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Identifying high risk for proximal endograft failure after endovascular aneurysm repair in patients suitable for both open and endovascular elective aneurysm repair

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ABSTRACT

Objective: Proximal endograft failure (type Ia endoleak or migration) after endovascular aneurysm repair (EVAR) is associated with hostile aneurysm neck morphology. Neck scoring systems were developed to predict proximal endograft failure but were studied in retrospective studies, which, due to selection bias, may have led to an overestimation of bad outcomes after EVAR. To predict patients who benefit from open repair, preoperative neck morphology and occurrence of long-term proximal endograft failure were investigated in patients enrolled in the endovascular arm of the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial who were suitable for open repair by definition and have long-term follow-up.

Methods: A post-hoc on-treatment analysis of patients after EVAR was performed in 171 patients. Aneurysm neck morphology was quantified using the aneurysm severity grading (ASG) neck score calculated on preoperative computed tomography angiography images. The ASG neck score was used to predict proximal endograft failure. Receiver operating characteristic analysis was performed to calculate a threshold to divide favorable and unfavorable aneurysm necks (low and high risk); positive and negative likelihood-ratios were calculated accordingly. Freedom from proximal endograft failure was compared between groups using Kaplan-Meier analysis.

Results: During a median follow-up of 7.6 years, 20 patients suffered proximal endograft failure. Receiver operating characteristic analysis showed an area under the curve of 0.77 (95% confidence interval [CI], 0.65-0.90; $P < .001$), indicating acceptable prediction. The threshold was determined at ASG neck score ≥5; 30 patients had unfavorable neck morphology, of whom 11 developed proximal endograft failure. The positive likelihood-ratio was 4.4 (95% CI, 2.5-7.8), and the negative likelihood-ratio was 0.51 (95% CI, 0.3-0.8). Twelve years postoperatively, freedom from proximal endograft failure was 91.7% in the favorable group and 53.2% in the unfavorable group, a difference of 38.5% (95% CI, 13.9-63.1; $P < .001$).

Conclusions: In this study, the ASG neck score predicted proximal endograft failure during the entire follow-up. This exhibits the persistent risk for proximal endograft failure long after EVAR and calls for ongoing surveillance especially in patients with unfavorable aneurysm necks. (J Vasc Surg 2022;76:1261-9.)

Keywords: Endovascular aneurysm repair; Secondary intervention; Sealing failure; Neck morphology

Secondary interventions remain necessary to maintain adequate aneurysm exclusion and prevent secondary rupture, in some patients years after endovascular aneurysm repair (EVAR).[1-3] A number of features of the infrarenal aortic neck have been associated with these secondary interventions and higher risk of secondary aneurysm rupture after EVAR.[4,5] This has allowed individual clinical decision making for abdominal aortic aneurysm (AAA) repair and has helped in choosing specific types of endografts to improve outcomes. However, a composite neck grading system based on various neck features has not found real-world application beyond reporting standards.

The aneurysm grading systems that were developed include variables describing aneurysm neck, sack, and iliac morphology. These grading systems are used to

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predict secondary interventions after EVAR.[6-8] In a previous publication, the St George's Vascular Institute score was successfully used to predict secondary interventions for all purposes in the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, but it lacks specificity for neck-related issues.[9]

One purpose of a neck grading system is to determine suitability for EVAR or to decide that open or no repair is a better option.[4] However, neck grading systems were designed and validated in retrospective studies. A proportion of the studied patients may not have been suitable for open repair due to comorbidity, and EVAR outside the instructions for use (IFU) may have occurred frequently.[6,7,10] Some risk factors for proximal endograft failure after EVAR may be associated with overall operative risk factors that had determined that these patients were unsuitable for open repair. This may have led to an overestimation of bad outcomes from these neck-grading systems after EVAR in retrospective studies. Investigating preoperative neck scores in patients who were suitable for both open and endovascular repair allows for a valid comparison of the predictive value for proximal endograft failure (type Ia endoleak or migration). This creates a more representative tool for patient selection on the basis of elevated risk for proximal endograft failure.

The neck grading systems were validated using short-term follow-up. Early proximal endograft failure, however, may be caused by different neck features than those that predict the occurrence of late proximal endograft failure. Long-term results may contribute to the prediction of proximal endograft failure and alter neck grading systems.

Therefore, the predictive value of a preoperative infrarenal aortic neck grading system for aortic neck-related adverse events and secondary interventions after EVAR was studied in a prospective cohort of patients with AAA suitable for both open and endovascular repair, with availability of long-term follow-up. The DREAM trial is particularly useful to investigate long-term secondary procedures because neck morphology was assessed prospectively after randomization, whereas long-term data was collected prospectively with high completeness of follow-up.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective multicenter study (data from the endovascular arm of the Dutch Randomized Endovascular Aneurysm Management [DREAM] trial)
- **Key Findings:** Aneurysm neck morphology was used to predict proximal endograft failure in 171 patients who underwent endovascular repair in the DREAM trial. Thirty patients (18%) had unfavorable neck morphology, of whom 11 (37%) developed proximal endograft failure. The positive likelihood-ratio was 4.4 (95% confidence interval [CI], 2.5-7.8), and the negative likelihood-ratio was 0.51 (95% CI, 0.3-0.8). Twelve years postoperatively, freedom from proximal endograft failure was 91.7% in favorable and 53.2% in unfavorable groups, a difference of 38.5% (95% CI, 13.9-63.1; $P < .001$). Both early and late proximal endograft failure were equally associated with preoperative neck morphology.
- **Take Home Message:** Aneurysm neck morphology predicted proximal endograft failure during the entire follow-up, highlighting the persistent risk for proximal endograft failure and need for surveillance long after endovascular aneurysm repair.

METHODS

Study design. To study the association between preoperative neck morphology and long-term proximal endograft failure (PEF) and secondary interventions, we used the aneurysm severity grading (ASG) neck score and registered neck related secondary complications in patients enrolled in the trial. The design and methods of the DREAM trial were described previously.[11] To summarize, 351 patients with unruptured, infrarenal AAAs measuring over 5 cm in diameter and suitable for both treatment modalities were randomized for open or endovascular repair in the Netherlands and Belgium. Patients with inflammatory aneurysms, anatomical variations, or connective tissue disease were excluded. The study was performed according to the principles of the Declaration of Helsinki, and the trial protocol was approved by the medical ethical comity of each participating hospital (ClinicalTrials.gov number: NCT00421330).

Suitability for endovascular repair was determined based on preoperative computed tomography (CT) angiography images; all patients were considered to have a sufficient aneurysm neck for EVAR, coherence to IFU was strictly warranted by the trial investigators. A post-hoc on-treatment analysis was performed in all patients who underwent EVAR in the DREAM trial. Aneurysm neck morphology was investigated in all aneurysm necks and used to predict secondary procedures. Secondary procedures in the DREAM trial were reported previously and were available during long-term follow-up.[2] PEF was scored in patients who underwent a first secondary procedure for PEF; repeated interventions in the same patient for PEF were not additionally scored in this analysis. PEF was also scored in patients who developed PEF but were unsuitable for intervention or those who suffered a secondary aneurysm rupture due to PEF without subsequent intervention. All performed follow-up images were cross-referenced to confirm the treatment indication and to prevent missing of PEF for which no treatment had followed.

Table I. Aneurysm severity grading (ASG) score neck characteristics

Characteristic severity (Points)	Absent (0)	Mild (1)	Moderate (2)	Severe (3)
Aortic neck length, mm	>25	>15 and ≤25	>10 and ≤15	≤10
Aortic neck diameter, mm	<24	≥24 and <26	≥26 and <28	≥28
Aortic neck angle, °	<30	≥30 and <45	≥45 and <60	≥60
Calcification and/or thrombus, %	<25	≥25 and <50	≥50	–

Morphology scoring. Preoperative morphological measurements derived from computed tomography planning were recorded in trial case report forms (CRFs). Neck morphology was based on the neck part of the Society for Vascular Surgery ASG score. The ASG score includes (points are displayed in brackets); neck length (>25 mm [0], >15 and ≤25 mm [1], >10 and ≤15 mm [2], and ≤10 mm [3]), neck diameter (<24 mm [0], ≥24 and <26 mm [1], ≥26 and <28 mm [2], and ≥28 mm [3]), neck angulation (<30° [0], ≥30° and <45° [1], ≥45° and <60° [2], and ≥60° [3]), and neck calcification and/or thrombus as a percentage of the circumference (<25% [0], ≥25% and <50% [1], and ≥50% [2]).[7] Missing CRF values were manually remeasured at the individual randomization sites. Validation of aneurysm neck morphology was performed by remeasuring 40 preoperative CT angiographies; these measurements were compared with CRF records for agreement. Kappa agreement test was used for categorial variables, and the Pearson correlation coefficient test was used for continuous variables. The ASG neck score was calculated in all patients who underwent EVAR, without weighting for any of the variables. The minimum ASG neck score is 0, and the maximum is 11; according to each variable, severity 0 to 3 (except maximum 2 for calcification and/or thrombus) points were scored. The ASG neck score was used to predict PEF and secondary interventions in the proximal aneurysm neck (Table I).

Data analysis. Statistical analysis was performed in SPSS version 24.0 (IBM Corp, Armonk, NY). The ASG neck score was determined as sum of the individual neck variables per patient and is provided as median and range for each group. A threshold of the ASG neck score, differentiating favorable from unfavorable necks to indicate low-risk and high-risk for PEF, was calculated with use of receiver operating characteristic (ROC) curve analysis. Sensitivity and specificity were calculated based on the threshold with use of crosstabs. Positive and negative predicting value and positive and negative likelihood ratios with 95% confidence intervals (CIs) were calculated using MedCalc Software Ltd. Diagnostic test evaluation calculator. (https://www.medcalc.org/calc/diagnostic_test.php [version 20.027; accessed February 4, 2022]).[12] This threshold value was afterwards used to divide patients into two groups; a group with low ASG neck scores (score ≤4/11) and a group with high ASG neck scores (score ≥5/11), representing favorable neck morphology (low risk for PEF) and unfavorable neck morphology (high risk for PEF), respectively. Differences in ASG neck variables were calculated between groups with the use of the Fisher exact test. Freedom from PEF was compared between favorable and unfavorable neck morphology groups with use of Kaplan-Meier analysis. Differences were calculated using log-rank tests. Cox regression analysis was performed to calculate hazard ratios (HRs) for the ASG neck score and threshold value. To determine risk-adjusted survival free from PEF, we created a multivariate Cox proportional hazards model adjusting for (1) preoperative aneurysm diameter; (2) oversizing; (3) proximal fixation; and (4) baseline characteristics. All values are provided with 95% CIs. All reported *P*-values are two-sided without correction for multiple testing.

RESULTS

Study descriptives and baseline. After randomization and cross-overs, 171 patients were treated by endovascular means and were analyzed as treated.[11] The implanted endografts are listed in Table II; 163 endografts were self-expanding. Only two manufacturers provided active proximal fixation; the Zenith (n = 57; Cook Medical Inc, Bloomington, IN) was provided with transrenal fixation, and the Ancure (n = 4; Guidant-EVT Corp, Indianapolis, IN) was provided with infrarenal fixation. The remaining endografts (n = 110) did not have proximal fixation. There were no differences in use of proximal fixation between patients with favorable and unfavorable aneurysm necks. Preoperative CRFs were complete in 169 patients (98.8%); additional calcification and/or thrombus measurements could be performed in the remaining two (1.2%). The baseline characteristics are presented in Table III.

The median follow-up length was 7.6 years (range, 0.1-17.9 years), during which PEF was observed in 20 patients. Of these failures, 18 patients received a first reintervention for PEF. Two additional patients developed PEF but did not receive treatment. One patient was unsuitable for both open and endovascular secondary intervention for a type Ia endoleak and remained in follow-up. One patient suffered a secondary aneurysm rupture due to an already diagnosed type Ia endoleak. The median time to intervention for PEF or time to detection in case no treatment was performed was 4.9 years (range, 0.1-17.1 years).

Table II. Endograft type and manufactures used in the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial

Type and manufacturer	Number	Graft type	Proximal fixation
Endologix, Bard/Impra	1	SE	None
Lifepath, Baxter Healthcare Corp	4	SE	None
Zenith, Cook Inc	57	SE	Transrenal active fixation
Quantum LP, Cordis Corp (J&J)	8	BE	None
Excluder, W. L. Gore and Assoc. Inc	37	SE	None
Ancure, Guidant-EVT	4	SE	Infrarenal active fixation
AneuRx, Medtronic	12	SE	None
Talent, World Medical/Medtronic	48	SE	None
Total	171	163 SE	61 active fixation

Table III. Baseline characteristics

Characteristic	Favorable neck (n =141)	Unfavorable neck (n = 30)	Total (N = 171)	*P*-value (2-tailed)
Age, years	70.5 ± 6.6	70.9 ± 6.0	70.5 ± 6.5	.74
Male gender	131 (92.9)	29 (96.7)	160 (93.6)	.45
SVS/ISCVS risk-factor score				
Diabetes mellitus	17 (12.1)	0 (0.0)	17 (12.0)	.045
Tobacco use	93 (66.0)	17 (56.7)	110 (64.3)	.34
Hypertension	84 (59.6)	16 (53.3)	100 (58.5)	.53
Hyperlipidemia	63 (46.3)	14 (46.7)	77 (46.4)	.97
Carotid disease	19 (13.5)	5 (16.7)	24 (14.0)	.65
Cardiac disease	59 (41.8)	14 (46.7)	73 (42.7)	.63
Renal disease	12 (8.5)	1 (3.3)	13 (7.6)	.33
Pulmonary disease	39 (27.7)	7 (23.3)	46 (26.9)	.63
Sum SVS/ISCVS risk-score	4.5 ± 2.7	4.1 ± 1.9	4.4 ± 2.5	.48
Body mass index, kg/m^2	26.3 ± 3.5	26.0 ± 3.1	26.2 ± 3.4	.73
Aneurysm diameter, mm	59.6 ± 8.5	64.9 ± 10.3	60.6 ± 9.1	.004
Lowest ABI	95.3 ± 19.0	95.6 ± 14.0	95.4 ± 18.1	.86
ASA class				
ASA I	27 (19.1)	11 (36.7)	38 (22.2)	.04
ASA II	103 (73.0)	17 (56.7)	120 (70.2)	.08
ASA III	11 (7.8)	2 (6.7)	13 (7.6)	.83
Stent graft oversizing	1.2 ± 0.2	1.1 ± 0.1	1.2 ± 0.2	.14
Proximal fixation	48 (34.0)	13 (43.3)	61 (35.7)	.40

ABI, Ankle brachial index; *ASA*, American Society of Anesthesiologists; *ISCVS*, International Society for Cardiovascular Surgery; *SVS*, Society for Vascular Surgery.
Data are presented as number (%) or mean (standard deviation).

ASG neck score and threshold. The median ASG neck score was 2 (range, 0-9). The median aneurysm neck length was 20.0 mm (range, 6.0-67.0 mm), the median aneurysm neck diameter was 23.0 mm (range, 10.0-32.0 mm), the median angulation was >150°, and the median circumference with calcification or thrombus was <25%, displayed in Table IV. Validation of the neck morphology measurements showed good agreement for the calcification and/or thrombus measurements and excellent agreement for all other neck variables. The ASG neck score and its threshold showed excellent agreement as well.

The threshold for prediction of PEF based on ASG neck score was determined at ≥5 based on ROC analysis. The ROC analysis showed an area under the curve of 0.77 (95% CI, 0.65-0.90; $P < .001$), corresponding to acceptable prediction. The ROC curve is displayed in Fig 1. An ASG neck score ≤4 was observed in 141 patients, and a score ≥5 was present in 30 patients. Within the favorable neck morphology group (ASG ≤4), nine of

Table IV. Neck morphology score

ASG variable	Group No. (%)		Total (n = 171)	*P*-value (2-tailed)
	No endograft failure (n = 151)	With endograft failure (n = 20)		
Aneurysm neck length, mm				
0: >25	57 (37.7)	1 (5.0)	58 (33.9)	.001
1: >15 and ≤25	65 (43.0)	10 (50.0)	75 (43.9)	
2: >10 and ≤15	25 (16.6)	5 (25.0)	30 (17.5)	
3: ≤10	4 (2.6)	4 (20.0)	8 (4.7)	
Aneurysm neck diameter, mm				
0: <24	83 (55.0)	8 (40.0)	91 (53.2)	.015
1: ≥24 and <26	31 (20.5)	1 (5.0)	32 (18.7)	
2: ≥26 and <28	17 (11.3)	3 (15.0)	20 (11.7)	
3: ≥28	20 (13.2)	8 (40.0)	28 (16.4)	
Aneurysm neck angulation, degrees				
0: <30	112 (74.2)	5 (25.0)	116 (67.8)	<.001
1: ≥30 and <45	22 (14.6)	5 (25.0)	23 (13.5)	
2: ≥45 and <60	11 (7.3)	4 (20.0)	12 (7.0)	
3: ≥60	6 (4.0)	6 (30.0)	20 (11.7)	
Aneurysm neck calcification and/or thrombus, %				
0: <25	128 (84.8)	15 (75.0)	143 (83.6)	.244
1: ≥25 and <50	18 (11.9)	4 (20.0)	23 (13.5)	
2: ≥50	5 (3.3)	1 (5.0)	5 (2.9)	

ASG, Aneurysm severity grading.

141 patients (6.4%) developed PEF, compared with 11 of 30 patients (36.7%) in the unfavorable neck morphology group (ASG ≥5). At baseline, patients in the unfavorable neck morphology group were less frequently diagnosed with diabetes and had larger aneurysms (Table III). No overall survival differences were found between groups with favorable and unfavorable neck morphology as between those with or without PEF. Stent graft oversizing did not differ between groups. Sensitivity of the calculated ASG neck threshold ≥5 was 55.0% (95% CI, 31.5%-76.9%), whereas the specificity was 87.4% (95% CI, 81.5%-92.3%), with a positive predictive value of 36.7% (95% CI, 24.5%-50.8%) and a negative predictive value of 93.6% (95% CI, 90.0%-96.0%). The positive likelihood ratio was 4.4 (95% CI, 2.5-7.8), and the negative likelihood ratio was 0.51 (95% CI, 0.3-0.8).

Morphology. When comparing the morphological variables between the favorable group and the unfavorable group, shorter aneurysm neck lengths, wider aneurysm neck diameters, and higher angulation were observed. No differences were seen between groups in the circumferential percentage of calcification and/or thrombus. When comparing patients who developed PEF with those who did not, similar differences were seen as between favorable and unfavorable groups (Table IV). No differences were observed between patients in the unfavorable group who developed PEF and those who did not develop PEF.

Proximal endograft failure. The cumulative percentage free from PEF was compared between favorable and unfavorable groups, based on the ASG threshold ≥5. Twelve years after randomization, the cumulative rates free from PEF were 91.7% for the favorable group and 53.2% for the unfavorable group, for a difference of 38.5% (95% CI, 13.9%-63.1%; $P < .001$). The Kaplan-Meier graph is displayed in Fig 2. When comparing all first indications for secondary interventions between groups, a smaller difference was found, a difference of 16.8 percentage points ($P = .028$). Cox proportional hazard analysis showed an increased risk for endograft failure in the proximal aneurysm neck based on the ASG neck score (calculated HR, 1.7; 95% CI, 1.4-2.1; $P < .001$). The calculated HR for the unfavorable group based on the threshold ≥5 was 7.7 (95% CI, 3.1-19.2; $P < .001$). After correction for preoperative aneurysm diameter, oversizing, proximal fixation, and baseline characteristics, the ASG neck score and its calculated threshold remained independently associated with PEF. No differences were seen between early PEF (within 5 years after treatment) and late PEF (more than 5 years after treatment).

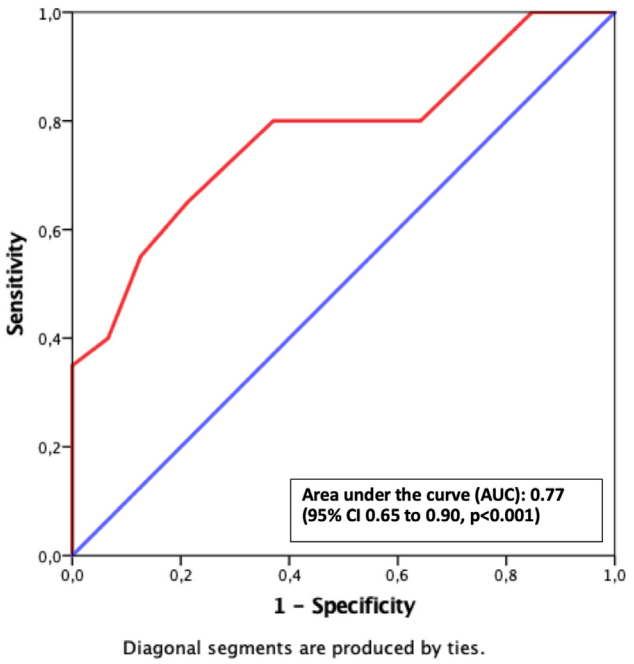

Fig 1. Receiver operating characteristic (ROC) curve (*red*); the area under the curve (*AUC*) is 0.77. A trend line is displayed in *blue*. *CI*, Confidence interval.

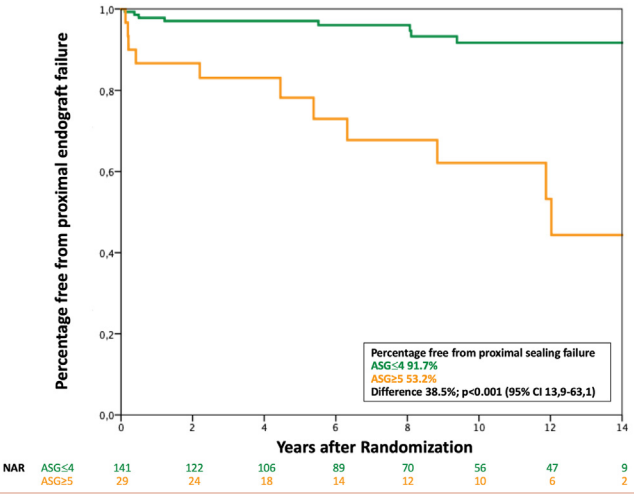

Fig 2. Kaplan-Meier graph showing freedom from proximal endograft failure (PEF) on the y-axis, with the x-axis indicating years after randomization. Favorable necks (*green*); unfavorable necks (*orange*). Difference 38.5%; $P < .001$. *ASG*, Aneurysm severity grading; *CI*, confidence interval.

DISCUSSION

The need for secondary intervention to maintain adequate aneurysm exclusion and prevent secondary rupture is of main concern in patients after EVAR.[1,2] The loss of wall apposition resulting in PEF (type I endoleak and/or migration) is more frequently described in patients with unfavorable aneurysm neck morphology.[4,13,14] The ASG score, an indicator for aneurysm morphology, has been validated to predict complications and technical complexity with short-term follow-up.[7,10,15] However, this score lacks opportunity to specify different indications for secondary interventions, such as PEF. Predicting PEF and adverse events causative for secondary intervention after EVAR probably requires analysis of preoperative neck morphology rather than aneurysm sack morphology or iliac morphology. Therefore, the current study demonstrates that the ASG neck score is an acceptable predictor for the occurrence of PEF not only during short-term follow-up but during the entire follow-up. A subgroup analysis for PEF within the first 5 years after EVAR and late PEF occurring more than 5 years after EVAR showed a similar area under the curve, and comparable positive and negative likelihood ratios. Of 10 patients with early PEF, six (60%) were classified unfavorable, whereas five of 10 (50%) were classified unfavorable in the patients who developed late PEF. The overall incidence of PEF in patients after EVAR in this study was just less than 12%. The ASG neck score is especially useful in patients with low scores because PEF hardly occurs in these patients; however, the risk for secondary interventions increases seven-fold in patients with unfavorable neck morphology. Due to the low incidence, the occurrence of PEF in this group is still just 36.7%. Future studies would have to prove if these patients benefit from complex endovascular techniques or if close surveillance might be enough after all.

This is a new observation; previous studies demonstrated the risk for short-term secondary interventions due to hostile neck anatomy. Meanwhile, the latest updates of the major randomized trials investigating outcomes after EVAR showed a continued risk for secondary interventions following EVAR during the entire follow-up.[1,2] The current study also demonstrates an increased risk for PEF in patients with unfavorable neck morphology far beyond 5 years of follow-up. If all secondary interventions were compared, a smaller difference was observed than when comparing neck-related interventions. The remaining difference was most likely caused by the incidence of PEF. It is possible that patients with a first secondary intervention for PEF underwent secondary interventions for other purposes later during follow-up. Meanwhile, no difference was observed in overall survival between groups. The DREAM trial was particularly useful for this investigation due to the availability of long-term secondary interventions and high completeness of follow-up.

Secondary procedures in the first years of follow-up are associated with both aneurysm morphology and procedural complications. For this reason, strict preoperative screening is indispensable, and patients with unfavorable neck anatomy should be at least considered for open treatment, especially when exceeding the IFU as seen in patients with hostile aneurysm neck morphology.

The etiology of long-term secondary interventions is less obvious and might be multicausal.[4,9,15] For example, stent graft durability is linked to PEF by loss of adequate aneurysm exclusion. Increased rates of secondary interventions observed in the major clinical trials have been associated with stent graft durability.[16] These results may be related to obsolete or earlier generations of devices being used in the major trials. A recent publication comparing real-world outcomes after elective open and endovascular aneurysm repair showed a decrease of secondary interventions with newer generation endovascular devices.[17] However, real-world data is prone for selection bias because patients with hostile neck morphology might be selected to undergo open repair.

Furthermore, PEF may also be the result from disease progression and neck dilatation.[18-21] The reported increase in aneurysm neck dilatation after endovascular repair is partly considered to be caused by radial force of the implanted endograft exerted on the vascular wall and is dependent on type and oversizing of the endograft.[20-23] However, progressive dilatation beyond the nominal diameter of the inserted endograft is described as well; this phenomenon is often explained by disease progression and may contribute to late onset of PEF.[20,23,24] Yet, a significant increased occurrence of late PEF was observed in patients with preoperative unfavorable neck morphology. This dilatation of the proximal seal zone may contribute to the development of type Ia endoleaks or proximal migration of the endovascular device, which creates the urgency for secondary procedures.[23] Even though dilatation of the proximal neck is a common phenomenon, it is hard to predict based on preoperative morphologic parameters.[23,25,26] Kouvelos et al showed that proximal neck dilatation already occurs in the first years after EVAR, and, in a smaller proportion, progressive neck dilatation is witnessed over time.[23] A possible explanation is a loss of wall apposition, initially induced by the radial force of the stent graft, leading to pressure transmission on the aortic wall. This can ultimately induce progressive dilatation of the proximal neck and necessitate secondary interventions. Future research should focus on the association between PEF and incidence of neck dilatation beyond the nominal endograft diameter as well as differences in neck dilatation between patients with favorable and unfavorable neck morphology prior to treatment.

In the current study, the preoperative ASG neck score showed an increased risk for PEF even after correcting for oversizing and preoperative aneurysm size on multivariate analysis. In this study, 10 patients (6%) suffered PEF late during follow-up. The ASG neck score was a comparable predictor for late PEF after EVAR as well as for early PEF. This suggests that long-term PEF can also be explained by preoperative neck morphology and that patients with unfavorable neck morphology remain at constant risk to lose adequate aneurysm exclusion. This corresponds to the ongoing need for secondary interventions after EVAR.[1,2] A delay in treatment after diagnosis of PEF may cause selection bias by contributing to late onset of secondary interventions, while in fact, the loss of adequate aneurysm sealing already occurred earlier during follow-up.

Study strengths and limitations. To our knowledge, there are no reports analyzing the association between preoperative aneurysm morphology and late PEF. Preoperative neck morphology was available in all patients enrolled in the DREAM trial; however, preoperative aneurysm sack volumes were not available for comparison, and therefore no correction for aneurysm volume shrinkage could be performed. All patients in the DREAM trial were suitable for both open and endovascular repair; no patients were treated outside the manufacturer's IFU. This reduces the chance of misrepresentation of the risk to develop endograft failure. Within the DREAM trial, 171 patients were treated by endovascular means, and long-term follow-up and occurrence of complications was already available. Approximately 70% of the patients were still alive 5 years after randomization, of whom 90.0% remained under surveillance. This number dropped to 68.3% after 10 years. The number of patients who underwent repeated CT imaging more than 5 years after treatment was 93 of the surviving patients (75.6%) at that time. However, the decision for continued follow-up after 5 years was made by the treating vascular surgeon, which could cause missing of PEF.

Despite follow-up being available for more than 12 years, only 20 patients suffered PEF; of them, 10 developed PEF more than 5 years after treatment. The number of events is small, as was the number of patients with unfavorable neck morphology, which could have induced a type I error. The decision for treatment was made by the treating vascular surgeon, treatment indications were cross-referenced, and PEF without intervention was included in this study as well, which reduces the risk for information bias.

This study compared favorable and unfavorable neck morphology and is a representation of EVAR in the early 2000s without availability of complex endovascular approaches. The stent grafts used in the DREAM trial have been replaced by newer generations or are no longer available. It is suggested, but not proven, that the durability of new generation stent grafts is superior to the ones used in this study.[17,27] This also allowed for a relatively small number of patients with short aneurysm necks to be randomized in the DREAM trial. These patients may contribute to the increased number of secondary procedures performed in the DREAM trial, although divided equally between favorable and unfavorable neck groups. It has to be emphasized that no

endovascular treatment alternatives were available at that time. Still, this study accentuates that unfavorable neck morphology is associated with increased rates of secondary interventions. Due to continued development of endografts, no strong recommendation could be made regarding current generation endografts. Nonetheless, durability of creative infrarenal EVAR for unfavorable neck morphology can be doubted based on these results, especially given the current availability of complex EVAR with good results. Long-term studies investigating outcomes after complex EVAR are required to prove its superiority over open repair.

Neck morphology measurements were performed in the individual trial centers by trained radiologists, while at the time of inclusion, no thin slice CT images or measuring software was available. This may contribute to interobserver variability and information bias; still, validation analysis of the CRF values showed high agreement in all measurements. The distribution of favorable and unfavorable neck morphology was based on an arbitrary margin of the ASG neck score derived from ROC analysis. The ASG score including aneurysm sack and iliac morphology was validated in cohort studies, whereas the ASG neck score was not individually validated in these studies. Nevertheless, the calculated ASG neck threshold was in coherence with and proportional to the complete ASG score threshold validated in these earlier cohort studies.[6,10] Withal, individual assessment of the proximal neck has been performed earlier and is a known predictor for early secondary interventions.[7,28] This is in line with the results of our current study using the ASG neck score as part of the ASG score. Future studies might be able to validate the ASG neck threshold calculated in this study.

Last, baseline characteristics differed between patients with favorable and unfavorable neck morphology. Within the unfavorable group, more patients were classified as American Society of Anesthesiologists 1, suggesting an overall slightly healthier patient population. Aneurysm size was expectedly higher in patients with unfavorable neck morphology, which corresponds to the aneurysm severity and disease progression prior to treatment. Diabetes was not present in patients with unfavorable neck morphology; this is in line with the existing literature that suggests that diabetes and in particularly the use of anti-diabetics reduces the risk of aneurysm progression.[29-31]

In this study, the ASG neck score was used to predict PEF, and a threshold was calculated to compare patients at low risk and high risk for endograft failure. The risk for PEF was increased for patients with unfavorable neck morphology (high ASG neck scores), even on multivariate analysis and correction for oversizing, proximal fixation, and preoperative aneurysm size during the entire follow-up.

CONCLUSIONS

Unfavorable aneurysm neck morphology is associated with PEF during short-term and even long-term follow-up after endovascular aneurysm repair in patients suitable for open and endovascular repair. Due to this persistent risk of failure, patients with unfavorable neck morphology should be followed with increased awareness, and secondary intervention might be required even late after treatment.

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AUTHOR CONTRIBUTIONS

Conception and design: TGS, KY, JDB
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