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Interwoven Nitinol Stents *versus* Drug Eluting Stents in the Femoro-Popliteal Segment: A Propensity Matched Analysis

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WHAT THIS PAPER ADDS

Percutaneous transluminal angioplasty (PTA) is a common treatment for femoro-popliteal segment (F-P) atherosclerotic disease. The use of biomimetic nitinol stents (Supera peripheral stent, SPS) or drug eluting stents (DES) may improve F-P PTA patency. These devices, however, have not been compared in a pragmatic setting taking plaque characteristics into account. This case matched analysis shows that SPS and DES have comparable results in F-P PTA. Using a DES did not confer a measurable benefit in terms of patency or clinical results at two years. At the same time, the SPS also did not confer a benefit in the heavily calcified plaques.

Background: Percutaneous transluminal angioplasty (PTA) is a common procedure in patients with peripheral arterial disease (PAD) affecting the femoropopliteal segment (F-P). Biomimetic nitinol stents (Supera peripheral stent, SPS) and drug eluting stents (DES) were designed to improve the longevity of F-P PTA; however, their performance has not been compared in a pragmatic setting, taking atherosclerotic plaque characteristics into account.

Methods: Overall, 296 consecutive patients (mean age: 73 y, SD: 11 y, 65% male, 68% with chronic limb threatening ischaemia) who underwent F-P PTA using SPS or DES between 2013 and 2018 were identified from a prospectively maintained institutional database. Patient and plaque characteristics, including F-P plaque characterisation based on computed tomography, were collected; 121 case matched pairs were created using a propensity score based on patient and plaque data.

Results: During the median two year follow up, 28% of the cohort (32% SPS *vs.* 24% DES, $p = .07$) developed target lesion restenosis (TLR) $>$ 50%. Among the 121 case matched pairs of patients, those with SPS *vs.* DES were not significantly more likely to develop TLR $>$50% (31% *vs.* 27%, $p = .34$), or stent occlusion (13% *vs.* 12%, $p = .85$ – secondary patency rate 87% *vs.* 88%), have a major amputation (10% *vs.* 6%, $p = .16$), require re-intervention (14% *vs.* 9%, $p = .12$), or die (7% *vs.*4%, $p = .31$). Plaque calcification did not predict restenosis or occlusion in either stent group, both in the matched and non matched populations. Multivariable analysis adjusted for patient and plaque characteristics revealed that the main predictors of restenosis $>$50% at two years were female sex [odds ratio (OR): 2.05, $p = .01$], hypertension (OR: 2.10, $p = .04$) and previous F-P occlusion (OR: 1.35, $p = .04$).

Conclusion: Medium term results following F-P PTA with either SPS or DES are comparable, regardless of plaque calcification and patient characteristics.

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INTRODUCTION

Percutaneous transluminal angioplasty (PTA) is a routine treatment in lower limb peripheral arterial disease (PAD) and is recommended by international guidelines.[1] The femoropopliteal segment (F-P) is the most commonly treated site, although durability of PTA in this area is challenged by vessel mobility, multilevel disease, presence of calcified plaque, and neointimal hyperplasia.[2]

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Endovascular stents are used increasingly to address these issues and improve long term patency.[3] Complications of stent implantation in the F-P segment however, include in stent restenosis or occlusion and stent compression or fracture.[4] Initial designs of laser cut bare nitinol stents have now evolved to target these issues. The Supera peripheral stent (SPS; Abbott Laboratories, IL, USA), a self expanding biomimetic nitinol stent formed of interwoven wires, is designed to adapt to arterial anatomy and reduce stent fracture.[5] Drug eluting stents (DES), which combine a stent platform with a cytostatic or cytotoxic drug such as paclitaxel, may prevent restenosis by inhibiting neo-intimal hyperplasia over the long term. Some studies suggest superiority of paclitaxel eluting stents over bare metal stents.[6–9] At the same time, they may be less cost effective and some investigators have suggested that the use of paclitaxel may be associated with increased long term mortality.[10] To the authors' knowledge, there has been no direct comparison of SPS and DES in the treatment of F-P stenotic/occlusive disease.

Heavy calcific plaque burden is a major predictor of restenosis and a common reason why a stent may be advocated following angioplasty. The present study group has previously reported that the percentage of calcified plaques independently predicts restenosis at one year and absolute volume of calcified plaque was independently associated with amputation free survival after PTA in the F-P segment.[11]

In view of the above, the performance of SPS and DES in the F-P segment remains unclear, especially in patients with calcified plaques. The aim of this study therefore, was to compare outcomes after implantation of SPS or DES in the F-P segment in two propensity matched groups and to investigate the influence of calcific plaque composition on outcomes.

METHODS

Patient selection

A prospectively maintained database (2013—2018) in a tertiary referral centre was screened for consecutive patients meeting the following inclusion criteria: patients with incapacitating intermittent claudication or chronic limb threatening ischaemia (Rutherford stage 3—6); F—P disease (>70% stenosis based on a computed tomography angiogram following an initial duplex assessment) undergoing endovascular treatment by stenting of the F-P segment using either a SPS or a DES [Zilver PTX stent (Cook Medical, IN, USA) or Eluvia stent (Boston Scientific, Marlborough, MA, USA)]. Stenting of the F-P segment in the institution during the study period was reserved for patients requiring an F-P angioplasty who had residual stenosis >50% and/or flow limiting dissection post plain balloon angioplasty (POBA). The decision to use a stent was made intra-operatively based on the lesion response to POBA and the preferences of the operator; all operators were qualified consultant endovascular surgeons or interventional radiologists. All devices were used as per the manufacturers' instructions for use.

Exclusion criteria were intervention for acute limb ischaemia; previous F-P stenting; F-P intervention proximal to a bypass; significant aorto-iliac or common femoral stenosis; previous F-P angioplasty within one year. The study complied with the Declaration of Helsinki and NHS Caldicott principles. Approval was granted by the King's Health Partners and Guy's and St Thomas' NHS Foundation Trust Audits and Service Evaluation Department.

Imaging

All CTAs were obtained as part of routine clinical care. As per departmental policy, patients presenting with symptoms of claudication or chronic limb threatening ischaemia undergo a duplex scan first and then a CTA to plan intervention. All CTAs were performed using a standardised protocol in helical scanning mode from the aortic bifurcation to the toes. Studies were collimated at 0.625 mm, with a peak kilovoltage of 120, automated milliamps and a rotation time of 64 × 0.75 s. Approximately 100 mL of iodinated contrast were administered at 4 mL/s using a power injector. Both duplex and CTAs were analysed and reported as per the Society for Vascular Surgery reporting standards.[12] All procedures were planned using the latest pre-operative CTA; duplex was used as the initial assessment method prior to CTA. The CTA proportion of stenosis was calculated using 3D reconstruction and estimating the proportion (area) taken by plaque at the level of the lesion. During follow up (surveillance) all interventions were again planned using CTA, following an initial assessment with duplex. Patients with a peak systolic velocity (PSV) of >180 cm/s within the treated site and PSV ratio of >2.5 across the lesion were further investigated by CTA during surveillance.

Plaque analysis

Detailed information regarding plaque analysis was published in a pilot study.[11] Three investigators (AS, NR, HZ) analysed the morphology of the plaques using TeraRecon (Aquarius iNtuition Viewer, Aquarius, TeraRecon, San Matteo, CA, USA) based on the pre-operative CTA. Inter- and intra-observer variability were tested using a random sample of 10 CTAs.

Clinical follow up and outcomes

All patients underwent standardised follow up including duplex surveillance with a scan at three and six months and annually thereafter. All duplex assessments were performed by a qualified vascular scientist in the same department. This constitutes standard care after F-P endovascular intervention in this unit. All follow up data were recorded in a digital database.

The main outcome of interest was occlusion or restenosis of the F-P segment exceeding 50% of the luminal diameter based on duplex imaging two years after the index procedure.

Diagnoses and clinical events were defined as per the American Heart Association (AHA) guidance for cardiovascular studies[13] and the reporting standards of the Society for Vascular Surgery for endovascular treatment of lower limb PAD.[12] As per these definitions, technical success was defined as successful use of a device or technique to re-establish vessel patency with a residual stenosis of <30%.

Statistical analysis

The SPSS 24.0 package (IBM, Armonk, NY, USA) and R software (version 3.5.2 for Windows) were used. Continuous values are reported as mean and standard deviation (SD) or median and interquartile range (IQR), depending on the normality of their distribution. Follow up duration is presented as median and range. Categorical variables are reported as absolute values and proportions (%). Parametric variables were compared using Student *t* test. Non-parametric variables were compared using Mann—Whitney *U* test. Fisher's test was used to compare categorical variables. Spearman's rank correlation co-efficient was used to assess interobserver variability, reported with a 95% confidence interval (CI). To assess which parameters contribute to future restenosis at the end of follow up, variables found to differ between those with and without restenosis on univariable analysis ($p < .05$) were entered into a logistic regression model, together with all available plaque data. To further compare outcomes relating to restenosis between those receiving an SPS or a DES, a propensity score analysis was performed. As per previous epidemiological simulation experiments, in certain situations where the relationship between treatment assignment and patient characteristics is complex (e.g. it depends on the interaction between the covariates), regular Cox models with simple linear covariable combination may have an elevated Type I error rate.[14] Therefore, it was decided to proceed with propensity score based case matching. This also provides effect estimates for every stratum used in the propensity score. More specifically, binary logistic regression with backward conditional selection was performed to calculate the "risk" of patients receiving either an SPS or a DES. Demographic information, all available clinical details and anatomical data were compared in univariable models between groups. Variables found to differ between groups ($p < .05$) were then included in a logistic regression model. The Hosmer—Lemeshow's test was used to assess model fit. Receiver operating characteristic (ROC) curve analysis estimated the area under the curve of the model predicting the probability of being included into either intervention. The calculated propensity score was employed for one to one matching based on a score difference < .005. Analyses in propensity score percentiles were not possible because of the relatively small number of patients. Kaplan—Meier curves were constructed and the log rank test was applied to compare outcomes. A *p* value < .05 was considered to be statistically significant.

RESULTS

Patient characteristics

A total of 296 patients (mean age: 73 years, SD: 11 years, 65% male) met the inclusion criteria; 32% presented with severe claudication (class 3), 22% with rest pain (class 4), 43% with minor tissue loss (class 5), and 2% with severe tissue loss (class 6), as per Rutherford classification. A total of 1801 lower limb angioplasties were performed in the department during this period. No patients were excluded because of non-availability of computed tomographic angiogram (CTA) at baseline. Further baseline characteristics are listed in Tables 1 and 2.

Procedural details

A total of 198 patients (67%) had at least one occlusion in the F-P segment; 31 (10%) had disease of the distal popliteal artery (P3), 59 (20%) of P2 and 92 (31%) of P1 — all (P3, P2 and P1) with co-existent superficial femoral artery disease. The median number of patent tibial runoff vessels was two (IQR: 2). Based on the Trans-Atlantic Inter-society Consensus (TASC) classification,[15] disease severity was classified as TASC II A in 66 (23%) patients, TASC II B in 87 (30%), TASC II C in 72 (25%), and TASC II D in 67 (23%) patients. The median length of treated artery was 150 mm (IQR: 180 mm) and the median maximum F-P stenosis was 83% (IQR: 40%). A subintimal approach was necessary in 171 (58%) patients. Following plain balloon angioplasty, 136 patients (46%) received a SPS and 160 (64%) patients a DES (121 a Zilver PTX and 39 an Eluvia stent). Most patients required implantation of more than one stent: a single stent was used in 175 patients (49%), while 80 (27%) received two stents, 60 (20%) three stents, and 11 (4%) four stents. The decision of whether to use a SPS or DES was taken intra-operatively, and was operator dependent. The immediate technical success rate was 99%. All procedures were performed by a qualified consultant endovascular surgeon or interventional radiologist, as per departmental policy; six operators performed all the procedures.

Clinical events during follow up

During the median two year follow up (range: 2—38 mo; 182 had completed two year follow up), a total of 83 patients (28%; 32% of those with an SPS *vs.* 24% of those with a DES, $p = .07$) developed a restenosis >50% within the treated F-P segment (primary outcome of interest). All patients with a restenosis >50% were discussed in a multidisciplinary meeting. Those who were offered re-intervention had deterioration in clinical symptoms (12 individuals) or a decrease in ankle brachial index of ≥20% (11 individuals).

Among those 83 patients, a total of 38 (13% of the whole cohort) had developed stent occlusions (13% SPS *vs.* 12.7% DES, $p = 1.0$ — patency rate 87% *vs.* 81.3% at the end of follow up) and 62 (23%) underwent re-intervention, including re-intervention for occlusion (24% SPS *vs.* 19% DES, $p = .26$); only eight (3%) required a surgical bypass —

Table 1. Baseline characteristics and between group univariable comparisons for patients who did and did not develop restenosis exceeding 50%

	Cohort	No restenosis <50%	Restenosis >50%	*p* value
N of patients	296	213	83	NA
Age, y [a]	73 (11)	73 (11)	73 (11)	.53
Male sex	65%	69%	53%	.02
Rest pain or tissue loss	45%	44%	46%	.61
Current smoker	38%	34%	37%	.58
IHD	42%	37%	42%	.50
Hypertension	79%	68%	81%	.03
Hypercholesterolaemia	45%	44%	45%	1.0
Diabetes	53%	52%	54%	.80
CKD > stage 3	47%	41%	48%	.30
Aspirin	67%	61%	63%	.89
Clopidogrel	33%	34%	29%	.49
Anticoagulation	10%	9%	12%	.39
Statin therapy	81%	81%	81%	1.0
Occlusion	67%	61%	83%	<.01
Popliteal involvement	24%	22%	25%	.53
Previous ipsilateral angioplasty	22%	18%	24%	.21
TASC II stage D	23%	21%	29%	.18
Thrombus present	2.4%	1.9%	3.6%	.31
Subintimal crossing	58%	24%	76%	<.001
More than one stent used	52%	48%	59%	.27
Plaque morphology				
Lesion length (mm)[b]	150 (180)	130 (160)	175 (220)	.03
Soft (cm^3)[b]	4.4 (7.9)	4.4 (8.7)	4.5 (6.5)	.78
Fibrocalcific (cm^3)[b]	1.4 (1.9)	1.4 (1.8)	1.4 (1.9)	.83
Calcified (cm^3)[b]	0.4 (1.5)	0.4 (1.4)	0.4 (1.7)	.75
Calcified % [b]	6.6 (17)	7.2 (14)	5.3 (15)	.56

CKD = chronic kidney disease; IHD = ischaemic heart disease; NA = not applicable; TASC = Trans-Atlantic Inter-society Consensus.
[a] Mean (standard deviation).
[b] Median (interquartile range).

the rest were treated endovascularly, including eight (3%) intra-arterial thrombolysis salvage procedures.

During follow up, 69 patients (23%) died (32.3% SPS *vs.* 17.7% DES, $p = .005$). Causes of death were available for 34 patients: 21 patients died from a cardiovascular event, nine from sepsis, and four because of a malignancy. Twenty-one patients (7%) had undergone a major amputation at the end of follow up (9.8% SPS *vs.* 5.4% DES, $p = .13$) and 27 (9%) had suffered a major cardiovascular event (14.5% SPS *vs.* 5.4% DES, $p = .009$). Amputation free survival at two years was 87%. One patient with an Eluvia stent had developed aneurysmal dilatation in the F-P segment but that did not lead to occlusion or further intervention.

Plaque analysis

The inter-observer correlation (10 CTAs analysed by two investigators) was 0.91 (95% CI 0.81—0.98) and intra-observer correlation (10 CTAs analysed by the same observer twice) was 0.93 (95% CI 0.82—0.95) for calcified plaque volume, 0.93 (95% CI: 0.77—0.90) and 0.90 (95% CI 0.76—0.99) for fibrocalcific plaque volume, 0.92 (95% CI 0.84—0.96) and 0.92 (95% CI 0.83—0.97) for soft plaque volume. Four patients with occlusive F-P thrombus did not undergo analysis of the F-P plaque morphology. The median arterial wall volume on CTA within the treated length of artery was 12.2 cm^3 (IQR: 12.3 cm^3). Plaque analysis showed this to be composed of a median 4.4 cm^3 (IQR: 7.9 cm^3) of soft plaque, 1.3 cm^3 (IQR: 1.9 cm^3) of fibrocalcific plaque and 0.4 cm^3 (IQR: 1.5 cm^3) of calcified plaque. The overall proportion of calcified plaque volume was 6.6% (IQR: 17%). Tables 1 and 2 summarise differences between plaque characteristics in the various groups (those with and without restenosis >50% and those with an SPS *vs.* DES).

Propensity score analysis

To assess differences between treatments with SPS *vs.*DES, a matched analysis using a propensity score, including data relating to plaque morphology/calcification, was performed. The following variables were included in the propensity score: age (β −0.40), lesion length (β −0.10), hypercholesterolaemia (β 0.97), current smoker (β −0.71), history of IHD (β 0.48), occlusive target lesion (β 0.67), calcific plaque content volume (β −0.175), and fibrocalcific plaque content volume (β −0.402).

The observed area under the curve for the propensity score was 0.79 [standard error (SE) 0.03; 95% CI 0.73—0.86, $p < .0001$).

Case to case propensity score matching provided 121 pairs of patients (242 individuals) who underwent either

Table 2. Baseline characteristics and between group univariable comparisons for patients who had a Supera peripheral stent (SPS) *vs.* those with a drug eluting stent (DES)

	Cohort	SPS	DES	*p* value
Patients	296	136	160	NA
Age, y [a]	73 (11)	76 (10)	70 (12)	<.001
Male sex	65%	63%	66%	.63
Rest pain or tissue loss	45%	44%	46%	.54
Current smoker	38%	26%	42%	.003
IHD	42%	44%	33%	.07
Hypertension	79%	75%	69%	.3
Hypercholesterolaemia	45%	52%	38%	.03
Diabetes	53%	52%	52%	1.0
CKD > stage 3	47%	45%	41%	.41
Aspirin	67%	59%	63%	.55
Clopidogrel	33%	30%	35%	.39
Anticoagulation	10%	14%	6%	.02
Statin therapy	81%	82%	81%	1.0
Occlusion	67%	78%	59%	<.001
Popliteal involvement	24%	24%	24%	1.0
Previous ipsilateral angioplasty	22%	19%	23%	.13
TASC II stage D	23%	22%	24%	.12
Thrombus present	2.4%	2.2%	2.5%	1.0
Subintimal crossing	58%	48%	52%	.03
More than one stent used	52%	54%	50%	.43
Plaque morphology				
Lesion length (mm)[b]	150 (180)	150 (220)	122 (153)	<.001
Soft (cm^3)[b]	4.4 (7.9)	5.0 (8.5)	4.3 (6.6)	.31
Fibrocalcific (cm^3)[b]	1.4 (1.9)	1.5 (2.6)	1.3 (1.7)	.22
Calcified (cm^3)[b]	0.4 (1.5)	0.5 (1.9)	0.4 (1.3)	.25
Calcified % [b]	6.6 (17)	6.2 (12)	6.6 (16)	.47

CKD = chronic kidney disease; IHD = ischaemic heart disease; NA = not applicable; TASC = Trans-Atlantic Inter-society Consensus.
[a] Mean (standard deviation).
[b] Median (interquartile range).

SPS or DES treatment. These two groups were comparable at baseline in terms of demographics (age: 75 ± 10 years for SPS *vs.* 70 ± 11 years for DES, $p = .06$; 60% male *vs.* 66% male, $p = .44$) and cardiovascular as well as plaque composition characteristics (Table 3).

Among the 121 case matched pairs of patients, those with SPS *vs.* those with a DES were not significantly more likely to develop restenosis >50% (31% *vs.*27%, $p = .57$), develop an occlusion (13% *vs.*12%, $p = 1.00$ — primary patency rate was 73% for SPS *vs.* 79% for DES and secondary patency rate was 87% for SPS *vs.* 88% for DES at the end of follow up), have a major amputation (10% *vs.* 6%, $p = .22$), require re-intervention (14% *vs.* 9%, $p = .32$), or die (7% *vs.* 4%, $p = .41$).

The median freedom from target lesion restenosis >50% was 2.7 y for those with SPS (SE: three months) *vs.* three years for those with DES (SE: six months), $p = .16$ (log rank test, Fig. 1). Amputation free survival at two years was 83% for those with an SPS *vs.*89% for those with a DES.

For the subgroup with a calcified plaque volume of ≥1.1 cm^3, which was the cut off point identified in the pilot study,[11] 38% of those who received an SPS developed restenosis *vs.*20% of those who received a DES ($p = .13$). For the subgroup with a proportion of calcified plaque ≥9.6%, which again was the % cut off point identified in the pilot study,[11] 38% of those who received an SPS developed re-stenosis *vs.*20% of those who received a DES ($p = .07$).

Predictors of binary restenosis >50% at two years

Multivariable analysis (Table 4) adjusted for all plaque morphology data and parameters that differed at univariable analysis, revealed that the main predictors of restenosis >50% at two years in the whole group were: female sex [OR 2.05, $p = .01$], hypertension (OR 2.10, $p = .04$), and previous F-P occlusion (OR 1.35, $p = .04$). For the subgroup of patients receiving an SPS (Table 5), none of these parameters, when entered in a multivariable model, predicted restenosis >50% at two years. For the subgroup of patients receiving a DES (Zilver PTX or Eluvia) (Table 6), a subintimal recanalisation was a major determinant of restenosis >50% at two years (OR 7.61, $p = .04$).

The previous pilot study had identified a calcified plaque volume of ≥1.1 cm^3 and a proportion of calcified plaque ≥9.6% as predictors of restenosis following F-P intervention. A calcified plaque volume ≥1.1 cm^3 was not associated with a higher proportion of restenosis >50% at the end of follow up (30.5% *vs.* 29.9%, $p = 1.0$, univariable analysis) nor was a proportion of calcified plaque ≥9.6% (30.4% *vs.* 29.5%, $p = .89$, univariable analysis).

Table 3. Baseline characteristics and between group univariable comparisons for patients who had a Supera peripheral stent (SPS) *vs.* those with a drug eluting stent (DES) in the case matched population based on propensity scores

	SPS	DES	*p* value
Patients	121	121	NA
Age, y [a]	75 (10)	72 (11)	.08
Male sex	60%	66%	.44
Rest pain or tissue loss	44%	45%	.51
Current smoker	38%	41%	.57
IHD	39%	28%	.08
Hypertension	76%	71%	.47
Hypercholesterolaemia	54%	31%	.001
Diabetes	54%	45%	.29
CKD > stage 3	46%	45%	.88
Aspirin	58%	65%	.33
Clopidogrel	13%	11%	.22
Anticoagulation	14%	6%	.06
Statin therapy	82%	80%	.90
Occlusion	78%	59%	<.001
Popliteal involvement	22%	24%	.87
Previous ipsilateral angioplasty	19%	22%	.11
TASC II stage D	23%	25%	.12
Thrombus present	2.2%	2.6%	1.00
Subintimal crossing	47%	53%	.44
More than one stent used	52%	51%	.70
Plaque morphology			
Lesion length (mm)[b]	157 (210)	132 (102)	<.001
Soft (cm^3)[b]	4.4 (8)	4.3 (6.2)	.30
Fibrocalcific (cm^3)[b]	1.5 (2.6)	1.3 (1.5)	.24
Calcified (cm^3)[b]	0.4 (1.0)	0.4 (1.3)	.78
Calcified % [b]	6.4 (11)	6.6 (12)	.51

CKD = chronic kidney disease; IHD = ischaemic heart disease; NA = not applicable; TASC = Trans-Atlantic Inter-society Consensus.
[a] Mean (standard deviation).
[b] Median (interquartile range).

DISCUSSION

This analysis has demonstrated that, when necessary, using an interwoven nitinol stent (SPS) in the F-P segment is associated with similar medium term patency compared with a DES. This was independent of patient related risk factors and plaque characteristics. The degree of plaque calcification was not a predictor of future restenosis or occlusion.

Endovascular intervention for F-P steno-occlusive disease is recommended by international guidelines and has become a common treatment for claudication.[1] Stents were initially seen only as a "bail out" option, but some studies suggest that primary stenting may yield superior results.[2] Guidance of the European Society for Vascular Surgery (ESVS) acknowledges the potential benefits of stenting and/or drug elution in the F-P segment, although the strength of recommendation is limited by the lack of high quality evidence.[1]

Early stent designs suffered from technical shortcomings, resulting in fractures and high rates of restenosis.[16] The improved mechanical properties of the biomimetic SPS and the antiproliferative properties of DES represent substantial advancements in stent design. In this study, analysis of the two propensity score case matched groups showed that there were no significant differences found in target lesion binary restenosis, stent occlusion, and re-intervention at two years. There were no stent fractures recorded; however, one patient with an Eluvia stent developed aneurysmal dilatation (no further sequelae). Mortality in the two matched groups did not differ either, which is an interesting finding in the context of recent literature suggesting a potential association between the use of paclitaxel based devices and long term mortality risk.[10] However, the

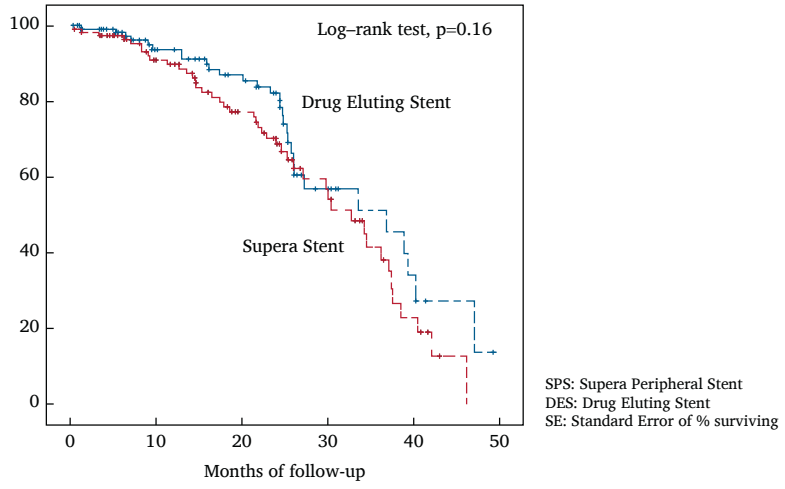

Figure 1. Freedom from target lesion restenosis >50% between those with a Supera peripheral stent and those with a drug eluting stent in the propensity score case matched analysis.

Table 4. Multivariable regression assessment of parameters associated with restenosis exceeding 50% (at two years)

	p value	Hazard ratio	95% confidence interval	
Female sex	.01	2.05	1.11	3.79
Hypertension	.04	2.10	1.04	4.20
Previous occlusion	.04	1.35	0.46	4.02
Lesion length	.06	1.00	1.00	1.01
Subintimal crossing	.21	1.87	0.71	4.94
Soft plaque volume	.85	1.00	0.96	1.03
Fibrocalcific plaque volume	.51	0.92	0.69	1.20
Calcified plaque volume	.62	1.09	0.76	1.57
Proportion of calcified plaque	.95	1.00	0.97	1.07

present study was not powered or designed to detect differences in long term mortality.

The outcomes reported in this study are comparable to those in the published literature, taking into consideration that the study cohort included a majority of patients with chronic limb threatening ischaemia and almost half had TASCII C/D lesions. Also, two thirds of patients had occlusive F-P lesions and the median length of vessel treated was 150 mm. The rates for target lesion binary restenosis, stent occlusion, and overall freedom from re-intervention at two years, are comparable with previous literature.[5,8,9]

Among the 121 case matched pairs of patients, those with SPS *vs.* DES were not significantly more likely to develop target lesion restenosis or an occlusion. The recently published IMPERIAL study, comparing Eluvia and Zilver PTX stents, reported target lesion restenosis rates of 13—18% and freedom from re-intervention rate of 94% at one year.[7,17] IMPERIAL, however, included only patients with claudication and lesions treated were between 82 and 87 mm, with far fewer occlusions (33%) and a lesser degree of calcification.[17] The Zilver PTX randomised controlled trial reported target lesion restenosis rates of 10% and 28% at one and five years, and a freedom from target lesion revascularisation of 85% at five years.[6,7] The MAJESTIC study of Eluvia DES reported a target lesion restenosis rate of 16.5% at two years and freedom for target lesion revascularisation of 85.3% at three years.[8,9] Similarly, more than 90% of patients in the Zilver PTX trial and all of the patients in the MAJESTIC study were claudicants and lesions treated in both studies were shorter, with little calcification.[6—9,18] The SUPERB study of SPS reported a target lesion restenosis rate of 17% and a freedom from target lesion revascularisation of 84% at two years.[5] There were, however, no patients with chronic limb threatening ischaemia, and only 6% of patients had TASC II C/D lesions. Mean lesion length was 80 mm.[5] Among patients who underwent SPS implantation in this study, the target lesion restenosis rate was 32% and the freedom from target lesion revascularisation rate was 76% at two years. Of note, nearly 80% of these patients had occlusive disease and lesion lengths were long (median 150 mm), often requiring sub-intimal recanalisation (48%). These observations reflect the fact that the industry funded trials may not fully reflect outcomes in patients with chronic limb threatening ischaemia, and those with longer and more calcified lesions, which this series attempted to address.

A previously published study on the utility of CTA plaque analysis in predicting outcomes in patients undergoing F-P intervention suggested that amputation free survival was significantly worse in those with a calcified plaque volume $\geq$1.1 cm^3 and those with a percentage calcified plaque >9.6%.[11] In this current study, neither calcified plaque volume nor percentage calcified plaque was associated with binary restenosis. A subgroup analysis of patients with a calcified plaque volume $\geq$1.1 cm^3 showed no difference in >50% restenosis rate at two years between the matched SPS and DES groups. The present authors still advocate the use of CTA plaque analysis as a reliable and standardised technique for objective lesion characterisation. Further research is required to fully establish its role in guiding treatment decisions.

The analysis also showed that female sex, hypertension, and previous F-P segment occlusion were found to be predictors of restenosis at two years. Patients with these

Table 5. Multivariable regression assessment of parameters associated with restenosis exceeding 50% (at two years) for patients receiving an interwoven uncovered nitinol stent (Supera)

	p value	Hazard ratio	95% confidence interval	
Female sex	0.07	2.22	0.84	5.18
Hypertension	0.05	3.01	0.99	9.06
Previous occlusion	0.09	4.24	0.79	22.59
Lesion length	0.10	1.00	0.99	1.01
Subintimal crossing	0.91	1.08	0.31	3.74
Soft plaque volume	0.81	0.99	0.92	1.06
Fibrocalcific plaque volume	0.65	0.93	0.66	1.30
Calcified plaque volume	0.93	1.02	0.61	1.71
Proportion of calcified plaque	0.97	1.00	0.95	1.05

Table 6. Multivariable regression assessment of parameters associated with restenosis exceeding 50% (at two years) for patients receiving a drug eluting stent (DES)

	p value	Hazard ratio	95% confidence interval	
Female sex	0.10	2.14	0.86	5.37
Hypertension	0.98	1.02	0.38	2.70
Previous occlusion	0.16	0.26	0.04	1.72
Lesion length	0.65	1.00	1.00	1.01
Subintimal crossing	0.04	7.61	1.12	51.79
Soft plaque volume	0.95	0.99	0.95	1.05
Fibrocalcific plaque volume	0.51	0.84	0.51	1.40
Calcified plaque volume	0.40	1.35	0.67	2.71
Proportion of calcified plaque	0.82	1.00	0.94	1.05

risk factors reasonably therefore could be offered targeted surveillance with the aim of early detection and treatment of target lesion restenosis. Interestingly, some parameters in the case matched populations (SPS *vs.* DES) did also differ, namely the number of patients with hypercholesterolaemia or those with prior occlusive plaque; indeed the SPS could have performed even better had these differences not existed. It is impossible to remove all differences between the two groups without significantly decreasing the sizes of the groups, which would add more Type II errors. A randomised approach would address this issue in the future. This analysis has shown that the percentage of calcified plaque has no relationship with the restenosis risk (as an imaging based outcome), and a previous work showed that the percentage of calcification does relate to amputation free survival.[11] Restenosis is a "local" outcome whereas amputation free survival is a result of systemic cardiovascular disease; previous work has shown that calcification in the F-P segment is indeed associated with cardiovascular risk.[19] This further supports the fact that future randomised prospective research should include amputation free survival as a primary endpoint in this disease area.

Limitations

The limitations of this study are acknowledged, which include the retrospective nature of the analyses, inclusion of only a single high volume centre, relatively short follow up duration and possible ascertainment bias, as data collectors were not blinded. Furthermore, potential residual stenoses have not been taken into account during follow up as any in stent stenosis after angioplasty and stenting would have been treated with in stent balloon post-dilatation, as per standard practice, which means that no significant residual stenosis was present in these patients after their index procedure. It is also impossible to conduct separate analyses for the two types of DES included in this series because of the size of the cohort and the fact that only a minority received an Eluvia stent. One important point raised in the SUPERB study[5] was that patency rates and re-intervention rates are based on deployment characteristics of the SPS; best outcomes are achieved with longitudinal compression of the stent during deployment. This series did not have data relating to SPS compression, which is indeed a limitation of the study design and may in part have contributed to the findings. Finally, no information is held regarding the potential effect of SPS shortening or elongation on future re-stenosis.

CONCLUSION

This study shows that stenting of the F-P segment for steno-occlusive disease with either SPS or DES has acceptable two year outcomes, independent of plaque calcification. Outcomes following SPS appear to be equivalent to those following DES. Interestingly, the rate of restenosis >50% based on cross sectional imaging was 32% for those with an SPS *vs.* 24% for those with a DES, but this did not reach statistical significance. Randomised controlled trials comparing SPS and DES are warranted to confirm or refute these findings; the exact role of calcium plaque analysis in risk stratification for patients having F-P angioplasty also remains to be fully explored.

CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

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