Proximal seal dilatation following fenestrated endovascular repair for complex abdominal aortic aneurysms

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ABSTRACT

Objective: Although proximal neck dilatation following infrarenal endovascular aneurysm repair (EVAR) is common and is associated with proximal graft failure, little is known about sealing zone dilatation and its clinical relevance following fenestrated EVAR (FEVAR). We studied proximal seal dilatation (PSD) dynamics following FEVAR and assessed its clinical significance.

Methods: We included all consecutive patients treated for a juxta-/supra-renal aneurysm with fenestrated EVAR using the Zenith Fenestrated Endovascular Graft (Cook Medical, Bloomington, Ind) from 2008 to 2018 in two large teaching hospitals in the Netherlands. The primary outcome was PSD over time and was determined using a linear mixed-effects model. Secondary outcomes included associations for early PSD and difference in aortic dilatation at the level of the covered stent compared with the bare stent. Proximal seal-related adverse events were also obtained.

Results: Our cohort included 84 patients with a median computed tomography angiography follow-up time of 24.5 months (interquartile range [IQR], 17-42 months). Maximum aneurysm diameter was 60.1 mm (IQR, 56.9-67.2 mm). Mean proximal seal diameter at baseline was 26.2 mm (standard deviation [SD], ±2.8 mm), mean stent oversizing was 20.1% (SD, ±9.1%), and mean proximal seal length was 29.5 mm (SD, ±11.7 mm). Proximal seal dilatation of 1.7 mm (95% confidence interval [CI], 1.4-2.1 mm) was found in the first year, decelerating thereafter (second year, 0.9 mm/year; 95% CI, 0.7-1.1 mm/y). Over 10% PSD at 1 year occurred in 22 patients (27%) and was associated with stent graft oversizing (odds ratio, 1.1; 95% CI, 1.03-1.2; $P = .008$) and a lower number of target vessels (four fenestrations/ref two fenestrations: odds ratio, 0.13; 95% CI, 0.02-0.74; $P = .029$). At last available imaging, dilatation difference was higher at the level of the covered stent compared with the bare stent (3.0 mm [IQR, 1.3-5.1 mm] vs 1.6 mm [IQR, 0.8-2.5 mm]; $P < .001$). During the study period, only one patient (1.2%) developed a proximal seal-related adverse event (type IA endoleak).

Conclusions: PSD is present following FEVAR, occurring at a faster rate in the first year and subsequently decelerating thereafter, similarly to neck dilatation after standard infrarenal EVAR. Although its clinical implication seems to remain limited in the first years following implantation, further research is required to assess the effect of PSD on long-term FEVAR outcomes. (J Vasc Surg 2022;■:1-9.)

Keywords: Abdominal aortic aneurysm; Endoleak; Endovascular procedures; FEVAR; Juxtarenal aneurysm; Proximal sealing zone

Fenestrated endovascular aneurysm repair (FEVAR) has expanded the applicability of endovascular aneurysm repair (EVAR) to abdominal aortic aneurysms (AAAs) with short necks (<1-15 mm) and to juxtarenal and suprarenal AAAs. Current studies on fenestrated technology show a high technical success and improved perioperative outcomes compared with open surgical repair.[1,2] Although EVAR is increasingly used, its long-term outcomes remain the Achilles' heel, with a low but continuous risk of rupture and high rate of reinterventions

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Author conflict of interest: H.V. is a consultant for Medtronic, WL Gore, Terumo, Endologix, and Philips. F.B.G. has received proctoring and speaker fees from W. L. Gore, Cook Medical, and Medtronic.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2021.12.061

over time.[3,4] In case of infrarenal EVAR, an important cause of technical failure is dilatation of the proximal sealing zone, resulting in type IA endoleaks, endograft migration, and AAA rupture.[5] Apart from natural disease progression, proximal seal dilatation (PSD) following EVAR has been reported to be associated with the radial force of the stent graft on the aortic wall and stent graft oversizing.[6] One of the presumed advantages of FEVAR is the use of a healthier segment of the aorta as proximal sealing zone, which is possibly less prone to dilatation over time, but published data on PSD following FEVAR is scarce.

In addition to the complications as described for standard EVAR, dilatation of the FEVAR proximal sealing zone could also lead to migration with target vessel stent kinking, subsequently causing acute visceral ischemia,[7,8] making it clinically of great importance to characterize PSD at this aortic level.

The objective of our study is to assess PSD following FEVAR, to identify factors associated with PSD, and to determine the clinical significance of seal dilatation at this level.

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter retrospective cohort study
- **Key Findings:** Using longitudinal mixed-effects methods in 84 patients with custom-made fenestrated endovascular aortic repair (EVAR), a proximal seal dilatation rate of 1.7 mm/y (95% confidence interval, 1.4-2.1 mm/y) was found in the first year, significantly decelerating thereafter (second year, 0.9 mm/year; 95% confidence interval, 0.7-1.1 mm/y). During the study period, only one patient (1.2%) developed a proximal seal-related adverse event (type-IA endoleak).
- **Take Home Message:** Proximal seal dilatation is present following fenestrated EVAR, occurring at a faster rate in the first year and subsequently decelerating thereafter, similarly to neck dilatation after standard EVAR. However, its clinical implication seems to be limited in the mid-term.

METHODS

Design and population. We performed a retrospective cohort study, including all eligible patients undergoing elective repair with the Zenith fenestrated endovascular graft (ZFEN; Cook Medical, Bloomington, Ind) for degenerative/non-atherosclerotic (no aortopathy/mycotic/known connective tissue disorders) AAA at two large teaching hospitals in the Netherlands (Erasmus University Medical Center and Maasstad Hospital) between 2008 and 2018. In one of the hospitals, all aneurysm patients are offered genetic screening, and none of the included patients were found to have known connective tissue disorders. In the other hospital, genetic screening was only performed when clinical suspicion was raised. Imaging and clinical follow-up were captured until June 2020. Patients treated with the Vascutek Anaconda stent graft were excluded. (Supplementary Fig, online only) Also, thoraco-abdominal aortic aneurysms treated with FEVAR (n = 4) were excluded due to the location of the proximal sealing zone in a different segment of the aorta. Finally, patients with incomplete imaging (follow-up less than two computed tomography angiographies [CTAs]; n = 9) were excluded. Causes for incomplete imaging in this group were in-hospital death (n = 2), death before imaging at 1 year (n = 3), and loss to follow-up (n = 4). This study conforms to the Declaration of Helsinki in research ethics with the study protocol being approved by both hospitals' institutional and ethical review boards.

Postoperative surveillance. Surveillance imaging protocols were standardized and included a CTA performed within 6 weeks, followed by a yearly CTA. Depending on physician's risk assessment and patient's renal function, duplex ultrasound or noncontrast computed tomography (CT) were performed alternatively to CTA in selected cases. As intraoperative DynaCT had only recently become available in the institutions, any measurements from this imaging modality could not be included.

Measurements. All measurements were obtained using dedicated image-processing software (3-mensio, Bilthoven, the Netherlands) by a method that has previously been validated and described by our group.[9] All CTAs were reconstructed according to vessel center lumen line. The outer-to-outer aortic neck-diameter was measured in two axes (anterior-posterior and transverse) at a plane determined by the endografts' first covered stent on the first postoperative CTA imaging. The average of each two diameter measurements was used. In the presence of a scallop, the diameter was measured at both the start of the covered stent and at the bottom of the scallop and averaged as well. To determine the corresponding aortic reference plane on baseline imaging, as well as on subsequent imaging, the distance from the start of the proximal covered stent to the uppermost renal artery on the first postoperative CTA was used as reference.

Two additional aortic planes were measured: the first 1 cm above the start of the covered stent (at the level of the bare-metal stented portion of the main aortic device) and the second 1 cm below the start of the covered stent (at the level of the covered portion). In the presence of a scallop, the diameter increases from first to last postoperative CTA were also compared 1 cm above and below the bottom of the scallop. The sealing length

was considered to be the distance where the entire circumference of the aortic wall and the endograft were completely adjacent (scallop length not counted).[9]

Definitions. Patient comorbidities and aneurysm-related outcomes were reported according to the Society for Vascular Surgery reporting standards for complex abdominal aortic aneurysm repair.[10] PSD (mm/y), often referred to as aortic neck dilatation in infrarenal EVAR, is determined by measuring the aortic diameter at the start of the covered portion of the FEVAR/stent graft on the first postoperative CTA imaging. PSD was determined relative to the aortic diameter measured on the first postoperative CTA. Significant dilatation was considered to have occurred at >10% of the baseline diameter (at first postoperative CTA).

Graft oversizing was calculated by dividing the device diameter by the preoperative sealing zone diameter, which was defined as the diameter at the plane determined by the top of the first covered stent. Neck thrombus and calcification were classified into quartiles of circumferential involvement. Rates of endograft migration were reported, using as reference the distance from the start of the proximal covered stent to the beginning of the uppermost renal artery at 30-day imaging. Migration exceeding >10 mm was reported. Excessive dilatation was defined as the occurrence of a PSD that is larger than the nominal endograft diameter, causing loss of contact of the graft with the aorta throughout that specific aortic plane.

Two reference aortic planes were determined: the first one being 1 cm above the start of the covered stent (bare-metal stented portion of the aorta), and the second one being 1 cm below the start of the covered stent (covered portion). In the presence of a scallop, the diameter increases from first to last postoperative CTA were also compared 1 cm above and below the bottom of the scallop.

Proximal seal-related adverse events were defined as a composite outcome of type IA endoleaks, endograft migration (>10 mm), or secondary intervention related to the proximal sealing zone (ie, proximal cuff/thoracic EVAR, open conversion/other endovascular treatment due to proximal seal-related complications).[6]

Outcomes. The primary outcome was PSD over time. Secondary outcomes included morphological and device-related factors associated with PSD (>10%) at 1 year, and differences between PSD at different aortic levels including the covered and bare stent. Finally, the rate of excessive PSD and subsequent proximal seal-related adverse events were determined.

Statistical analysis. Categorical variables are presented as count and percentage and continuous variables as mean or median, plus standard deviation (SD) or interquartile range (IQR), respectively, according to their distribution. Differences in characteristics between groups were compared using the χ^2 or Fisher exact tests where appropriate for categorical variables. Continuous variables were checked for normal distribution using visual aid of histograms and Q-Q plots and the Shapiro-Wilk test. Student *t* tests and Mann-Whitney *U* tests were used to test these continuous variables depending on their parametric or non-parametric nature, respectively. Confidence intervals (CIs) of 95% were used, and statistical significance was considered for $\alpha < .05$.

To investigate the relationship between postoperative PSD over time, a longitudinal mixed effects model was made, in which time was entered as the independent variable and PSD as the dependent variable, assuming random intercepts and slopes to allow individual variation per patient (fixed: time + time^2 + time^3; random: ~time). To compare the time-sensitivity of the models, we ran the models with and without different polynomial terms time, and calculated the difference in likelihood ratios.[11] To understand associations of the occurrence of significant PSD (>10%) at 1 year, a multivariable logistic regression was performed. Variables for the model were selected a priori based on univariable outcomes and previous literature, including preoperative proximal seal diameter and stent graft oversizing.[5,12,13] Rates of excessive dilatation over the course of 48 months were estimated by using Kaplan-Meier methods.

CIs of 95% were used, and statistical significance was considered for $\alpha<.05$. Statistical analyses were performed with the "R" Project for Statistical Programming (version 4.0.3, R Foundation for Statistical Computing, Institute for Statistics and Mathematics, Vienna, Austria) and Stata 15.1 (StataCorp LLC, College Station, Tex).

RESULTS

A total of 84 patients undergoing FEVAR treated with ZFEN between 2008 and 2018 were included, with a median follow-up time of 24.0 months (IQR, 15.0-42.0 months). Baseline characteristics and anatomic details are presented in Table I. Seventy-seven patients (91.7%) were men, and the mean age was 73.7 years (SD, ±6.5 years). Seventy-nine patients were treated for a juxtarenal aneurysm and five patients for a suprarenal aneurysm with the proximal sealing zone landing within the visceral segment of the aorta. The majority of patients were treated with three fenestrations (n = 44; 52%), followed by 20 patients (24%) that were treated with four fenestrations and 19 patients (23%) with two fenestrations. One patient (1.2%) was treated with one fenestration. A total of 251 fenestrations (scallops not counted) were included, with an average of 3.0 (SD, ±0.71) fenestrations per patient. Of all patients, 13 patients (15.5%) had a scallop for the superior mesenteric artery, and 35 patients (41.7%) had a scallop for the celiac trunk. The median preoperative maximum aneurysm diameter was 60.1 mm (IQR, 56.9-67.2 mm), and the

Table I. Baseline clinical, anatomical, and device-related variables

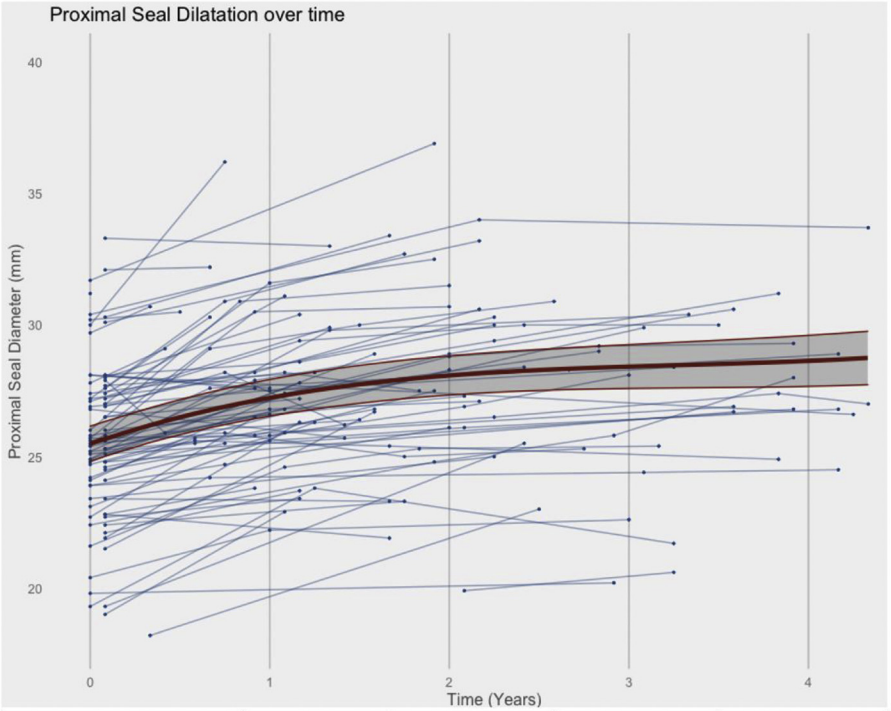
	Overall cohort (N = 84)	PSD >10% at 1 year (n = 22)	PSD ≤10% at 1 year (n = 62)	*P* value
Follow-up CT imaging, months	24.5 (16.8-42.3)	22.5 (15.3-39.0)	26.5 (17.5-43.0)	.60
Age, years	73.7 (±6.5)	73.1 (±6.5)	74.0 (±6.5)	.62
Male gender	77 (91.7)	18 (81.8)	59 (95.2)	.13
Hypertension	65 (81.3)	17 (77.3)	48 (77.4)	>.99
Diabetes mellitus	11 (13.4)	5 (22.7)	6 (9.7)	.26
eGFR <60 mL/min/1.73m^2	25 (29.8)	5 (22.7)	20 (32.3)	.57
Smoking at FEVAR[a]	25 (32.5)	9 (40.9)	16 (25.8)	.28
ASA class III/IV[b]	42 (64.6)	11 (57.9)	31 (67.4)	.66
Cardiac status ≥2	12 (13.0)	4 (18.2)	21 (33.9)	
PAOD	40 (49.4)	11 (50.0)	29 (49.2)	>.99
COPD	29 (36.3)	10 (45.5)	19 (32.8)	.43
Anti-platelet	52 (63.4)	16 (72.7)	36 (61.0)	.71
Maximum AAA diameter, mm	60.1 (56.9 – 67.2)	60.0 (56.7 – 67.8)	60.1 (57.1 – 66.7)	.94
AAA volume, mm^3	252.6 (200.9 – 302.1)	244.4 (190.3 – 305.2)	252.8 (202.3 – 301.5)	.71
Preoperative sealing zone diameter, mm	25.4 (±2.7)	25.6 (±2.6)	25.3 (±3.1)	.91
Proximal seal diameter at 30 days, mm	26.2 (±2.8)	25.9 (±2.8)	26.3 (±2.9)	.51
Proximal seal length, mm	29.5 (±11.7)	27.7 (±10.5)	30.9 (±11.5)	.26
PSZ thrombus	5 (6.0)	2 (9.1)	3 (4.8)	.60[c]
PSZ calcification	0 (0.0)	0 (0.0)	0 (0.0)	NA
Oversizing, %	20.1 (±9.1)	23.7 (±6.3)	18.8 (±9.7)	**.012**
Nominal diameter endograft, mm	32.0 (30.0-34.0)	32.0 (32-35.5)	32.0 (30.0-34.0)	.12
Distance endograft to uppermost renal, mm	25.0 (17.8-41.0)	25.0 (20.1-38.4)	26.1 (17.3-41.8)	.79
No. fenestrations				**.027**
1	1 (1.2)	0 (0.0)	1 (1.6)	
2	19 (22.6)	7 (31.8)	12 (19.4)	
3	44 (52.4)	12 (54.5)	32 (51.6)	
4	20 (23.8)	3 (13.6)	17 (27.4)	

AAA, Abdominal aortic aneurysm; *ASA*, American Society of Anesthesiologists; *COPD*, chronic obstructive pulmonary disease; *CT*, computed tomography; *eGFR*, estimated glomerular filtration rate; *FEVAR*, fenestrated endovascular aneurysm repair; *NA*, not applicable; *PAOD*, peripheral arterial occlusive disease; *PSD*, proximal seal dilatation; *PSZ*, proximal sealing zone.
Data are presented as number (%), mean ± standard deviation, or median (interquartile range).
Boldface *P* values indicate statistical significance.
P-values for comparison of groups with PSD >10% and PSD ≤10% at 1 year.
[a]Missing values >10%.
[b]Missing values >20%.
[c]Fisher exact test.

median effective proximal seal length was 29.5 mm (SD, ±11.7 mm). The median nominal endograft diameter was 32 mm (IQR, 30-34 mm), whereas the mean device oversizing was 20.1% (SD, ±9.1%).

PSD. At last available CTA imaging, the median PSD was 9.5% (IQR, 4.6%-18.3%), and PSDs of >10% and >20% at the level of the first covered stent was found in 40 (47.6%) and in 17 (20.2%) patients, respectively. At 1-year follow-up, 22 patients (26.2%) developed PSD >10%. Patients who developed early significant PSD (>10%) at 1 year had higher proximal endograft oversizing (23.7% [SD, ±6.3%] vs 18.8% [SD, ±9.7%]; $P = .01$) and a lower number of target fenestrations (4 fenestrations [PSD >10% vs PSD ≤10% at 1 year]: 13.6% vs 27.4%; $P = .027$) compared with patients without >10% PSD at 1 year.

Fig 1 shows the longitudinal mixed effect model-derived time curves for proximal seal diameter as a function of time, where time curves are fitted with the predicted values of the mixed-effects model. Our model demonstrated an annual PSD of 1.7 mm/y (95% CI, 1.4-2.0 mm/y) in the first year, declining to 0.9 mm/y (95% CI, 0.8-1.1 mm/y) in the second year, and 0.3 mm/y (95% CI, 0.2-0.5 mm/y) in the third year (Table II).



Proximal Seal Diameter	Coefficient	SE	t-value	P-value
Fixed portion				
Time	2.33	0.28	8.2	<.001
(Time)^2	-0.64	0.15	-4.4	<.001
(Time)^3	0.06	0.02	3.5	<.001
Constant	25.5	0.34	75.1	<.001

Fig 1. Linear mixed-effects model displaying proximal seal diameter (mm) over time. *SE*, Standard error.

Table II. PSD estimates from linear mixed effects model

Time point	No.	Proximal seal diameter, mm (95% CI)	Cumulative dilatation, mm (95% CI)	Annual growth rate, mm (95% CI)
Baseline	84	25.4 (24.8-26.2)	NA	NA
1 year	84	27.1 (26.5-27.9)	1.7 (1.4-2.0)	1.7 (1.4-2.0)
2 year	48	27.9 (27.3-28.8)	2.5 (2.2-3.0)	0.9 (0.8-1.1)
3 year	33	28.2 (27.6-29.3)	2.8 (2.3-3.4)	0.3 (0.2-0.5)
4 year	22	28.4 (27.6-29.7)	3.0 (2.3-3.7)	0.2 (0.1-0.4)

CI, Confidence interval; *NA*, not available; *PSD*, proximal seal dilatation.

Factors associated with >10% PSD at 1 year. In multivariable analyses, >10% PSD at 1 year imaging was associated with greater degrees of stent graft oversizing (odds ratio [OR], 1.1; 95% CI, 1.03-1.21 per %; $P = .008$), and trended towards an association with wider preoperative sealing zone diameter (OR, 1.2; 95% CI, 0.99-1.6 per 1 mm; $P = .063$) (Table III). Inversely, patients with a higher number of target vessels were associated with a lower risk of developing >10% PSD at 1 year (OR [4 vs 2 fenestrations], 0.13; 95% CI, 0.02-0.74; $P = .029$).

Effect of covered self-expandable stent and oversizing on PSD. At last available follow-up, the overall diameter increase was larger at the level of the covered stent compared with the level at the bare-metal stent (3.0 mm [IQR, 1.3-5.1 mm] vs 1.6 mm [IQR, 0.8-2.5 mm]; $P < .001$) (Fig 2). Similarly, among those patients with a proximal scallop (n = 56), a larger increase of diameter was found 1 cm below the bottom of the scallop compared with 1 cm above the bottom of the scallop (3.3 mm [IQR, 2.1-5.3 mm] vs 2.1 mm [IQR, 1.1-3.6 mm]; $P < .001$).

Table III. Multivariable logistic regression analysis for associative factors with >10% PSD at 1 year

Variables	OR	95% CI	*P* value
Preoperative sealing zone diameter (/10 mm)	1.2	0.99-1.6	.063
Stentgraft oversizing (/%)	1.1	1.03-1.2	**.008**
No. fenestrations	(Reference: 2)		
3	0.40	0.99-1.5	.17
4	0.13	0.02-0.74	**.029**

CI, Confidence interval; *OR*, odds ratio.
Boldface *P* values indicate statistical significance.

Excessive seal dilatation and clinical consequences. On the last available CT scan, the aorta did not surpass the nominal endograft diameter in 73 patients (86.9%), whereas in 11 patients (13.1%), this diameter had been exceeded. For these 11 patients, the median time to excessive dilatation was 41.1 months (IQR, 21.2-62.2 months). At 3 and 5 years, freedom from excessive dilatation was 92.3% (95% CI, 85.9%-99.1%) and 81.6% (95% CI, 69.7%-95.5%), respectively (Fig 3).

During the study period, one patient (1.2%) developed a proximal seal-related adverse event. Specifically, the male patient who underwent a 3-vessel FEVAR without scallop to the celiac trunk acquired a type IA endoleak after 61.3 months and was left untreated, as further treatment options were declined due to severe comorbidity. The preoperative proximal seal diameter of this patient was 25.4 mm, stent graft oversizing of 19.5%, and with an initial effective sealing length of 36 mm. Two patients developed a secondary type IB endoleak. One of these type IB endoleaks presented in the patient who developed a type IA endoleak too, whereas the other was acquired by a patient who did not develop either excessive dilatation or PSD >10% within the first year. Finally, only four (4.8%) of the included patients developed patency loss of one of the target vessels during follow-up (1.6% of all fenestrations), which were all unrelated to PSD >10% within 1 year, or excessive sealing.

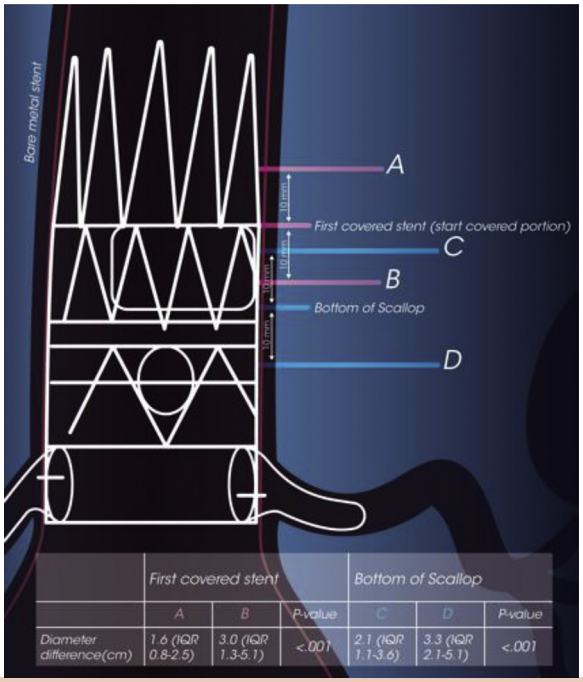
DISCUSSION

Following standard infrarenal EVAR, aortic neck dilatation is a well-known and important factor for endograft failure, leading to proximal neck-related secondary interventions, migration, type IA endoleaks, and/or rupture. Fenestrated endografts obtain a proximal seal in a more proximal segment of the aorta, including the visceral proportion of the aorta, presumed to be more resistant to dilatation over time. However, very little is known regarding dilatation in this portion of the aorta, making it of importance to study the occurrence of seal dilatation in this segment. Especially, as similar to infrarenal EVAR, excessive dilatation may potentially lead to major complications.[6] In the current study, we demonstrated that PSD occurs following FEVAR, at a faster rate in the first year and decelerating over time. Stent graft oversizing and number of target fenestrations were associated with development of >10% PSD at 1 year. Furthermore, we found a significant increase in overall dilatation at the level of the covered stent compared with the level of the bare-metal stent. Finally, our study showed that, although excessive dilatation occurred in 11 patients (13%), the clinical relevance of PSD appeared limited in the short-term, with only one patient acquiring a type IA endoleak. Nevertheless, long-term studies on this subject should reveal the true clinical consequences as proximal seal-related adverse events may take longer to develop.[14,15]

Many assume the visceral segment to be a more stable part of the aorta compared with the infrarenal part, and therefore less prone to dilation. Consequently, it was hypothesized that using this area as A sealing zone would result in negligible dilation of the proximal sealing zone after FEVAR, reducing the risk of proximal graft failure.[8] However, as demonstrated here, PSD also occurs following treatment with FEVAR using the Cook fenestrated device. We could not perform any direct comparisons between infrarenal PSD after standard EVAR and PSD of the visceral segment after FEVAR due to different stent grafts used. Nevertheless, the results of the current study and our previous study[6] show quite similar trends, demonstrating PSD fastest in the first year, decelerating over time.

The occurrence of PSD following FEVAR has been previously described by Tran et al in 43 patients undergoing FEVAR.[13] Our study confirms the development of PSD at this aortic level with a larger sample size, but also demonstrated that PSD following FEVAR decelerates over time. The subsequent deceleration that we found is in concordance with previous studies on infrarenal EVAR,[6] and with Zetterval et al and Qaderi et al, who reported on proximal neck dilatation following FEVAR with physician-modified endografts (PMEGs).[12,16] Interestingly, compared with the latest PMEG paper by Zettervall et al, the dilatation rates seemed similar at the measured aortic levels (PMEG at level of SMA: ~18 mm at first year vs ZFEN at level of first covered stent ~17 mm at first year).

It has previously been suggested that the deceleration of PSD occurs due to the gradual reduction in radial



	First covered stent			Bottom of Scallop		
	A	B	P-value	C	D	P-value
Diameter difference(cm)	1.6 (IQR 0.8-2.5)	3.0 (IQR 1.3-5.1)	<.001	2.1 (IQR 1.1-3.6)	3.3 (IQR 2.1-5.1)	<.001

Fig 2. Overall dilatation in covered and bare-metal stented portion of aorta. *IQR*, Interquartile range.

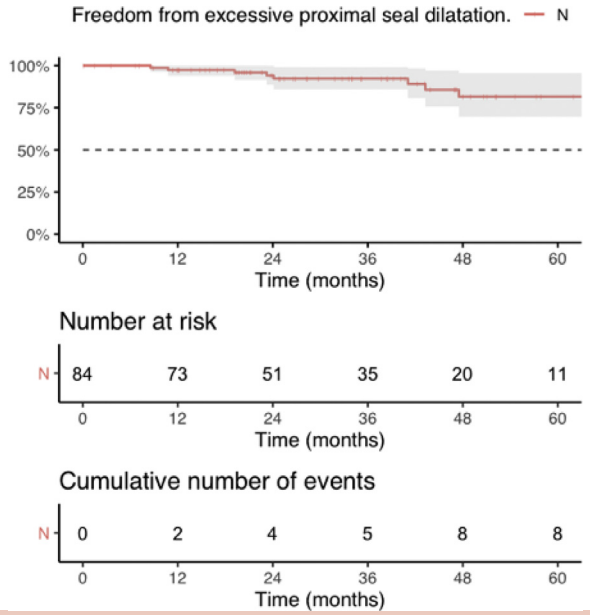


Fig 3. Kaplan-Meier curve displaying the freedom from excessive proximal seal dilatation (*PSD*).

force from the stent graft on the aortic wall as the endograft approaches its nominal diameter.[6] Interestingly, our results show that the covered portion of the aorta dilates faster than at the level of the bare-metal stent of the main device, potentially adding validity to the hypothesis that radial force does contribute to PSD. Alternative theories suggest that endografts may contribute to wall hypoxia, subsequently promoting neck degeneration.[13] Otherwise, the difference in overall dilatation at these two aortic levels could potentially be due to the fact that the covered portion is closer to a diseased part of the aortic wall, thus potentially leading to more wall degradation and dilatation.

We found that increased stent graft oversizing was associated with an additional risk of >10% PSD at 1 year, confirming findings from previous reports that studied PSD in the visceral segment.[12,13,16] Furthermore, these findings matched the associations found for neck dilatation after standard infrarenal EVAR, as reported in a systematic review by Kouvelos et al.[5] Although increased oversizing does seem to be associated with PSD, we do not know whether increased oversizing will eventually lead to adverse outcomes too. Thus, our data do not yet provide enough information to suggest whether the existing common practice for oversizing should be altered. Although not significant, our results demonstrate a trend that wider preoperative proximal seal diameters are associated with increased risk of >10% PSD at 1 year, which is in conjunction with earlier findings for FEVAR[12,13,16] and standard infrarenal EVAR.[5] Such a relation was not visible in univariable analysis, which we believe is the result of the small variety in proximal seal diameters within the cohort, and as diameters differ greatly at different aortic levels.

Furthermore, in the study by Tran et al, proximal seal length was significantly correlated with aortic neck dilatation, which was defined as neck dilatation of >3 mm at any given moment in time during follow-up. This contrasts with our results, which do not display an association between PSD >10% within 1 year and the sealing length at baseline. We believe that the differences in definition for the occurrence of neck/seal dilatation, diversity in endografts configurations/disease extent (as Tran et al included a majority of 2-vessel fenestrated endografts vs. 3-4 vessel fenestrated endografts, likely due to regulatory differences between the United States and Europe), and measurement techniques may have to do with the contrasting results regarding this association.

Due to our limited sample size, we were unable to assess any other associations between characteristics of the proximal seal such as calcium/thrombus or (reverse-) tapering within the sealing zone, with early PSD. Some of these components have proven to be of effect in infrarenal EVAR, and future studies will need to establish whether this is of effect in the visceral aorta too. Besides the prior associations, we found that a lower number of target fenestrations was associated with an increased risk of >10% PSD at 1 year. It can be hypothesized that a higher number of fenestrations and a subsequent higher, or longer, proximal landing zone is more protective for future proximal dilatation and graft failure. Nonetheless, whether the more proximal aortic level, or

the structural stability of the endograft due to a higher number of target vessels is the causative factor for a lower risk of early PSD cannot be answered with our data, and remains to be investigated.

Our results suggest that radial force is already present at the level of the scallop, albeit in a lesser degree given the circumferential discontinuity of the top stent at this level. The variability in scallop heights, however, complicated interpretation regarding the influence of radial force at this level. Tran et al measured seal dilatation at various heights within the seal, reporting that diameter differences were highest 1 cm below the start of the first covered stent and were also present at the level of the bare metal stent,[13] in agreement with our findings. Taking into account that both stent graft oversizing and wider sealing zone diameters are associated with increased dilatation, these findings could suggest that both biological components combined with the radial force of the stent graft are causal to PSD.

Our group previously reported that, following infrarenal EVAR, excessive neck dilation at 5 years was present in 3.4% (95% CI, 2.1%-4.7%) of patients.[6] Although no direct comparison was made with the infrarenal EVAR cohort, we found a higher rate of patients that achieved excessive dilation following FEVAR (13.1%). In spite of these higher rates, proximal seal-related complications such as type iA endoleaks, endograft migration, or proximal seal-related interventions were rare within the short- to mid-term, supporting findings from previous FEVAR studies reporting low rates of proximal graft failure.[12,13,16] We agree that this is most likely due to longer sealing lengths, as suprarenal stent grafts provide enough length to avoid endoleak development, even after excessive dilation occurs at the start of the covered stent. However, it is important to realize that only relatively short follow-up periods are described so far and that proximal sealing zone failure may take longer to develop. Furthermore, it will take longer follow-up periods to study whether dilatation of the proximal sealing zone will continue after the nominal diameter of the implanted FEVAR stent graft is reached and radial force on the aorta has diminished. Therefore, future studies with more patients and longer follow-up are necessary to understand how PSD will affect proximal graft failure following FEVAR.

Our study should be interpreted within the context of the study design. First, given its retrospective nature, our cohort size is limited and was not based on power calculations. Due to the limited sample size, our linear mixed effect model or multivariable logistic regression model did not have enough power to include additional variables such as endoleaks and proximal seal length. This remains important for future investigation. Furthermore, we only included patients with at least 1 year of CTA follow-up, potentially leading to a selection bias as we did not account for PSD in patients with early death. Lastly, the follow-up duration of our cohort was limited to ascertain clinical relevance of PSD following FEVAR. Further prospective research with higher population sizes and long-term follow-up are required to get a better understanding of the clinical significance of PSD following EVAR of complex abdominal aortic aneurysms.

CONCLUSION

PSD occurs following FEVAR, at a faster rate in the first year and decelerating over time, similarly to neck dilatation following infrarenal EVAR. Stent graft oversizing (%) and a lower number of target vessels are associated with >10% PSD at 1 year. Furthermore, dilatation occurs at a faster rate at the level of the covered stent when compared with the level of the bare-metal stent, potentially suggesting that PSD is a multifactorial process including biological and mechanical causes. Although dilatation is not unusual following FEVAR, the clinical implications of seal dilatation seems to remain limited in the short- to mid-term. Future studies will need to assess the effect of PSD after FEVAR on long-term outcomes and evaluate whether this follows the same course as PSD after standard infrarenal EVAR.

The authors thank Muis Kortland for support with conducting images.

AUTHOR CONTRIBUTIONS

Conception and design: VR, JB, RV, NO, EB, MR, FG, MS, BF, HV

Analysis and interpretation: VR, JB, NO, SH, SR, FG, MS, BF, HV

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Final approval of the article: VR, JB, RV, NO, EB, SH, SR, MR, FG, MS, BF, HV

Statistical analysis: VR, RV, EB, SH

Obtained funding: Not applicable

Overall responsibility: VR

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Submitted Sep 23, 2021; accepted Dec 10, 2021.

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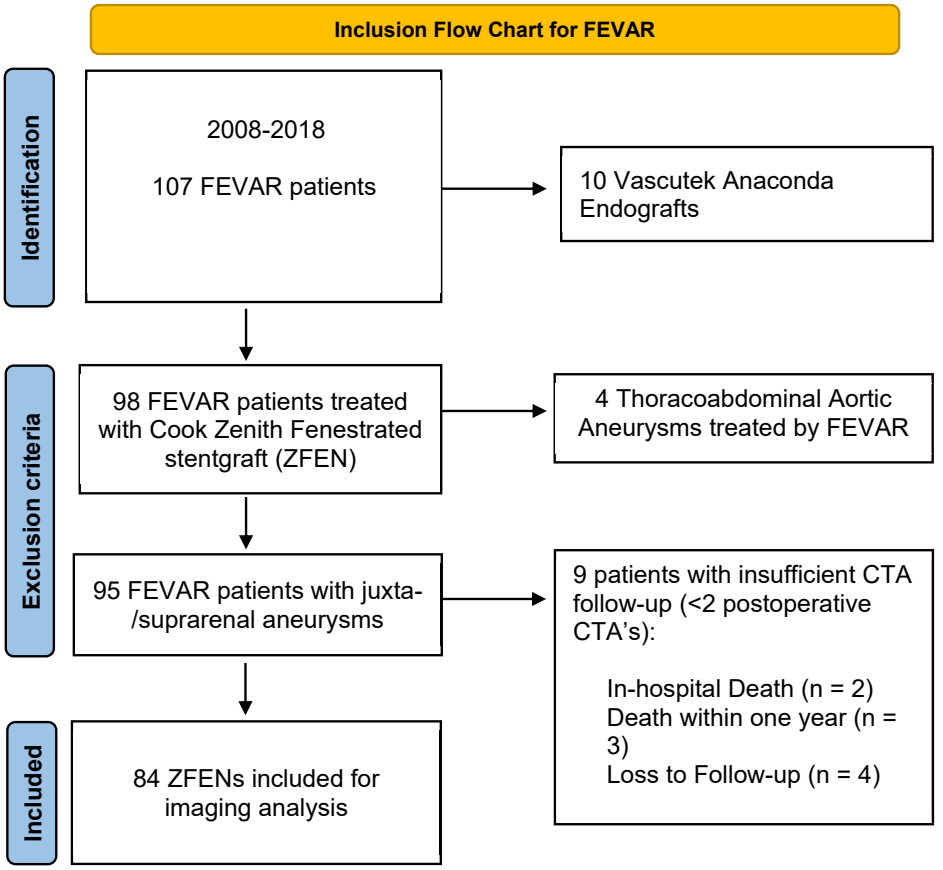

Supplementary Fig (online only). Inclusion flow chart for patients undergoing fenestrated endovascular aneurysm repair (*FEVAR*). *CTA,* Computed tomography angiography; *ZFEN,* Zenith fenestrated stent graft.