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ORIGINAL ARTICLE
PERIPHERAL ARTERIAL DISEASE

Real-world outcomes of Cook Zilver PTX in femoro-popliteal district from multicenter experience

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ABSTRACT

Background: The purpose is to evaluate the follow-up outcomes after femoro-popliteal stenting with Cook Zilver PTX in a multicenter experience.

Methods: Collected data from four Units were retrospectively joined and analyzed considering Zilver PTX deployed from August 2009 according to the instruction for use. Patient demographics, preoperative comorbidities, Rutherford classification, arterial characteristics and stent data were considered. Target lesion revascularization (TLR) was defined as reintervention performed for ≥50% diameter stenosis after recurrent clinical symptoms. Primary outcome was the freedom from TLR (ffTLR) and its risk factors. Secondary outcomes were primary patency (PP) of the stent, amputation-free survival (AFS) and their risk factors.

Results: Considering 203 patients (mean age: 73.5 years ±10.6; male: 66.5%) and 263 stents (median 2 stents/patient, range 1-5stent/patient), chronic limb-threatening ischemia (CLTI) affected 154 patients (75.9%). The length of the treated lesion was <120 mm in 99 (48.8%), ≥120 mm and <200 mm in 65 (32%) and ≥200 mm in 39 (19.2%) cases, respectively; the reference vessel mean diameter was 5.5±0.7 mm; chronic total occlusion was treated in 153 (75.4%) patients, the popliteal artery was involved in 56 (27.6%) cases and prior endovascular intervention was performed in 27 (13.3%) cases. Two or more crural run-off vessels were patent in 124 (61.1%). Mean follow-up was 23.2 months ±21.3. At 1, 2 and 3 years, the ffTLR was 90.6±4.2%, 86.4±6.1% and 80.4±8.3%, respectively, and the PP was 85.6±5.0%, 74.2±7.6% and 72.7±8.2%, respectively. Negative prognostic factor for ffTLR and PP was the reference vessel diameter (P=0.001 and P<0.001, respectively). At 1, 2 and 3 years, the AFS was 81.8±6.0%, 75.5±7.1% and 74.2±7.5% respectively; coronary artery disease (P=0.041) and CLTI (P=0.011) resulted negative prognostic factors.

Conclusions: In the real-world practice, around 3/4 of patients were treated for CLTI. The rate of ffTLR is high, and PP is substantially lower. A small vessel diameter (<5 mm) is a negative factor for both ffTLR and PP. The rate of AFS is about 75% at 2 years and CLTI and coronary artery disease are negative prognostic factors.

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Key words: Peripheral arterial disease; Endovascular procedures; Drug-eluting stents; Chronic limb-threatening ischemia.

Drug eluting stents (DES) are largely deployed in coronary district[1] and since the first decade of 2000 have been proposed for peripheral arterial disease (PAD) in femoro-popliteal district.[2]

The Zilver PTX (Cook Medical, Bloomington, IN, USA) has been the first drug-eluting peripheral stent obtaining the CE mark in 2009. A randomized control trial reported a >40% relative risk reduction for restenosis and target lesion revascularization (TLR) through 5 years.[3] Other premarket and postmarket studies confirmed the clinical benefit with this DES reporting >80% freedom from TLR (ffTLR) at 2 years.[4-6]

However, the majority of the current publications includes high rate of claudicant patients[6] and are directly supported by Cook.[3-6] For these reasons, obtained data risk to be poor comparable with other experiences and does not reflect the daily practice activity. The real-world data on the Zilver PTX DES device in the femoro-popliteal district are scarcely reported.

The aim of the study is to report the outcomes of Zilver PTX drug-eluting stent in femoro-popliteal district from a multicenter real-world experience.

Materials and methods

Study design

The study is a retrospective observational multicenter study without any sponsorship or financial support. The included centers are three high-volume hospital for peripheral arterial procedure. Each center has a prospectively collected database including surgical and peripheral procedure for PAD. Each database was retrospectively analyzed and a unique datasheet was created including patients treated with Zilver PTX for chronic PAD (Figure 1). The project was approved by the Institutional Review Boards.

Inclusion and exclusion criteria

The considered interval period was from August 2009 (date of European Commission approval) to August 2021.

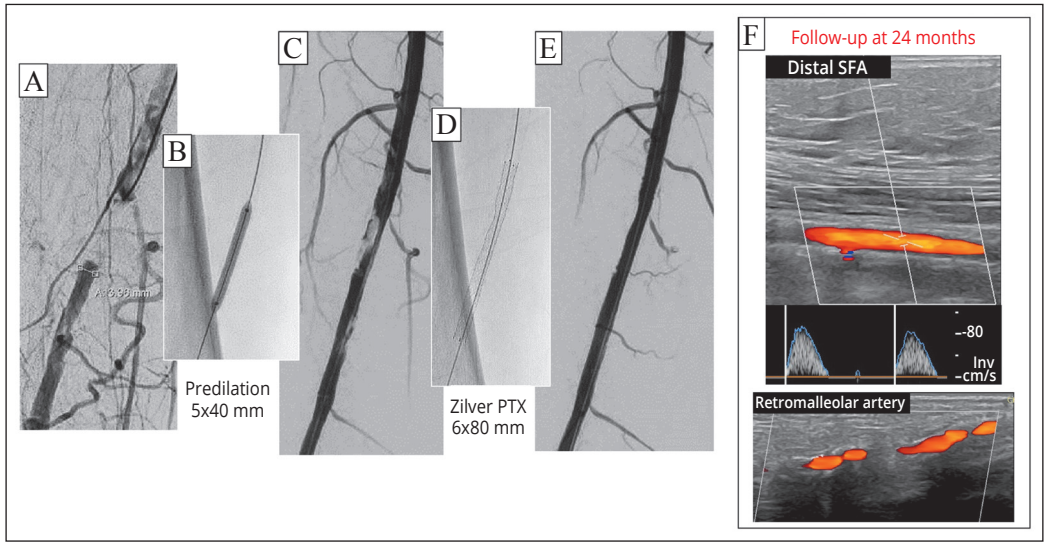


Figure 1.—Superficial femoral artery (SFA) treatment with Cook - Zilver PTX in a 62-year male patient with rest pain (Rutherford 4). A) Preoperative angiography shows a short-calcified lesion at the distal third of SFA; B) predilation with a 5x40 mm balloon; C) result after predilation; D) the Cook - Zilver PTX after the deployment; E) completion angiography; F) Duplex follow-up after 24 months shows the patency of the distal SFA and retromalleolar artery with direct flow.

All patients treated for femoro-popliteal chronic PAD with at least one Zilver PTX stent were included in the datasheet, and both endovascular and hybrid procedures were considered. Hybrid procedure was considered a surgical intervention with concomitant intraoperative endovascular step (*e.g.* femoral endoarterectomy and transluminal angioplasty and stenting of superficial femoral artery). Patients with <6-month follow-up were excluded. In case of Zilver PTX deployment out of instruction for use (symptomatic vascular disease of the above-the-knee femoropopliteal artery with the proximal end of the stent at least 1 cm below the origin of the superficial femoral artery and the distal end of the stent above the plane of the femoral epicondyles), patient was excluded.

Data collection

The following data were extracted from the database of each center: patient demographics (age, gender), preoperative comorbidities (arterial hypertension, diabetes mellitus, dyslipidemia, smoke habit, chronic renal failure, coronary artery disease, obesity), Rutherford classification and chronic limb-threatening ischemia (CLTI), arterial characteristics (length of the treated lesion, reference vessel diameter, popliteal involvement of the lesion, chronic total occlusion, prior endovascular intervention of the treated segment, tibial run-off vessels) and stent data (number, length and diameter). The majority of data were also reclassified as reported in the Zilver PTX prediction model (https://cooksfa.z13.web.core.windows.net/); due to different classification in database of each center, the arterial lesion length was reclassified in three groups (<120 mm, between 120 mm and <200 mm and ≥200 mm); arterial lesion calcification was not considered because of value was not available in all centers. Further specifications of the collected data are reported in Table I.[7]

Treatment

The DES delivery and deployment was performed in operating room, angio-suite or hybrid room according to the center, in accordance with normal procedural of each center. The indication for the Cook Zilver PTX drug eluting stent was determined by the first operator during the procedure according his experience. The stent diameter was at least 1mm larger than the reference vessel; however, the diameter and length of the DES were chosen by the first operator in accordance with product recommendations. In case of multiple stent necessity, the distal stent was deployed first, followed by the proximal, with an overlap zone at least of 20 mm.

Postprocedural therapy

The standard protocol for postoperative medical therapy after the femoro-popliteal stenting was the same in three centers: 1) in cases of preoperative single antiplatelet therapy, double antiplatelet therapy was postoperatively prescribed for 3 months; 2) in case of indication to anticoagulation for other comorbidities (*e.g.* atrial fibrillation), one antiplatelet therapy was suggested with anticoagulation; 3) if double antiplatelet therapy was already assumed for other indication, this therapy was assumed lifelong. However, postprocedural medical therapy was chosen according to the type of the procedure and patient comorbidities and risk of thrombosis/hemorrhage.

Follow-up

Each center performed own standard schedule of follow-up for peripheral arterial endovascular procedure consisting in clinical examination and duplex ultrasound at least 1 per year. The follow-up data of the patients were retrospectively gathered from outpatient clinic medical reports, clinical charts, picture archiving and communication system (PACS) and hospital management software.

Outcomes

The primary outcome was to assess the freedom from target lesion revascularization (ffTLR) during the follow-up and to define risk factors. According with previous publications,[6] ffTLR was defined reintervention performed for ≥50% diameter stenosis after recurrent clinical symptoms.

The secondary outcomes were to assess the primary patency (PP) of the stent and amputation-free survival (AFS) during follow-up, defining their possible risk factors. PP was considered as absence of occlusion or ≥50% diameter stenosis at duplex ultrasound or digital subtraction angiography. AFS was a composite endpoint adding survival and limb salvage (defined as lack of major amputation for any cause).

Statistical analysis

The continuous variables were reported as mean±standard deviation in case of normal distribution and median and inter-quartile range in case of no-normal distribution. The outcomes were calculated with Kaplan-Meier analysis; Kaplan-Meyer estimates were reported in the graphs only so long as the standard error remains <10% and the at risk patients in all groups were ≥10. Uni- and multivariate analyses for each outcome were calculated with Cox regression; patient demographics, preoperative comorbidities, CLTI, arterial characteristics and treatment data were

TABLE I.—*Definition, frequencies and means of patient and stent data.*

Parameters	Definition	N.=203
Patient demographics		
Mean age±SD, years		73.5±10.6
<65 years		41 (20.2%)
≥65 and <75 years		60 (29.6%)
≥75 and <85 years		74 (36.5%)
≥85 years		28 (13.8%)
Gender: male		135 (66.5%)
Preoperative comorbidities		
Arterial hypertension	Systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mmHg or patient in treatment with antihypertensive drug.	173 (85.2%)
Diabetes mellitus	Fasting plasma glucose level ≥126 mg/dL or plasma glucose ≥200 mg/dL 2 hours after a 75-g oral glucose load as in a glucose tolerance test or symptoms of hyperglycemia and plasma casual glucose >200 mg/dL or glycated hemoglobin ≥6.5%.	115 (56.7%)
Dyslipidemia	Total cholesterol ≥200 mg/dL or triglycerides ≥180 mg/dL, or high-density lipoprotein cholesterol ≤35 mg/dL.	124 (61.1%)
Smoker	An adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes.	33 (16.3%)
Ex-smoker	An adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview.	76 (37.4%)
Chronic renal failure	Glomerular filtration rate <60 ml/min/1.73 m^2 (Cockcroft-Gault formula)[7]	65 (32%)
Coronary artery disease	Clinical history of myocardial infarction or angina pectoris or previous endovascular/surgical coronary revascularization.	93 (45.8%)
Obesity	Body Mass Index ≥30 kg/m^2	50 (24.6%)
Rutherford classification		
3	Severe claudication	49 (24.1%)
4	Rest pain	49 (24.1%)
5	Minor tissue loss	77 (37.9%)
6	Major tissue loss	28 (13.8%)
CLTI	Rutherford cat. ≥4	154 (75.9%)
Arterial characteristics		
Length of the treated lesion		107±77.7 mm
<120 mm		99 (48.8%)
≥120 mm and <200 mm		65 (32%)
≥200 mm		39 (19.2%)
Reference vessel diameter	Diameter of the healthy artery in proximity of the arterial lesion	5.5±0.7 mm
<5 mm		14 (6.9%)
≥5 mm		189 (93.1%)
Popliteal involvement of the lesion		56 (27.6%)
Chronic total occlusion		153 (75.4%)
Prior endovascular intervention	Any prior endovascular treatment of the study lesion	27 (13.3%)
Tibial run-off vessels	Patent tibial vessels	
0/1		79 (38.9%)
2+		124 (61.1%)
Treatment data		
Number of stents		263
1 stent/patient		154 (75.9%)
≥2 stent/patient		49 (24.1%).
Stent data		N.=263
Length (median, range)		100 mm (40-140)
40 mm		10
60 mm		20
80 mm		50
100 mm		57
120 mm		71
140 mm		55
Diameter (median, range)		6 mm (5-7 mm)
5 mm		72 (27.4%)
6 mm		160 (60.8%)
7 mm		31 (11.8%)

CLTI: critical limb-threatening ischemia; SD: standard deviation.

considered as possible correlated factors. The statistical significant threshold was set at P<0.05. For multivariate analysis, risk factors with P≤0.200 were considered.

Results

Patients and stents

Patients treated with Zilver PTX were retrospectively found since January 2014. Since then, the total number of treated patients was 203 (mean age: 73.5 years ±10.6; male: 66.5%). The preoperative comorbidities, Rutherford classification, arterial characteristics and treatment data were reported in Table I. CLTI and claudication intermittens were present in 154 (75.9%) and 49 (24.1%) patients, respectively. The length of the treated lesion was <120 mm in 99 (48.8%), ≥120 mm and <200 mm in 65 (32%) and ≥200 mm in 39 (19.2%) cases. The mean reference vessel diameter of treated lesion 5.5±0.7 mm. The lesion consisted in chronic total occlusion in 153 (75.4%) patients and involved the popliteal artery in 56 (27.6%) cases. A previous endovascular intervention was already performed in 27 (13.3%) cases. Two or more tibial run-off vessels were patent in 124 (61.1%).

Total number of deployed stents was 263 (median 2 stents/patient, range 1-5stent/patient). Two or more stents were used in 49 patients (24.1%). Length and diameter of deployed stents were reported in Table I.

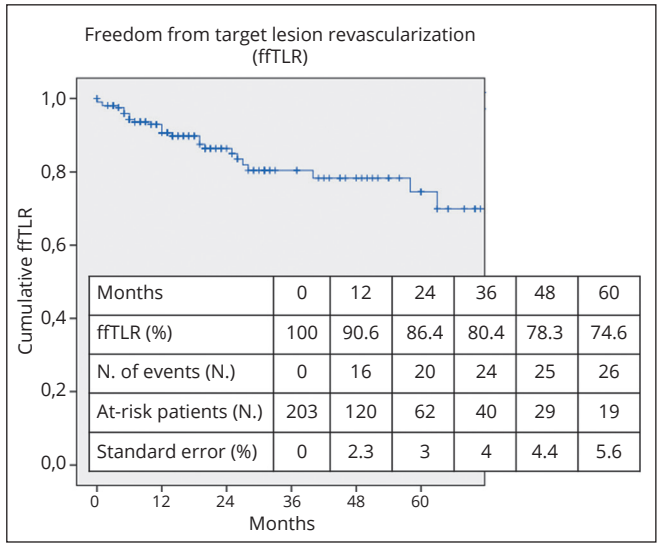
The mean follow-up was 23.2 months ±21.3. Excluding 22 patients with death or major amputation occurred in the postoperative period <6 months, all patients had at least 6 months of follow-up.

Outcomes

At 1, 2 and 3 years, the ffTLR was 90.6±4.2%, 86.4±6.1% and 80.4±8.3% (Figure 2). Twenty-nine events (14.3%) occurred during the whole follow-up and 16/29 (55.2%) within 12 months. At univariate analysis (Table II), risk factor for ffTLR was the reference vessel diameter (P<0.001); treated artery with a diameter ≥5 mm have higher ffTLR than artery <5 mm (P=0.002). At multivariate analysis (Table II), reference vessel diameter resulted a negative prognostic factor for ffTLR (P=0.001).

At 1, 2 and 3 years, the PP was 85.6±5.0%, 74.2±7.6% and 72.7±8.2% (Figure 3). The total number of events was 44 (21.7%); 27/44 (61.4%) occurred within 1 year, and 22/44 (50%) of events at 7 months. At univariate and multivariate analysis (Table III), the sole negative risk factor for PP was the reference vessel diameter (P<0.001).

At 1, 2 and 3 years, the AFS was 81.8±6.0%, 75.5±7.1%



Months	0	12	24	36	48	60
ffTLR (%)	100	90.6	86.4	80.4	78.3	74.6
N. of events (N.)	0	16	20	24	25	26
At-risk patients (N.)	203	120	62	40	29	19
Standard error (%)	0	2.3	3	4	4.4	5.6

Figure 2.—Estimated freedom from target lesion revascularization (ffTLR) rates according to Kaplan-Meier analysis.

and 74.2±7.5% (Figure 4). Events occurred in 49 patients (24.1%): 40 deaths and 9 major amputations. At 1 year, 34/49 (69.4%) events occurred; 25/49 events (51%) occurred at 7 months. At univariate analysis (Table IV), negative risk factors for AFS resulted: age (P=0.001), female gender (P=0.004), coronary artery disease (P=0.043), CLTI (P=0.002), small reference vessel diameter (P=0.003), less than 2 tibial run-off vessels (P=0.001). At multivariate analysis (Table IV), negative prognostic factors for AFS were coronary artery disease (P=0.041) and CLTI (P=0.011).

Discussion

The current multicenter experience shows that in the real-world practice about 3/4 of patients were treated for CLTI. The rate of ffTLR is high, and PP is substantially lower; small reference vessel diameter is negative factor for both ffTLR and PP. The rate of AFS is about 75% at 2 years and CLTI and coronary artery disease are negative prognostic factors.

The scientific base for the utility of Cook Zilver PTX stent in femoro-popliteal district for PAD is solid, based on data from randomized controlled trial (RCT) and large case series with 5-year results.[6] However, patients included in RCT are largely different from the daily-practice patients; in particular, the Zilver PTX Randomized Study[8] included only 9% of CLTI patients, arterial lesion involved the popliteal artery in about 8% and consisted in occlusion only in 28% of cases. Moreover, the majority of large

Table II.—*Factors influencing freedom from target lesion revascularization (ffTLR) calculated by uni- and multivariate Cox regression analysis.*

	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
Patient demographics						
Age	0.877	0.997	0.961-1.034			
Male gender	0.584	0.800	0.360-1.776			
Preoperative comorbidities						
Arterial hypertension	0.675	1.293	0.388-4.291			
Diabetes mellitus	0.886	1.057	0.493-2.262			
Dyslipidemia	0.706	1.165	0.525-2.583			
Smoke						
No smoker	0.413	1.801	0.712-4.566			
Smoker	0.223	3.300	1.182-9.259			
Ex-smoker	0.274					
Chronic renal failure	0.430	0.707	0.300-1.669			
Coronary artery disease	0.357	0.698	0.325-1.497			
Obesity	0.114	0.425	0.147-1.228	0.342	0.590	0.199-1.748
Rutherford classification						
CLTI	0.342	1.526	0.637-1.485			
Arterial characteristics						
Length of the treated lesion	0.424	1.003	0.996-1.009			
<120 mm	0.370	1.956	0.750-5.102			
≥120 mm and <200 mm	0.632	1.474	0.559-3.891			
≥200 mm	0.589					
Reference vessel diameter	<0.001	0.332	0.186-0.594	0.001	0.368	0.200-0.678
≥5 mm	0.002	0.177	0.058-0.536			
Popliteal involvement of the lesion	0.053	2.096	0.990-4.424	0.280	1.538	0.705-3.344
Chronic total occlusion	0.378	1.503	0.607-3.731			
Prior endovascular intervention of the treated segment	0.472	1.479	0.509-4.310			
Tibial run-off vessels						
2 or 3	0.143	0.569	0.268-1.210	0.354	0.700	0.330-1.485
Treatment data						
Number of stents						
≥2 stents/patient	0.843	1.090	0.462-2.570			

CLTI: chronic limb-threatening ischemia.

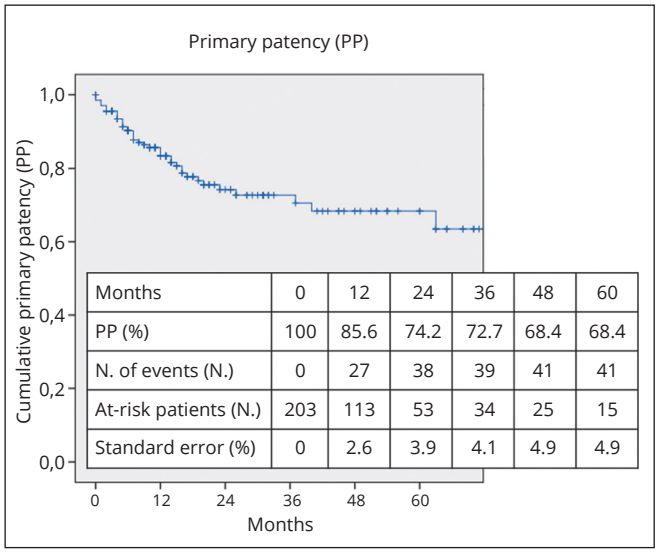


Figure 3.—Estimated primary patency (PP) rates according to Kaplan-Meier analysis.

series are supported by industry[6] and the industry-driven studies risk to be biased in favor of sponsored products.[9]

The current study includes all cases treated with this type of DES in three hospitals since its availability on the market. The non-experimental design permits to analyze data collected from daily practice, defining real-world data.[10] Specific publications on Zilver PTX without randomization and sponsor influence are few and include <200 patients without a follow-up ≥2 years.[11-14]

In real-world setting, the CLTI patient represent the majority of patients undergone to endovascular lower limb revascularization.[11, 15] Also in this case series, CLTI patients are prevalent (about 76%), while in many retrospective experiences this rate is largely inferior, ranging between 8 and 22%.[6, 16]

Considering the primary endpoint, rates of ffTLR during follow-up was comparable to a multistudy analysis including more than 2200 patients from 5 global studies.[6] In terms of arterial characteristics, both studies included arte-

TABLE III.—*Factors influencing primary patency (PP) calculated by uni- and multivariate Cox regression analysis.*

	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
Patient demographics						
Age	0.610	0.992	0.964-1.022			
Male gender	0.185	0.653		0.731	0.889	0.457-1.730
Preoperative comorbidities						
Arterial hypertension	0.219	2.092	0.645-6.756			
Diabetes mellitus	0.209	0.677	0.369-1.243			
Dyslipidemia	0.793	1.088	0.578-2.049			
Smoke						
No smoker	0.555	1.282	0.561-2.932			
Smoker	0.236	1.689	0.709-4.016			
Ex-smoker	0.473					
Chronic renal failure	0.335	0.711	0.356-1.420			
Coronary artery disease	0.711	0.891	0.486-1.633			
Obesity	0.220	0.330	0.129-0.840			
Rutherford classification						
CLTI	0.719	0.888	0.464-1.694			
Arterial characteristics						
Length of the treated lesion	0.704	1.001	0.995-1.007			
<120 mm	0.316	1.872	0.859-3.952			
≥120 mm and <200 mm	0.515	1.494	0.681-3.278			
≥200 mm	0.489					
Reference vessel diameter	<0.001	0.413	0.265-0.645	<0.001	0.435	0.274-0.689
≥5 mm	0.076	0.389	0.137-1.103			
Popliteal involvement of the lesion	0.153	1.584	0.843-2.985	0.368	1.329	0.698-2.531
Chronic total occlusion	0.668	1.162	0.584-2.314			
Prior endovascular intervention of the treated segment	0.949	1.030	0.404-2.624			
Tibial run-off vessels						
2 or 3	0.185	0.663	0.361-1.218	0.371	0.751	0.402-1.404
Treatment data						
Number of stents						
≥2 stents/patient	0.595	1.199	0.614-2.336			

CLTI: chronic limb-threatening ischemia.

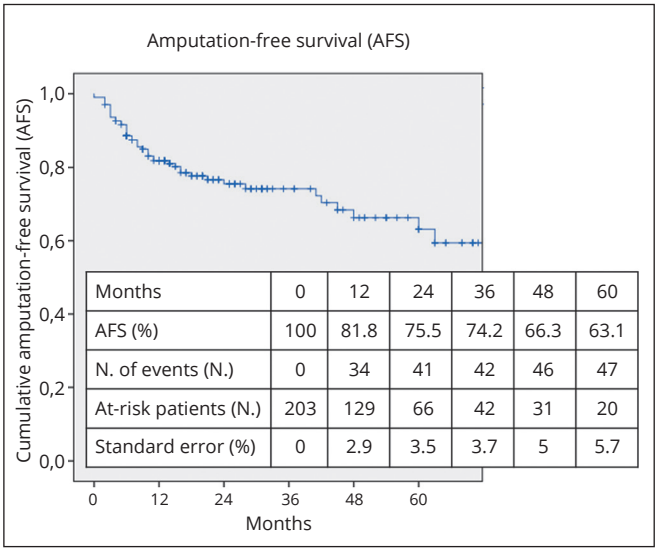


Figure 4.—Estimated amputation-free survival (AFS) rates according to Kaplan-Meier analysis.

rial lesion ≥200 mm in about 20% of cases. However, we treated more likely chronic occlusions (75% *vs.* 42%) and popliteal lesions (28% *vs.* 7.8%), with a worse tibial run-off (≥2 patent vessel: 61% *vs.* 71.4%). These considerable differences seem to confirm the utility of the Zilver PTX also in more challenging conditions. Instead of previous publications, no quantitative evaluation of arterial lesion calcifications was retrospectively available in our case series and no comparison was possible on this issue. Dake *et al.*[6] in 2020 developed a prediction model from ffTLR including 15 risk factors. Of those, only the reference vessel diameter resulted a negative prognostic factor in the current experience: an arterial diameter ≥5 mm reduces the risk of TLR of 0.3.

During the follow-up, the rate of stent PP was lower than ffTLR. At the considered intervals, the difference between ffTLR and PP ranged from 5% at 1 year to 12% at 2 years. At 2 years, 20 patients presented an intrastent restenosis or reocclusion requiring reintervention, while 18 patients

TABLE IV.—*Factors influencing amputation-free survival (AFS) calculated by uni- and multivariate Cox regression analysis.*

	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
Patient demographics						
Age	0.001	1.056	1.022-1.090	0.218	1.022	0.987-1.058
Male gender	0.004	0.435	0.246-0.771	0.097	0.556	0.278-1.111
Preoperative comorbidities						
Arterial hypertension	0.286	0.673	0.326-1.392			
Diabetes mellitus	0.289	1.377	0.762-2.487			
Dyslipidemia	0.831	1.067	0.589-1.926			
Smoke						
No smoker	0.366	0.510	0.197-1.321			
Smoker	0.972	1.088	0.389-3.039			
Ex-smoker	0.640					
Chronic renal failure	0.113	1.584	0.896-2.801	0.297	1.383	0.751-2.544
Coronary artery disease	0.043	1.814	1.019-3.236	0.041	1.912	1.026-3.571
Obesity	0.839	1.066	0.573-1.984			
Rutherford classification						
CLTI	0.002	22.222	3.086-166.666	0.011	13.513	1.821-100
Arterial characteristics						
Length of the treated lesion	0.765	0.999	0.994-1.005			
<120 mm	0.499	1.295	0.611-2.739			
≥120 mm and <200 mm	0.558	1.269	0.572-2.816			
≥200 mm	0.782					
Reference vessel diameter	<0.003	0.528	0.348-0.801	0.068	0.655	0.415-1.032
≥5 mm	0.052	0.393	0.153-1.007			
Popliteal involvement of the lesion	0.458	1.261	0.683-2.320			
Chronic total occlusion	0.954	1.018	0.545-1.901			
Prior endovascular intervention of the treated segment	0.340	0.607	0.218-1.692			
Tibial run-off vessels						
2 or 3	0.001	0.364	0.204-0.650	0.319	0.725	0.385-1.366
Treatment data						
Number of stents						
≥2 stents/patient	0.692	1.136	0.602-2.145			

CLTI: chronic limb-threatening ischemia.

an intrastent event with no clinical consequences. This finding confirmed that, despite high number of intrastent events, a considerable number of patients had no clinical consequences or remained pauci-symptomatic, without necessity of surgical or endovascular reintervention.

In literature, the rate of stent PP up to 5 years is rarely reported, especially considering non-sponsored studies (Table V).[3, 4, 8, 11, 12, 16-18] In the Zilver PTX Randomized Trial, 5-year PP of 319 stents is reported: at 1, 3 and 5 years, PP is 84.4%, 71.5% and 66.4%, respectively. In non-sponsored observational studies, PP resulted lower: at 1 year about 75% and at 2 years between 54% and 68%.[11, 12, 16] Differently from experience of Oberto *et al.*,[12] diabetics seems to have a comparable PP to the non-diabetic patients. As the ffTLR, our analysis reports that PP is influenced by the reference vessel diameter: 1-mm increase of arterial diameter reduces the risk of reocclusion/restenosis of 0.4.

Considering the AFS of the current study, one out four patients died or underwent major amputation within 2 years. AFS is not always reported in publications. AbuRahma *et al.*[11] included 115 limbs with Zilver PTX and reported AFS rates of 79% at 1 year and 71% at 2 years (mean follow-up 18.4 months); the majority of events are deaths, like in our experience. These AFS rates are comparable with our case series (at 1 and 2 years 82% and 76%, respectively) even if some differences in terms of patients' demographics and comoribilities are evident: outpatients were more likely male, older, with more diabetes, hypertension, dyslipidemia and CLTI; on the contrary, we had less patients with chronic renal failure and coronary artery disease. These differences in comorbility rates may explain the higher rate of AFS in our case series. The CLTI and coronary artery disease resulted independent risk factors for AFS: patients with rest pain or tissue loss have a 13-fold higher risk of major amputation or

TABLE V.—*Main publications reporting primary patency (PP) of Zilver PTX.*

First author and year of publication	Study design	Sponsored	DES limbs	Length of follow-up	1-year PP (%)	2-year PP (%)	3-year PP (%)	4-year PP (%)	5-year PP (%)
Current case series	Retrospective		203	23.2 months	85.6%	74.2%	72.7%	68.4%	68.4%
Tsujimura *et al.*[16] 2021	Retrospective with PSM		243	Median 2.4 years	74%	64%	59.5%	-	-
Lee *et al.*[17] 2021	Retro- and prospective cohort with PSM		102	Median 19.6 months	74.7%[a]	57.4%[a]	-	-	-
AbuRahma *et al.*[11] 2021	Retrospective cohort		115	18.4 months	75%	54%	-	-	-
Bosiers *et al.*[18] 2020	Randomized controlled trial		113	Not reported	74.5%	-	-	-	-
Dake *et al.*[3] 2016	Randomized controlled trial	X	305	Not reported	84.4%	76.3%	71.5%	67.4%	66.4%
Kichikawa *et al.*[4] 2018	Prospective, single-arm study	X	662	Not reported	85.5%	70.3%	-	-	-
Dake *et al.*[8] 2011	Prospective, single-arm study	X	787	Not reported	86.2%	-	-	-	-
Oberto *et al.*[12] 2015	Observational cohort		67	28 months	88%	68%	-	-	-

The length of follow-up is reported as mean; when mean is not available, median is reported.
PSM: propensity score matching.

death than claudicant patients, while patients with positive cardiologic anamnesis have about 2-fold higher risk. Since TASCII2007,[19] claudication and critical limb ischemia have been considered two conditions with completely different natural history and prognosis, and the extremely higher rate of AFS in claudicant patients is not surprising. Even the negative association between coronary artery disease and AFS is easily explainable and already reported in literature.[20, 21]

The hypothesis of lower survival in patients treated with drug-coated device[22] has been largely retracted both after femoro-popliteal and crural treatment.[23, 24] Recently, Ribeiro *et al.*[25] reported 57% of 5-year AFS after treatment with drug coating devices, comparable with 63% of our experience after Zilver DES.

Limitations of the study

The limitations of the study are several. Due to the retrospective design, some patient and lesion characteristics (*e.g.* hemodialysis, arterial calcification) were not available and these variables were not considered; moreover, type of endovascular recanalization (intraluminal *vs.* subintimal) was not reported in all databases and was not included in the analysis; no data on the patient compliance at the postoperative double antiplatelet therapy were available and no statins were considered in the pre- and postoperative periods; however, real-world non-sponsored case series including more than 200 patients with a >2 years follow-up are scarce in literature. The Zilver PTX were deployed in three different centers and four primary operators performed the DES deployment; however, the involvement of more centers permits to reach a consistent patient sample and more solid results. At last, some patients were lost at follow-up, reducing the overall length of mean follow-up.

Conclusions

In this real-world experience, results of Zilver PTX drug-eluting device in femoro-popliteal arterial lesions is promising. Despite high rate of CLTI patients, chronic total occlusion and popliteal involvement, the ffTLR and stent PP are comparable with previous large prospective. In small (<5 mm) femoro-popliteal arteries, the Zilver PTX reaches the worst results in terms of ffTLR and PP. The patients with CLTI or coronary artery disease have higher risk of major amputation and death. Further real-world studies with larger patient sample are needed to confirm or deny the results of sponsored trial and case series.

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