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Comparison Between Interwoven Nitinol and Drug Eluting Stents for Endovascular Treatment of Femoropopliteal Artery Disease

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WHAT THIS PAPER ADDS

This analysis compares the efficiency of interwoven nitinol stents with drug eluting stents for treatment of atherosclerotic lesions in the femoropopliteal artery with regard to clinically driven target lesion re-intervention at 12 months. Inverse probability treatment weighting was used to remove biased estimates given by data collection from non-randomly assigned treatment. The data do not provide conclusive evidence to favour one stent over the other including calcified lesions or popliteal artery involvement. Randomised controlled comparisons of different stent platforms with longer term follow up are needed to individualise treatment for patients with symptomatic femoropopliteal lesions.

Objectives: Information on performance of different stent platforms in endovascular revascularisation of femoropopliteal lesions is controversial and scarce.

Methods: Interwoven nitinol (INS, Supera) were compared with drug eluting (DES, Zilver PTx) stents with primary intervention for femoropopliteal lesions. The primary endpoint was time to clinically driven target lesion revascularisation (CD-TLR) within 12 months. Secondary endpoints were time to death, amputation and composite of death, amputation and CD-TLR. Due to the retrospective analysis, inverse probability treatment weighted (IPTW) Cox models were calculated to reach more similar patient populations with weights for the average treatment effect of the population. The two sensitivity analyses were propensity score matching and adjustment for covariates.

Results: At 12 months, the cumulative incidence of CD-TLR in the INS group (13%) and DES group (18%) did not differ (HR 1.36, 95% CI 0.56—3.31). A significant interaction between stents used and grade of calcification was observed ($p = .006$). HR for CD-TLR was 6.4 (95% CI 1.3—32.5) in none to mildly calcified favouring INS, and 0.3 (95% CI 0.1—1.3) for moderate to severely calcified lesions favouring DES. Stent efficiency did not differ comparing treatment of popliteal lesions (HR 0.80; 95% CI 0.21—3.13). Sensitivity analyses confirmed the primary efficacy outcome for either adjusted (HR 1.16; 95% CI 0.51—2.62) or matched analysis (HR 1.35; 95% CI 0.50—3.62)). Interaction of stents with calcification grade was lost for adjusted (HR 0.28; 95% CI 0.06—1.19) and matched analysis (HR 0.53; 95% CI 0.10—2.91).

Conclusion: Both stents (INS and DES) showed comparable results regarding CD-TLR in femoropopliteal lesions, so that one stent could not be favoured over the other, even for calcified or popliteal artery lesions.

Keywords: peripheral artery disease, lower extremity revascularisation, femoropopliteal segment, patency, drug eluting stents, self expanding interwoven nitinol stent
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INTRODUCTION

Peripheral artery disease (PAD) is a severe manifestation of atherosclerosis predominantly affecting the femoropopliteal segment causing intermittent claudication or critical limb ischaemia.

Endovascular revascularisation represents a standard, widely accepted, and recommended treatment for symptomatic PAD including chronic limb threatening ischaemia

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(CLTI).[1–4] Nevertheless, revascularisation of the femoropopliteal region remains challenging when looking at the full range of heterogenous lesion characteristics independently of the preferred treatment approach. Apart from morphology, length, and calcification grade of the target lesion, the distal femoral artery segment is especially exposed to physical forces through movement of the leg considered to be one causative factor for stent fracture and restenosis.[5,6]

To minimise re-intervention rates by overcoming mechanical challenges a bare metal interwoven nitinol stent (INS, Supera) is available offering better flexibility, radial strength and kink resistance. One of its advantages is the unique delivery system, which allows stacking of the stent especially in severely calcified lesions. Non-randomised trials and registry data have reported primary patency rates at one, two, and three years of up to 90%, 84% and 82%, respectively.[7,8] At present, the INS is regarded as the preferred choice for treatment of heavily calcified lesions.[9]

The most frequent mechanism causing restenosis and indication for target lesion revascularisation (TLR) is neointimal proliferation of the treated lesion. To reduce the rate of this undesired event, drug eluting stents (DES) were introduced, having shown their superiority compared with bare metal stents (BMS). Zilver PTx is a self expanding nitinol stent coated with polymer free paclitaxel on its outer surface. The primary patency at one and two years was shown to be 84% and 76%, respectively.[10] A recent five year study on stent performance showed a sustained clinical benefit superiority of DES over BMS.[11]

The aim of this study is to compare INS with DES in a wide range of femoropopliteal lesions of patients treated consecutively. Inverse probability weighted and sensitivity models were used to balance for confounding factors. Calcified and popliteal lesions were predefined as subgroups of interest.

METHODS

Study design

A retrospective, single centre analysis using hospital based patient data from a prospectively collected series of consecutive cases was conducted to compare the CD-TLR rate between an INS (Supera) and a DES (Zilver PTx) stent over a 12 month follow up period. All interventions were primary interventions for non-selected atherosclerotic femoropopliteal lesions. The analysis period from a tertiary vascular referral centre (Bern University Hospital, Switzerland) ranged between August 2012 and August 2016. Inclusion criteria were symptomatic PAD (Rutherford class 2–6) and evidence of severe stenosis or occlusion by duplex sonography (peak systolic velocity (PSV) ratio $>$ 2.4) or angiography. All lesion characteristics caused by atherosclerotic disease were included without restrictions by lesions length, grade of calcification or popliteal artery involvement. There were no limitations regarding prior percutaneous transluminal angioplasty (PTA) in other territories.

To enrol in the analysis patients had to be treated by implantation of either an INS or DES for any lesion located within the entire femoropopliteal segment (including P1 to P3).

Treatment was performed by four experienced operators according to institutional standards including digital subtraction angiography (DSA) prior to any manoeuvre as well as before termination of the intervention to assess procedural success and to rule out visible macro-embolisation. Vessel preparation to reference diameter using plain old balloon angioplasty (POBA) prior to stent placement as well as post-dilation of the stented segment were performed as standard. Use of debulking devices or stents other than study devices for the same target lesion or drug coated balloons were exclusions. Choice of access site, treatment of inflow and outflow lesions, use of additional devices for crossing total occlusions and choice of either INS or DES were at the discretion of the operator.

A 5000 IU bolus of unfractionated heparin was given intravenously during the intervention. An initial loading dose (clopidogrel 300 mg orally or aspirin 250 mg intravenously) was followed by dual antiplatelet therapy (aspirin/clopidogrel) for three months followed by long term antiplatelet monotherapy (either aspirin 100 mg/d or clopidogrel 75 mg/d), unless contraindicated or when patients were already taking oral anticoagulants.[1,12,13] Patients were assessed by oscillometric reading, ankle brachial and toe brachial pressure index (ABI/TBI) to confirm patency before discharge and at three, six and 12 months follow up.

The study was in accordance with the Declaration of Helsinki and was approved by the cantonal ethics committee.

DSAs were retrospectively evaluated in consensus between three investigators (A.H., M.J.S. and J.F.D.) to assess stent placement within one or more arterial segments including proximal, middle, distal superficial femoral artery (SFA) and popliteal artery (P1–P3). Lesion characteristics were rated for grade of vessel calcification (none, mild, moderate, severe) by visual assessment according to the PARC classification,[14] lesion length[17] and below knee vessel runoff (1, 2, or 3). For INS the ratio of the absolute stent length deployed compared with its length intended to use as fabricated was analysed if the primary endpoint (CD-TLR) was reached.[8]

Study endpoints

The primary efficacy endpoint was time to CD-TLR within 12 months. Secondary endpoints were time to death, time to amputation, and a composite of time to death, amputation, and CD-TLR. CD-TLR was defined as target lesion revascularisation performed for target lesion diameter stenosis $>$50% and either evidence of clinical or functional ischaemia (e.g. recurrent/progressive intermittent claudication, critical limb ischaemia) or recurrence of the clinical syndrome for which the initial procedure was performed. CD-TLR occurs in the absence of protocol directed surveillance ultrasound or angiography.[15]

Study devices

Briefly the INS (Supera®; Abbott Laboratories, Illinois, CE n° 0086) is built from six pairs of interwoven nitinol wires, arranged in a helical pattern, thus being both flexible and resistant to fracture. In this study stent diameters between 4 and 6 mm with reference to inner diameter and length from 40 to 200 mm were used.

The DES (Zilver PTx®; Cook Medical Inc., Bloomington, CE n° 0088) is coated with polymer free paclitaxel on its outer surface. During the trial, stent diameters between 4 and 6 mm with reference to outer diameter and length from 40 to 120 mm were used. Details for each stent are described in the manufacturer's manual.[12,13]

Statistical analyses

Since data were collected retrospectively with non-randomly assigned treatment, the two stent groups differed with respect to baseline patient and lesion characteristics (Table 1). Primary data analysis was performed by inverse probability treatment weighting (IPTW) to remove biased estimates and to achieve more similar patient populations in the two groups. IPT weights were calculated for the average treatment effect of the population (ATE), since the primary objective was a comparison between two stents, i.e. all patients were treated. To calculate IPT weights, propensity scores were first calculated using a logistic regression model with the stent group as response variable (INS group as control) and baseline pre-treatment characteristics as covariates (see Table S1 in supplementary material). Next, propensity scores were trimmed at the 2.5th percentile of the DES group and at the 97.5th percentile of the INS group. Patients with a propensity score outside of these limits were removed from the analysis, resulting in 77 patients treated with a DES and 74 patients treated with an INS in the primary analysis. Finally, inverse probability treatment weights were calculated as 1/(1 - ps) for the INS (control) group, and 1/ps for the DES (treatment) group, where ps denotes the propensity score.

Missing pre-treatment variable values used in the propensity score model were imputed using single imputation, assuming values to be missing at random. Continuous variables were imputed using predictive mean matching, and binary data using logistic regression. Single imputation was used because of the negligible number of missing values in pre-treatment variables, and since these variables were used for calculation of propensity scores only, and not to estimate effect sizes, standard errors or *p* values. Two sensitivity analyses were performed. First, the models were adjusted for covariates, using all patients available, i.e. 124 in the INS group, and 110 in the DES group (see Table S1, supplementary material). Second, propensity score matching was performed. Nearest neighbour matching with the same propensity score model as in the primary analysis was used, discarding observations at both tails, resulting in 54 patients in each group.

Time to event outcomes were analysed using the weighted Aalen (hazard based) estimator from Kaplan—Meier analysis, and hazard ratios (HR; relative risk) from Cox proportional hazard models, using a robust variance estimator. In subgroup analyses of the primary endpoint (CD-TLR), the interaction between calcification (none to mild *vs.* intermediate to severe) and stent group, and the interaction between popliteal involvement (binary) and stent group were tested. In the primary analysis, subjects were allocated to the subgroups based on the IPTW cohort. In sensitivity analyses, subjects were allocated to subgroups in the respective analysis sets, i.e. the matched cohort, or the complete case data set.

All statistical analyses were performed using R (Version 3.5.0 R Foundation for Statistical Computing, Vienna, Austria), with the packages survival (version 2.41.3) for weighted Cox proportional hazard models, survey (version 3.33.2) for weighted Kaplan—Meier analysis, MatchIt (version 3.0.2) for propensity score matching, and *mice* (version 3.0.0) for single imputation of pre-treatment characteristics.

RESULTS

Description of study population

As explained in the methods section, 234 consecutive patients overall were treated for femoropopliteal lesions using either INS or DES (Fig. 1, flow chart). Due to the retrospective character of the analysis, IPTW was performed in order to achieve more similar patient populations, leaving 151 patients (primary study population) to be included in the data set after weighting, for primary analysis (INS, $n = 74$ *vs.* DES, $n = 77$) with a high prevalence of male gender (69.7% *vs.* 64.1%), diabetes (45.7% *vs.* 49.3%), and critical limb ischaemia (38.1% *vs.* 36.2%, Table 1). Lesions were intermediately long (12.2 cm *vs.* 11.6 cm) with a high rate of occlusions (74.4% *vs.* 71.6%), severe calcification (38.9% *vs.* 40.1%), popliteal involvement (39.7% *vs.* 36.9%) and TASC C/D lesion type (34.2% *vs.* 32.2%).

Primary efficacy endpoint

The primary analysis was an IPTW analysis. The cumulative incidence of CD-TLR did not differ significantly between INS and DES (HR 1.36, 95% CI 0.56—3.31, Table 2). CD-TLR was 13% (95% CI, 5%—21%) in the INS group, and 18% (95% CI; 8%—27%) in the DES group at 12 months follow up (Fig. 2).

Secondary endpoints

INS and DES did not differ significantly regarding secondary endpoints. The cumulative incidence of death and amputation was comparable in both groups. The HR for reaching the composite endpoint of death, major amputation and CD-TLR was 1.2 (95% CI 0.59—2.47) for the DES over the INS (Table 3).

Table 1. Baseline patient and lesion characteristics and standardised differences for comparison between the two stent groups intervowen nitinol stents (INS) or drug eluting stents (DES) before and after inverse probability treatment weighting[a]. Due to the weighting absolute patient numbers are not provided

Characteristics	Crude (n = 234)						Weighted (n = 151)			
	INS		DES		Standardised difference	p	INS (n = 74)	DES (n = 77)	Standardised difference	p
	n	n (%) or mean ± SD	n	n (%) or mean ± SD						
Patient characteristics										
Gender – male	124	87 (70.2)	110	73 (66.4)	0.08	.63	69.7	64.1	0.12	.55
Age – years	124	77.3 ± 10.0	110	69.7 ± 10.0	0.77	<.001	73.0 ± 10.7	72.3 ± 8.8	0.06	.75
BMI	124	26.7 ± 4.4	110	26.9 ± 5.1	0.02	.85	27.6 ± 4.6	28.3 ± 6.4	0.12	.60
Smoking	124		110			.01				.14
Active		40 (32.3)		54 (49.1)	0.35		38.4	42.2	0.08	
Ex		48 (38.7)		38 (34.5)	0.09		36.1	41.6	0.11	
Never		36 (29.0)		18 (16.4)	0.31		25.5	16.2	0.23	
Diabetes	124	49 (39.5)	110	52 (47.3)	0.16	.29	45.7	49.3	0.07	.71
Hypertension	124	114 (91.9)	110	95 (86.4)	0.18	.24	87.9	88.4	0.01	.94
Hyperlipidaemia	124	100 (80.6)	110	97 (88.2)	0.21	.16	83.7	82.7	0.03	.90
CKD[b]	124	54 (43.5)	110	30 (27.3)	0.35	.01	33.5	35.4	0.04	.83
Rutherford St.	124		110			.13				.07
1		2 (1.6)		2 (1.8)	0.02		3.0	2.2	0.05	
2		20 (16.1)		17 (15.5)	0.02		19.5	11.3	0.23	
3		44 (35.5)		55 (50.0)	0.30		39.4	50.2	0.22	
4		11 (8.9)		8 (7.3)	0.06		11.1	7.3	0.13	
5		43 (34.7)		28 (25.5)	0.20		24.9	28.9	0.09	
6		4 (3.2)		0 (0.0)	0.26		2.1	0.0	0.21	
CAD	124	58 (46.8)	110	42 (38.2)	0.17	.23	40.5	38.6	0.04	.84
CVD	124	14 (11.3)	110	16 (14.5)	0.10	.58	9.3	16.4	0.22	.25
ABI before PTA	88	0.6 ± 0.2	83	0.6 ± 0.2	0.12	.44	0.6 ± 0.3	0.6 ± 0.2	0.01	.96
TBI before PTA	53	0.3 ± 0.1	50	0.4 ± 0.1	0.69	<.001	0.3 ± 0.2	0.4 ± 0.1	0.55	.04
Lesion characteristics										
Lesion length – cm	124	14.0 ± 9.0	110	10.1 ± 7.4	0.48	<.001	12.2 ± 7.7	11.6 ± 8.5	0.07	.72
Target lesion stenosis	124	38 (30.6)	110	46 (41.8)	0.23	.10	25.6	28.4	0.06	.71
Calcification	124		110			<.001				.52
None		6 (4.8)		30 (27.3)	0.64		9.8	12.1	0.07	
Mild		27 (21.8)		28 (25.5)	0.09		36.7	29.3	0.16	
moderate		25 (20.2)		24 (21.8)	0.04		14.6	18.5	0.11	
severe		66 (53.2)		28 (25.5)	0.59		38.9	40.1	0.02	
Popliteal involvement	124	87 (70.2)	110	22 (20.0)	1.17	<.001	39.7	36.9	0.06	.76
Runoff	124		110			.006				.03
1		38 (30.6)		34 (30.9)	0.01		25.9	30.3	0.10	
2		60 (48.4)		34 (30.9)	0.36		46.2	31.4	0.31	
3		26 (21.0)		42 (38.2)	0.38		27.9	38.3	0.22	
TASC Classification	124		110			<.001				.15
A		2 (1.6)		1 (0.9)	0.06		0.9	3.7	0.19	
B		66 (53.2)		80 (72.7)	0.41		64.9	64.1	0.02	
C		24 (19.4)		23 (20.9)	0.04		22.3	25.7	0.08	
D		32 (25.8)		6 (5.5)	0.58		11.9	6.5	0.19	

INS = Interwoven Nitinol Stent (Supera); DES = Drug Eluting Stent (Zilver PTx); BMI = Body Mass Index; CKD = Chronic Kidney Disease; CAD = Coronary Artery Disease; CVD = Cerebrovascular Disease; ABI = Ankle brachial Index; TBI = Toe Brachial Index; TASC = Trans-Atlantic Inter-Society Consensus; PTA = percutaneous transluminal angioplasty; SD = standard deviation. ABI and TBI have many missing values and were therefore not used for weighting. Further, gender, BMI, CAD, and CVD were assumed to have no influence on the outcome and were thus not used for weighting, either. P values for continuous variables are based on ANOVA models, categorical variables are compared with chi-square or fisher exact test. Absolute standardised differences are shown.

[a] Continuous data are presented as the mean ± standard deviation; categorical data are given as the counts (percentage).

[b] eGFR (estimated glomerular filtration rate) <60 ml/min.

Pre-specified subgroup analysis

Subgroups were only analysed for CD-TLR. Calcification significantly interacted with stent group ($p = 0.006$). The HR in non- or mildly calcified lesions was 6.42 (95% CI 1.27–32.48), with the incidence of CD-TLR of 6% in the INS group compared with 33% in the DES group. In contrast, the HR in moderate to severe calcified lesions was 0.32 (95% CI 0.08–1.26), with a high cumulative incidence of CD-TLR in the INS

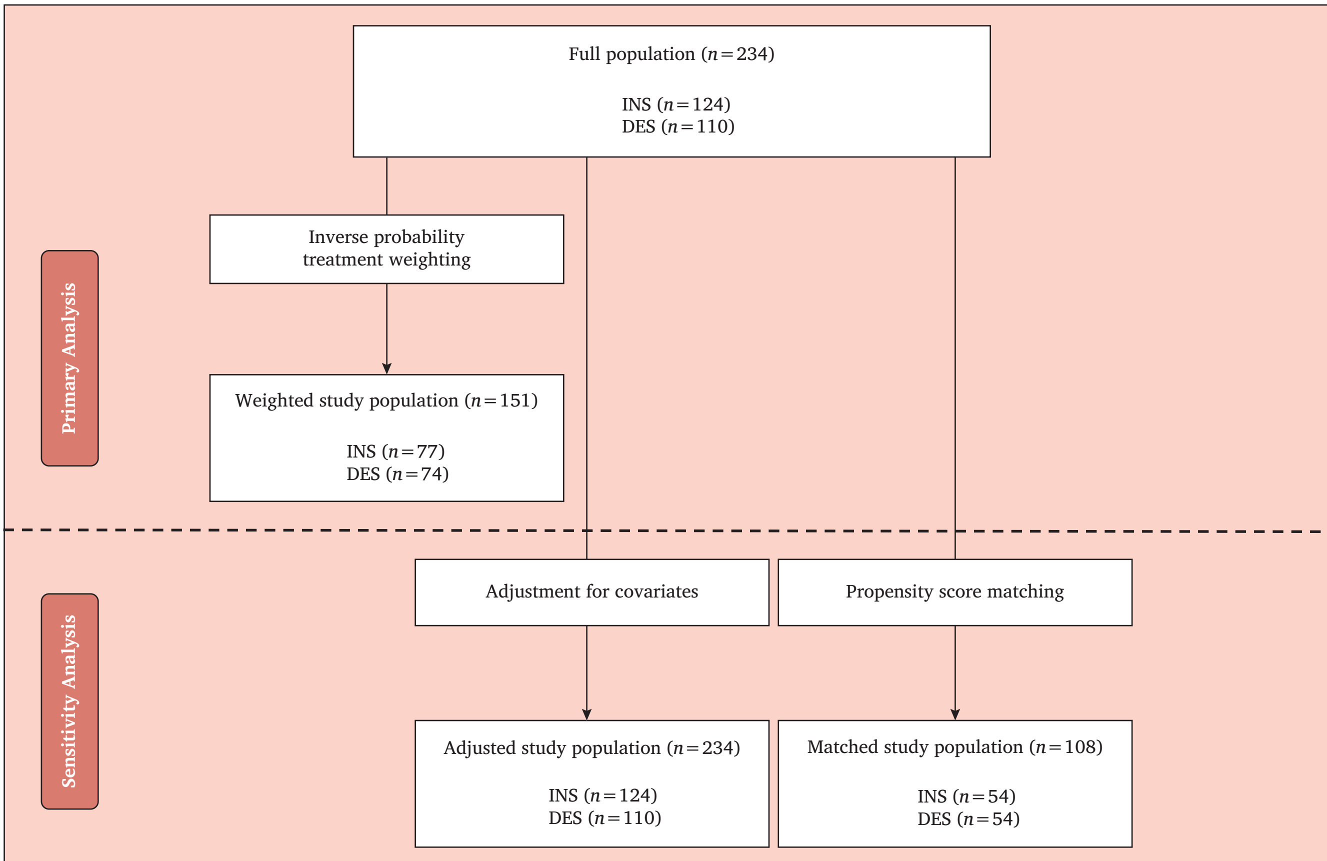

Figure 1. Flow chart of 234 consecutive patients treated for femoropopliteal lesions using either Intervowen Nitinol Stent (Supera) (INS) or Drug Eluting Stent (Zilver PTx) (DES) for comparison between the two stent groups. For primary analysis the statistical model of inverse probability treatment weighting (IPTW) was used. For sensitivity analyses, adjustment for covariates and a propensity score matched analysis were performed.

group and a low cumulative incidence of CD-TLR in the DES group (Fig. 3). Popliteal involvement did not significantly interact with the stent group (Fig. 3).

Sensitivity analyses

Two separate sensitivity analyses, one adjusting for covariates, another with propensity score matching, confirmed the primary analysis of primary and secondary outcomes with no significant difference in CD-TLR (see Fig. 4 A—C, Table S2 in supplementary material). Subgroup results regarding differences in CD-TLR related to calcification could not be confirmed and had to be discarded based on sensitivity analyses (see Table S3 in supplementary material).

In the full study population, fourteen patients from the INS group had CD-TLR. Of these patients, five had stent elongation (36%): one minimally (10—20%), three moderately (20—40%) and one severely (>40%) elongated.

DISCUSSION

Patients treated for symptomatic PAD including CLTI for whom there are only few high quality comparative data to guide the choice of a specific endovascular approach were analysed.[1,2] Patient and lesion characteristics differed significantly in the two stent groups showing the bias in syent use being effective in clinical routine. After inverse probability weighted and sensitivity analyses to compensate for confounding factors and to reduce imbalances, no clinically relevant differences were found for any of the endpoints to justify preference for one stent over the other in a wide range of femoropopliteal lesions including calcification or popliteal artery involvement.

Results from stringently designed RCTs using different stent platforms are scarce and prone to selection bias with limited information on patient subgroups.[16] Dake et al. were the first to report on the superiority of DES over BMS,[10] with a 43% lower risk of target vessel revascularisation for DES at 12 months.[17] However, comparing DES to BMS, no significant difference was shown regarding primary patency.[18] INS has never been tested *vs.* other stents in an RCT. In a large, single centre analysis of propensity score matched pairs, the INS demonstrated superior primary patency up to three years compared with other self expanding nitinol stents.[19] There was a striking coincidence with the present data regarding the preferred use of an INS in patients with severely calcified and popliteal lesions.[17,19]

Okuno *et al.* demonstrated independently worse clinical outcome after endovascular treatment of severely calcified at 12 months.[6,20] The INS is a stent promoted as specially

Table 2. Procedural and post-procedural characteristics of patients treated for femoropopliteal lesions from both Interwoven Nitinol Stent (INS) and Drug Eluting Stent (DES) groups after weighting. Due to the weighting absolute patient numbers are not provided

Procedural and post-procedural characteristics	Weighted		
	INS (n = 74)	DES (n = 77)	p
Mean number of investigated stents ± SD	1.2 ± 0.4	1.5 ± 0.8	.08
Mean stent length ± SD − mm	160.6 ± 83.8	124.1 ± 86.2	.04
Mean stent diameter ± SD − mm	5.3 ± 0.7	5.8 ± 0.7	.003
Medication			
Antiplatelet therapy at discharge − %			.004
None	0.0	0.8	
SAPT	12.5	3.9	
DAPT	72.6	68.8	
OAC	1.0	0.0	
SAPT or DAPT with OAC	13.9	26.5	
Statins	81.1	61.9	.03
Ezetimibe	11.4	3.9	.12
Laboratory data			
LDL-C	2.3 ± 1.2-mmol/L	2.4 ± 0.9-mmol/L	.83
Creatinine	99.5 ± 67.1-μmol/L	102.6 ± 94.7-μmol/L	.81
eGFR (CKD-EPI)	66.2 ± 22.0-ml/min	66.6 ± 20.0-ml/min	.93
HbA1c	6.2 ± 1.2-%	6.4 ± 1.3-%	.53

SD = standard deviation; INS = Interwoven Nitinol Stent (Supera); DES = Drug Eluting Stent (Zilver PTx); SAPT = Single Antiplatelet Therapy; DAPT = Dual Antiplatelet Therapy; OAC = Oral Anticoagulation; LDL-C = Low Density Lipoprotein Cholesterol; eGFR = estimated Glomerular Filtration Rate; HbA1c = Haemoglobin A1c; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration. p values for continuous variables are based on ANOVA (analysis of variance) models, categorical variables are compared with chi-square or fisher exact test.

designed for heavily calcified lesions, and its unique abilities[8,9] have been associated with the high primary patency rates (81%) and 12 month freedom from TLR (72%).[21,22] In contrast to expectations, in the initial primary analysis the two stents showed an opposite performance in none to mild and intermediate to severe calcified lesions. This result was not stable and was lost in sensitivity analyses, showing that many confounders come into play biasing reflection of stent performance. One confounder might be more or less rigorous vessel preparation depending on the stent being used.

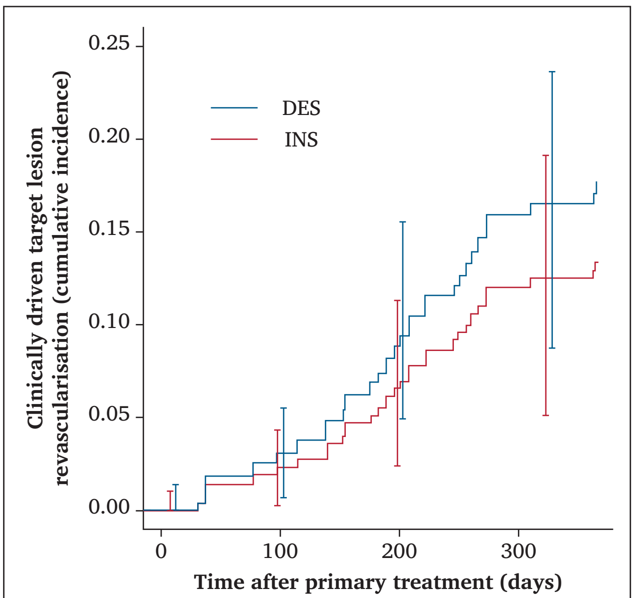

Figure 2. Clinically driven target lesion revascularisation at 12 months after treatment of femoropopliteal lesions with either Interwoven Nitinol Stent (Supera) (INS) or Drug Eluting Stent (Zilver PTx) (DES), Cumulative incidence of INS and DES in the inverse probability treatment weighted analysis up to 12 months after intervention. Confidence intervals are shown at 10, 100, 200 and 325 days after intervention (n = 151, weighted study population).

Based on several human studies, the effect of drug delivery seems to be reduce in highly calcified lesions.[18,23,24] On the other hand, DES demonstrated excellent results, with freedom from TLR above 90% at 12 months in patients with moderate to severely calcified lesions.[20] These contradictions remain unresolved and leave room for further clarification.

Next to calcification, popliteal artery treatment remains a problem regarding stent fracture and reduced patency rates and is explained by the tremendous physical forces within this segment.[25,26] Many stent trials are limited to the proximal popliteal artery segment. The INS theoretically has characteristics to be advantageous for this segment. Results from several single arm trials with cumulatively more than two hundred patients treated with INS in the popliteal artery demonstrated primary patency rates ranging from 70.3% to 89.6% at 12 months follow up.[27−30] The present data are discordant regarding preference of the INS over DES for popliteal artery treatment.

Considering stent deployment, pitfalls like absolute length inserted or intussusception have been analysed with discordant results for the INS regarding stent performance. Garcia *et al.* reported on the significant impact of gross oversizing in 26 out 177 patients on loss of patency at 12

Table 3. **Primary and secondary endpoints (target lesion revascularisation, death, amputation), up to 12 months after treatment of femoropopliteal lesion with either Interwoven Nitinol Stent (Supera) (INS) or Drug Eluting Stent (Zilver PTx) (DES). The cumulative incidence from Kaplan–Meier analysis, and the hazard ratio and *p* value from a weighted Cox proportional hazard model with robust variance estimator are presented**

Primary and secondary endpoint	INS ($n = 74$) Cumulative incidence (95% CI)	DES ($n = 77$) Cumulative incidence (95% CI)	Hazard Ratio (95% CI)	*p*
CD-TLR	0.13 (0.05–0.21)	0.18 (0.08–0.27)	1.36 (0.56–3.31)	.50
Death	0.06 (0.00–0.13)	0.13 (0.02–0.23)	2.12 (0.40–11.10)	.37
Amputation	0.09 (0.02–0.15)	0.05 (0.00–0.11)	0.63 (0.17–2.29)	.48
CD-TLR, death, and amputation	0.25 (0.13–0.35)	0.30 (0.17–0.41)	1.20 (0.59–2.47)	.62

INS = Interwoven Nitinol Stent (Supera); DES = Drug Eluting Stent (Zilver PTx); CD-TLR = clinically driven target lesion revascularisation; CI = confidence interval.

	Interwoven Nitinol Stent		Drug Eluting Stent		Hazard ratio (95% CI)	*p*
	n	Incidence (95% CI)	*n*	Incidence (95% CI)		
Overall	74	0.13 (0.05 – 0.21)	77	0.18 (0.08 – 0.27)	1.36 (0.56 to 3.31)	.50
Calcification						.006
None to mild	27	0.06 (0.00 – 0.14)	35	0.33 (0.13 – 0.49)	6.42 (1.27 to 32.47)	
Intermediate to severe	47	0.19 (0.06 – 0.31)	42	0.06 (0.00 – 0.13)	0.32 (0.08 to 1.26)	
Popliteal involvement						.25
No	41	0.16 (0.03 – 0.27)	19	0.31 (0.06 – 0.50)	2.25 (0.70 to 7.22)	
Yes	33	0.12 (0.00 – 0.22)	58	0.10 (0.01 – 0.18)	0.80 (0.21 to 3.13)	

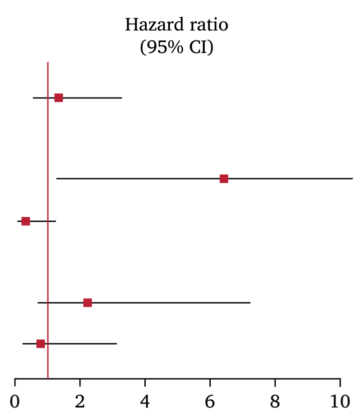

Figure 3. Subgroup analyses of calcification and popliteal involvement on clinically driven target lesion revascularisation at 12 months in patients treated for femoropopliteal lesion with either Interwoven Nitinol stent (Supera) (INS) or Drug Eluting Stent (Zilver PTx) (DES). Cumulative incidence of INS and DES up to 12 months after intervention from Kaplan–Meier analysis, and the hazard ratio and *p* value from a weighted Cox proportional hazard model with robust variance estimator are presented. CI = confidence interval.

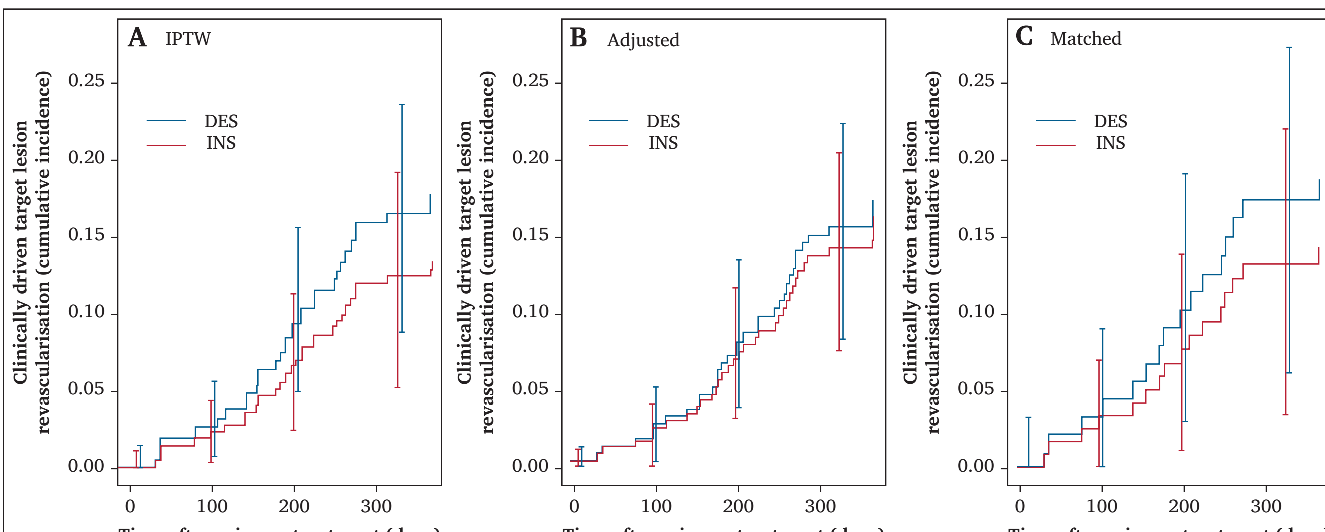

Figure 4. Sensitivity analyses of the primary endpoint of clinically driven target lesion revascularisation in patients treated for femoropopliteal lesions with either Interwoven Nitinol Stent (Supera) (INS) or Drug Eluting Stent (Zilver PTx) (DES). Cumulative incidence of INS and DES up to 12 months after intervention for A) inverse probability treatment weighted (IPTW, primary analysis) ($n = 74/77$), B) adjusted analysis of full population ($n = 124/110$) and C) propensity score matched analysis ($n = 54/54$). Confidence intervals are shown at 10, 100, 200 and 325 days after intervention.

months and freedom from CD-TLR 24 and 36 months after intervention.[8] Real world experience with smaller patient series did not find comparable results concerning loss of primary patency at 12 months.[31] In the present series, of those 14 patients from the full data set who had CD-TLR up to 12 months after stent placement, only one patient showed severe INS length elongation.

To the authors' knowledge this is the first direct comparison of frequently used stents for treatment of the full range of various femoropopliteal lesions. Both stents have different key characteristics to overcome previous limitations in endovascular treatment of femoropopliteal lesions. The strength of the present analysis is the consecutive data collection from a real world setting and a dedicated statistical analysis to reduce heterogeneities in patient and lesion characteristics. Undeniably, with several uncertainties remaining, there is need to supplement evidence from randomised controlled trials and other existing data by further well conducted trials. These must include follow up data beyond 12 months considering the ongoing discussion regarding the meta-analysis by Katsanos *et al.* on mortality risk associated with the use of paclitaxel eluting devices.[32,33]

There are several limitations which should be acknowledged. The study is a retrospective analysis reflecting single centre experience. It is not possible to report on details, i.e. balloon sizing, inflation time, regarding treatment algorithm with specific focus on vessel preparation which is accepted to be of great importance to improve outcome from endovascular treatment. Despite the attempt to rule out selection bias by using IPTW analysis additional confounding factors regarding the operator's decision for one stent over the other may remain. Moreover the operator's individual treatment approach, although equally experienced, may have had an impact on outcome measures that were not considered in the present analysis. Finally, the analysis was limited to 234 patients covering a time period during which both stents analysed were first choice. The analysis of subgroups and further confounders has methodological limitations due to the low number of patients, especially after weighting and propensity score matching, potentially resulting in a risk of type II error. Finally the survival time analysis may be too short to generate differences between stent performances.

The analysis results might be taken into account considering the 2017 ESVS PAD guidance that favours the use of a DES in their recommendations on revascularisation of femoropopliteal lesions.[1]

In conclusion, INS and DES showed comparable efficiency regarding CD-TLR in a large range of atherosclerotic femoropopliteal artery lesions, although with considerable uncertainty around the point estimate. Overall the data do not provide conclusive evidence to favour one stent over the other including calcified lesions or popliteal artery involvement. Undeniably, with several uncertainties remaining, there is need to supplement evidence from randomised controlled trials and other existing data by further well conducted trials.

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DECLARATION OF INTEREST

None.

APPENDIX A. SUPPLEMENTARY DATA

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