessed with McNemar test for categorical outcomes, Bonferroni correction for multiple comparisons was applied. Repeated measures outcomes were modelled using generalized linear mixed-effects models with appropriate link functions and family and considering patients nested in hospital as 2 levels multilevel analysis; Anscombe residuals were analyzed for normality; influential observations were identified and excluded from models; marginal effect plots were reported. Kaplan–Meier curves were reported for events at follow-up; univariate and multivariable Cox regression models were performed; covariates with $p < 0.2$ at univariate analysis were considered for multivariable model. Backward selection with AIC minimization was applied to multivariable models. Schoenfeld scaled and unscaled residuals were analyzed to assess proportional hazard assumption. Patients were censored at the date of the last available visit. Multicollinearity was assessed by using the variance inflation factor (VIF), variables with VIF >5 were excluded from models. All analyses were performed with STATA 18.0 SE (StataCorp LLC); p-values <0.05 were considered statistically significant.

Results

Overall, 95 patients were included. Median age was 72 years, 24% were female. Most frequent comorbidities were mainly related to cardiovascular conditions: hypertension (86.3%), dyslipidemia (83.2%), diabetes mellitus (44.2%). Below the knee, vascular disease was observed among 22.1% for right limb and 21.3% for left limb. Previous peripheral revascularization was performed on 42.1%, while previous limb amputation on 6.3%. Index lesion was located in 41.0% of cases in the right limb and for the remaining 59.0% in the left limb. Median lesion length was 250 millimetres, with 46.3% of the sample having a lesion between 200 and 300 mm, and 39.0% over 300 mm (Figure 1). Baseline laboratory parameters did not show out of range median values (Table 1).

Procedural success was reached in 87 patients (91.6%). Among the remaining 8 patients in which the procedure was unsuccessful, 7 were below the median age (median age 60, IQR = 52–66), all of them were males and had a higher BMI

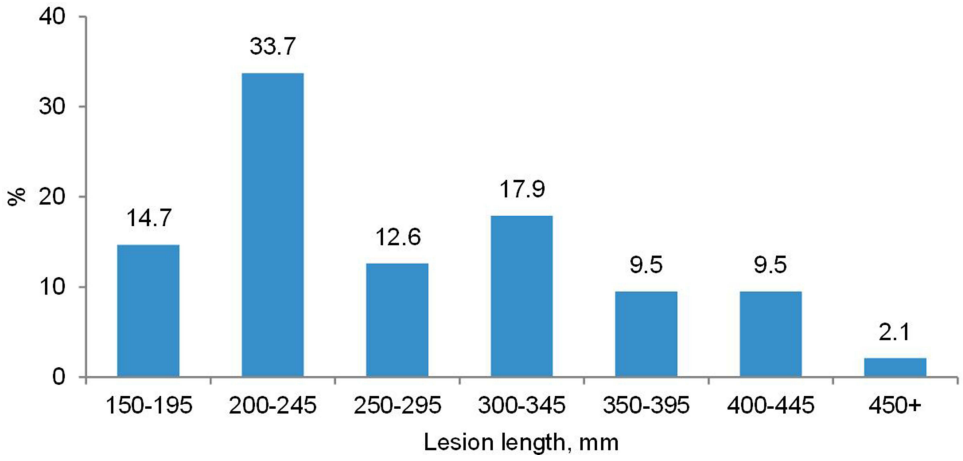


Figure 1 Distribution of patients according to lesion length.

(31.9, IQR = 27.1–32.3) as compared to the overall cohort. Moreover, 100% were affected by hypertension, 100% by dyslipidemia, 3 (37.5%) had diabetes mellitus and 7 (87.5%) were smoker.

At admission, 89.5% of patients showed severe claudication (grade I according to Rutherford classification) and 8.4% had ischemic pain at rest. At 6 months after the procedure, 61.2% were asymptomatic, 22.4% had mild claudication and 14.9% had moderate/severe claudication. At 12 months after the procedure, the percentages were, respectively, 56.7%, 11.7% and 31.7%; at 24 months 55.8%, 11.5% and 32.7%; at 36 months 43.8%, 12.5% and 43.8% (Figure 2). Similarly,

Table 1 Demographic and Clinical Characteristics

Total Patients, n	**95**
Female, n (%)	23 (24.2)
Age, median (IQR)	72 (64–76)
Weight, median (IQR)	77 (67–86)
Height, median (IQR)	168 (160–170)
BMI, median (IQR)	28.0 (24.6–30.1)
Systolic Blood pressure, median (IQR)	130 (120–140)
Diastolic Blood pressure, median (IQR)	80 (70–80)
Heart Rate, median (IQR)	69 (60–79)
Hypertension, n (%)	82 (86.3)
Dyslipidemia, n (%)	79 (83.2)
Diabetes Mellitus, n (%)	42 (44.2)
Subject insulin dependent, n (%)	20 (50.0)
Smoke, n (%)	66 (75.9)
Renal Insufficiency, n (%)	15 (16.0)
Subject on dialysis, n (%)	0 (0.0)
TIA, n (%)	6 (6.3)
Stroke, n (%)	6 (6.3)
MI, n (%)	19 (20.0)
CABG, n (%)	11 (11.6)
PCI, n (%)	35 (36.8)
Below the knee vascular disease, right limb, n (%)	17 (22.1)
Below the knee vascular disease, left limb, n (%)	16 (21.3)
Previous peripheral revascularization, n (%)	40 (42.1)
Previous limb amputation, n (%)	6 (6.3)
Lesion length mm, median (IQR)	250 (205–340)

(*Continued*)

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Table 1 (Continued).

Total Patients, n	**95**
150–195 mm (n, %)	14 (14.7)
200–245 mm (n, %)	32 (33.7)
250–295 mm (n, %)	12 (12.6)
300–345 mm (n, %)	17 (17.9)
350–395 mm (n, %)	9 (9.5)
400–445 mm (n, %)	9 (9.5)
450+ mm (n, %)	2 (2.1)
- Right limb, n (%)	39 (41.0)
- Left limb, n (%)	56 (59.0)
Laboratory parameters	
White Blood Cells (10^3/uL), median (IQR)	8.1 (7.1–9.6)
Red Blood Cells (10^6/uL), median (IQR)	4.8 (4.3–5.3)
Hemoglobin (g/dL), median (IQR)	13.6 (12.2–15.1)
Hematocrit (%), median (IQR)	41.2 (36.9–45.0)
Platelets (10^3/uL), median (IQR)	235.5 (203.5–276.5)
Serum Creatin (mg/dL), median (IQR)	1.0 (0.8–1.2)
Azotemia (mg/dL), median (IQR)	40.0 (33.0–57.0)
Total cholesterol (mg/dL), median (IQR)	148.0 (130.0–171.0)
HDL cholesterol (mg/dL), median (IQR)	46.0 (38.0–55.0)
LDL cholesterol (mg/dL), median (IQR)	79.0 (61.0–99.0)
Triglycerides (mg/dL), median (IQR)	131.0 (84.0–177.0)
Albumin (g/dL), median (IQR)	4.0 (3.7–4.2)
LDH (U/L), median (IQR)	177.0 (156.0–202.0)
GPT (U/L), median (IQR)	17.0 (12.0–22.0)
GOT (U/L), median (IQR)	17.0 (13.1–20.0)
CPK (U/L), median (IQR)	76.0 (55.0–116.0)

Abbreviations: IQR, interquartile range; BMI, body mass index; TIA, Transient ischemic attack; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary Intervention; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LDH, lactate dehydrogenase; GPT, glutamic-pyruvic transaminase; GOT, glutamic-oxalacetic transaminase; CPK, creatine phosphokinase.

Walking Impairment Questionnaire and EQ5D Questionnaire showed a statistically significant improvement at 6 and 12 months, with a decreasing trend over time, as seen for Rutherford classification (Figures 3 and 4). Patients who reported no problem in all 5 EQ5D items were 1.1% at baseline, 44.6% at 6 months, 43.1% at 12 months, 27.6% at 24 months,

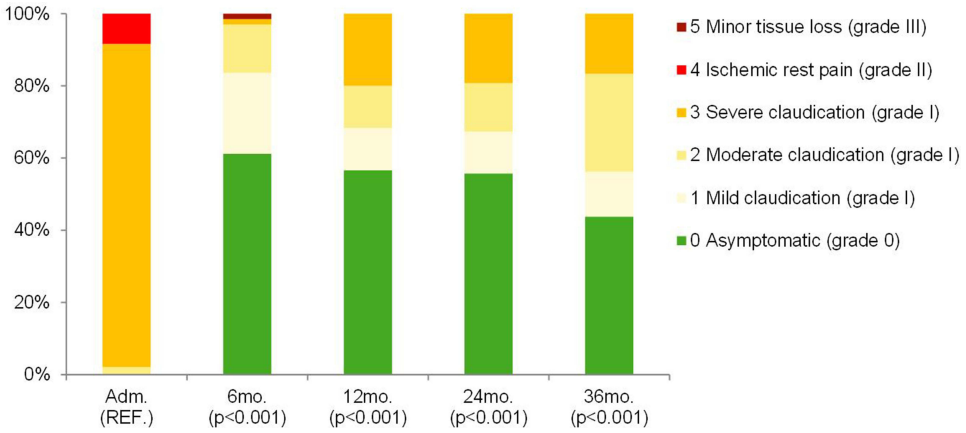

Figure 2 Distribution of patients according to Rutherford classification at different timepoints.
Abbreviations: Adm., admission; mo., months; REF., reference.

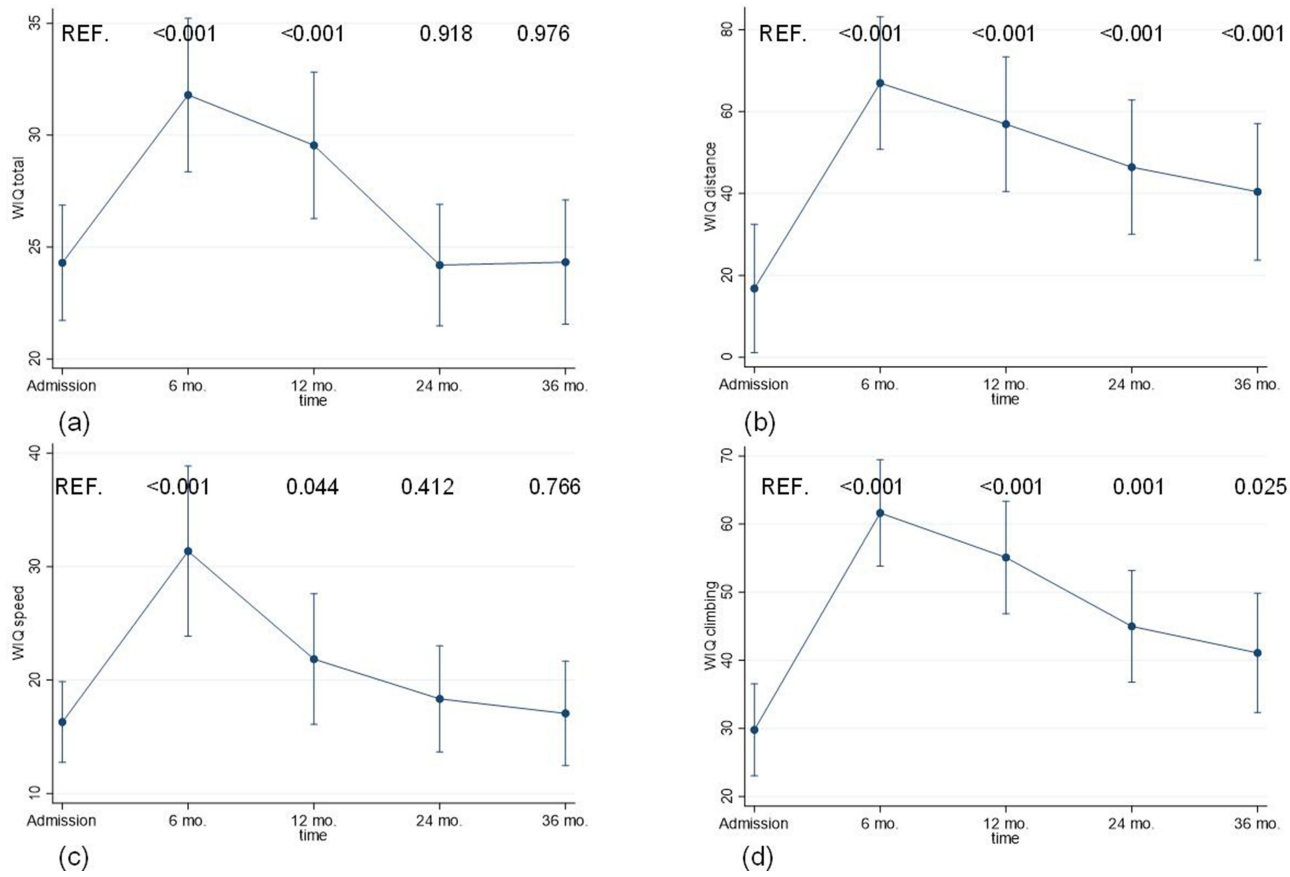

Figure 3 Walking Impairment Questionnaire (WIQ); marginal effects plot for total score (**a**), distance (**b**), speed (**c**) and climbing score (**d**) (predicted values and confidence intervals).
Abbreviations: Adm., admission; mo., months; REF., reference.

27.7% at 36 months. Analyzing the subsection of the Walking Impairment Questionnaire, it was observed that, even if a decreasing trend over time was present, an improvement in distance and climbing was maintained during the whole follow-up period, while an improvement in speed was attained only at 6 and 12 months.

No patients died during hospitalization; nine (9.5%) patients died during 36 months of follow-up. Specifically 3 patients died during the first year, 3 in the second year and 3 in the third year of follow-up; 3 patients died for cardiovascular diseases (non-atherosclerotic), 6 for non-cardiovascular diseases. At a multivariable Cox regression, only previous limb amputation resulted to be an independent predictor of death (HR = 7.4, p = 0.013) (Figure 5 and Table 2).

Primary patency, as defined as freedom from target limb revascularization or >50% restenosis (peak systolic velocity ratio, PSVR>2.4) at 12 months was reached by 76.5% of patients with at least one year of follow-up, with p=0.810 when compared to an expected reference rate p0=80%; lower primary patency rates were observed for patients affected by diabetes (66.7%), patients having a BMI over 28 (66.7%), with previous peripheral revascularization (65.2%), affected by a below the knee vascular disease (63.6%), previous myocardial infarction (55.6%); other conditions have similar success rates as the overall sample; patients over 72 years had 87.1% of success rate. PSVR≤2.4 was maintained over time (median survival time free from PSVR>2.4 was not assessable as it exceeded the 36 months of follow-up); survival rate free from PSVR>2.4 were 89.3 (80.9–94.1) at 6 months, 76.1 (65.6–83.7) at 12 months, 62.1 (50.7–71.5) at 24 months, 51.8 (40.1–62.3) at 36 months (Figure 5); at Cox models, no prognostic factors were identified as statistically significant.

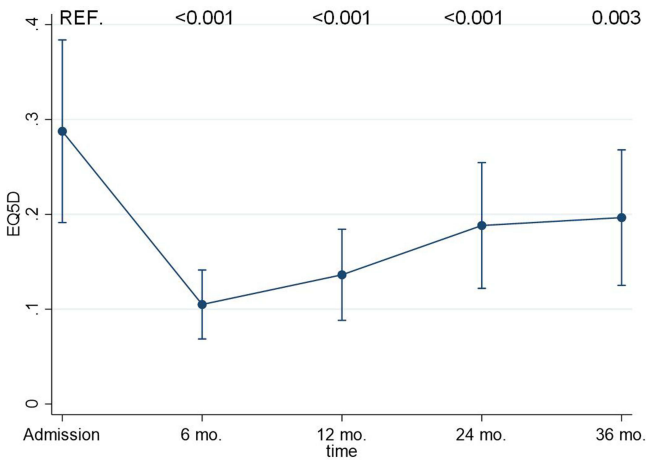

Figure 4 EQ5D questionnaire, marginal effects plot (predicted values and confidence intervals).
Abbreviations: Adm., admission; mo., months; REF., reference.

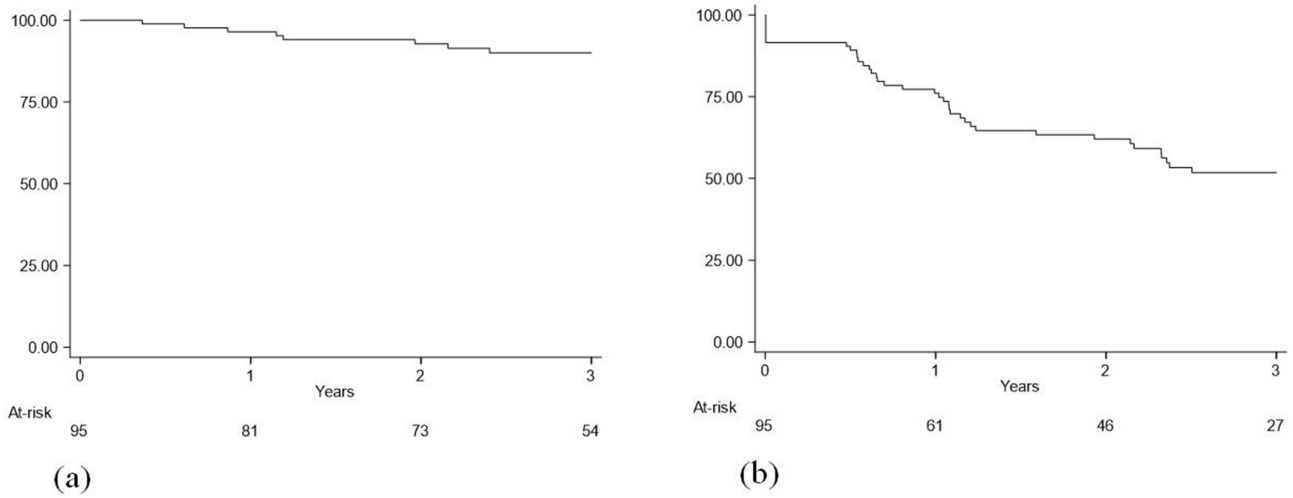

Figure 5 Kaplan Meier curves: death for any cause (**a**) and survival free from PSVR>2.4 (**b**).

Discussion

The optimal revascularization strategy for symptomatic patients with long femoropopliteal lesions remains a subject of debate. Initially, endovascular treatment of femoropopliteal artery disease involved PTA, with stents used only in cases of PTA failure or late recurrences. Compared to surgery, the main limitation of endovascular interventions is reduced long-term patency. Primary patency after angioplasty is highest in the common iliac artery and diminishes with increasing lesion length, diffuse disease, and more distal locations. Diffuse disease is particularly prevalent in the femoropopliteal segment. Conventional balloon angioplasty is limited by high restenosis rates (40–60%) within 6 to 12 months, with longer lesions having an even higher risk. Alternative therapies, such as brachytherapy, atherectomy, and cryoplasty, have not demonstrated superiority over PTA in clinical trials for both de novo and restenotic lesions. In contrast, paclitaxel-coated devices have been shown to enhance patency duration and reduce the need for repeat interventions compared to uncoated devices in the treatment of femoropopliteal lesions. The benefits of DCBs over nondrug therapies have been observed across various lesion lengths, including SFA lesions exceeding 100 mm.[18–20] RCTs comparing stenting with PTA for the treatment of moderate to long SFA lesions have not consistently demonstrated a significant reduction in restenosis with stents. Although stenting offers higher immediate success rates, routine stent placement did not lead to

Table 2 Death for Any Cause, Univariate and Multivariable Cox Regression Models

Univariate Models	**HR**	**95% CI**		**p**
Female	0.978	0.203	4.712	0.978
Age	1.033	0.953	1.119	0.432
Weight	1.017	0.966	1.072	0.515
Height	0.997	0.911	1.091	0.948
BMI	1.068	0.898	1.270	0.456
Systolic Blood pressure	0.977	0.932	1.025	0.340
Diastolic Blood pressure	0.953	0.886	1.024	0.186
Heart Rate	1.016	0.966	1.069	0.544
Hypertension	–			
Dyslipidemia	1.938	0.242	15.497	0.533
Diabetes Mellitus	2.816	0.703	11.278	0.144
Subject insulin dependent	2.193	0.548	8.773	0.267
Smoke	1.577	0.327	7.592	0.570
Renal Insufficiency	1.336	0.277	6.439	0.718
Subject on dialysis	–			
TIA	–			
Stroke	–			
MI	1.000	0.208	4.813	1.000
CABG	–			
PCI	2.272	0.609	8.466	0.222
Below the knee vascular disease, right limb	0.530	0.066	4.239	0.549
Below the knee vascular disease, left limb	–			
Previous peripheral revascularization	0.366	0.076	1.762	0.210
Previous limb amputation	7.549	1.558	36.586	0.012
Multivariable model	**HR**	**95% CI**		**p**
Diabetes Mellitus	2.765	0.690	11.084	0.151
Previous limb amputation	7.384	1.518	35.918	0.013

Note: Multivariable model was performed using a backward selection with AIC minimization.
Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; TIA, Transient ischemic attack; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary Intervention.

a significant decrease in restenosis or target vessel revascularization. The authors concluded that the evidence does not support routine stenting as the primary endovascular treatment for short SFA lesions.[4]

More recently, the introduction of self-expanding nitinol stents has led to primary nitinol stenting being recommended as a first-line treatment for intermediate-length superficial femoral artery lesions, owing to improved mid-term patency rates.[21] Restenosis rates after 1–2 years are 20–30% lower with primary stenting compared to angioplasty. The success in reducing restenosis with DES in coronary artery disease was not replicated in studies of sirolimus-coated stents for obstructive SFA disease. However, a recent clinical trial showed a significant improvement in primary patency at 1 and 2 years with paclitaxel-coated stents compared to PTA. Despite this, no significant advantage has been demonstrated for DES over bare-metal nitinol stents.[22] In long lesions, the high mechanical stress caused by normal patient movement in the femoropopliteal artery increases the risk of stent fractures and abnormal tortuosity in adjacent non-stented vessel segments, where deformations are exacerbated by the presence of stents.[23] Additionally, stents may pose a challenge for future surgical or endovascular interventions. As a result, alternative therapies that minimize the need for stent implantation—primarily reserved for sealing flow-limiting dissections—have been explored to reduce restenosis and improve clinical outcomes. The potential advantages of an efficacious stent-free approach and promising preclinical research led to consideration of DCB technology for prevention of restenosis in this complex PAD population. Recent RCTs comparing paclitaxel DCB with conventional PTA using uncoated balloon in patients with SFA disease were

undertaken and demonstrated significant reductions in restenosis rates 6 months after intervention in short SFA lesions.[24] In a prospective registry, our group evaluated 105 patients with femoropopliteal lesions/occlusions <15 cm treated with PEB balloon and provisional stenting in 12% of cases. Primary patency rate at 12 months was 84%.[25] Whether these positive results apply also to long SFA lesions remains to be investigated.

However, a meta-analysis published in 2018 suggested an increased rate of mortality over a long follow-up period with the use of paclitaxel-coated devices in the femoropopliteal arteries, despite subsequent studies did not confirm this association.[15]

In real world, the most frequent pattern of SFA steno-occlusion is long lesion disease, a condition prone to a high rate of restenosis, reaching 60% at one year for lesion longer than 15 cm.[23] So far, only very few data are available in long lesions.

The promising results seen with DCBs in short to mid-length lesions cannot be directly applied to long lesions due to various factors such as extension, compression, radial forces, and bending along the longer SFA tract, all of which contribute to higher restenosis rates. Given that long SFA lesions are prevalent in the real-world LEAD population, there is a clear need to evaluate the potential effectiveness of DCB technology in this setting. A variety of paclitaxel-based DCBs are available for peripheral artery applications, each differing in drug dosage, excipient type, and other characteristics that affect drug release kinetics. These variables influence the efficiency of drug delivery to target tissue, tissue drug levels, and drug loss during the procedure. As a result, the performance of specific devices may vary depending on their unique properties. While the benefits of DCBs over non-drug therapies have been demonstrated across a range of lesion lengths, including SFA lesions over 100 mm, limited evidence exists for some commercially available devices in this context.[17–19] The Stellarex® DCB is an over-the-wire dual lumen catheter with a distal semi-compliant balloon coated with low dose of paclitaxel (2 μg/mm^2 of the expanded balloon surface). It is characterized by an hybrid formulation, made of amorphous and crystalline paclitaxel combined with a polyethylene glycol excipient, allowing for maintenance of coating integrity and adequate drug release.[10]

The evidence in support of the clinical performance of Stellarex DCB in patients with long SFA lesions is limited. Moreover, additional device-specific evidence is advisable to rule out a possible increase of mortality rates with the use of different paclitaxel-coated devices in patients undergoing PTA of FPA. The 5-year results for the ILLUMENATE pivotal study showed no statistically significant difference among patients treated with the Stellarex DCB (21.2%) compared to those treated with PTA (20.2%).[26] Based on personal previous experience, we hypothesize that a significant improvement in patency for long SFA lesions treated with angioplasty when DCB use can be achieved. To test this hypothesis, we plan to conduct the present observational trial aimed at evaluating patency and clinical outcomes in patients with long SFA atherosclerotic lesions treated with DCB technology angioplasty.

Although few studies have focused on long lesions and long-term follow-up, similar results as reported in Figure 5 were observed for other DCB devices; in particular, in the Lutonix registry, for lesions >140mm, the clinical primary patency rate by Kaplan–Meier estimates was 76.9% at 12 months and 67.3% at 24 months, while survival was 90%,[27] while IN.PACT showed at 3 years a primary patency of 65.5% and a survival rate of 90%.[11] Moreover, DCB have showed better performances as compared to percutaneous transluminal angioplasty at 24 months: rate of freedom from revascularization was 81.6% vs 43.2% ($p < 0.001$), primary patency 46.9% vs 15.0% ($p = 0.003$), and better Rutherford class at 12 months ($p = 0.012$) but not at 24 months ($p = 0.127$); death showed no differences.[28] A meta-analysis published in 2023 conducted on 44 papers for a total of 4847 patients with long lesions showed that primary patency at 1 year were 83% for drug-coated balloons (DCBs), 74% for drug-eluting stents, 68% for bare metal stents and 67% for covered stents (CSs).[29]

Limitations

The Stellarex study was intended to enrol 150 patients (sample size calculation was based on proportion of patency rate at 12 months equal to 80 with 95% confidence interval plus or minus 0.10, $\alpha = 0.05$, $\beta = 0.20$ and 10% drop out rate). However, due to the COVID-19 pandemic, it was possible to enrol only two-third of the scheduled number of subjects. Therefore, it cannot be excluded that some of the non-statistically significant results found may be the consequence of the lower than expected number of enrolled patients.

Another potential limitation could be related to the follow-up period; while 36 months may generally be sufficient for high-risk patients, the variability in disease progression among individuals may render it inadequate for some.

Finally, the lack of external validation could limit the generalizability of the study findings.

Conclusions

In our sample, Stellarex showed to be safe and effective and it was associated with an event rate comparable to other devices reported in the literature. The use of the device in these patients with a median age of 72 years has also shown an improvement in mobility recovery as assessed by standardized questionnaires and scales (WIQ, EQ5D, Rutherford classification), resulting in an enhanced quality of life.

Data Sharing Statement

The data supporting the findings of this study are not publicly available, and no additional data will be shared.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflict of interest.

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