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Identifying Patients at High Risk for Post-EVAR Aneurysm Sac Growth

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Abstract

Purpose: Post-EVAR (endovascular aneurysm repair) aneurysm sac growth can be seen as therapy failure as it is a risk factor for post-EVAR aneurysm rupture. This study sought to identify preoperative patient predictors for developing post-EVAR aneurysm sac growth. **Material and Methods:** A systematic review was conducted to select potential predictive preoperative factors for post-EVAR sac growth (including a total of 34.886 patients), which were evaluated by a retrospective single-center analysis of patients undergoing EVAR between 2009 and 2019 (N=247) with pre-EVAR computed tomography scans and at least 1 year follow-up. The primary study outcome was post-EVAR abdominal aortic aneurysm (AAA) sac enlargement (≥5 mm diameter increase). Multivariate Cox regression and Kaplan-Meier survival curves were constructed. **Results:** Potential correlative factors for post-EVAR sac growth included in the cohort analysis were age, sex, anticoagulants, antiplatelets, renal insufficiency, anemia, low thrombocyte count, pulmonary comorbidities, aneurysm diameter, neck diameter, neck angle, neck length, configuration of intraluminal thrombus, common iliac artery diameter, the number of patent lumbar arteries, and a patent inferior mesenteric artery. Multivariate analysis showed that infrarenal neck angulation (hazard ratio, 1.014; confidence interval (CI), 1.001–1.026; p=0.034) and the number of patent lumbar arteries (hazard ratio, 1.340; CI, 1.131–1.588; p<0.001) were associated with post-EVAR growth. Difference in estimated freedom from post-EVAR sac growth for patients with ≥4 patent lumbar arteries versus <4 patent lumbar arteries became clear after 2 years: 88.5% versus 100%, respectively (p<0.001). Of note, 31% of the patients (n=51) with ≥4 patent lumbar arteries (n=167) developed post-EVAR sac growth. In our cohort, the median maximum AAA diameter was 57 mm (interquartile range [IQR] = 54–62) and the median postoperative follow-up time was 54 months (IQR = 34–79). In all, 23% (n=57) of the patients suffered from post-EVAR growth. The median time for post-EVAR growth was 37 months (IQR = 24–63). In 46 of the 57 post-EVAR growth cases (81%), an endoleak was observed; 2.4% (n=6) of the patients suffered from post-EVAR rupture. The total mortality in the cohort was 24% (n=60); 4% (n=10) was AAA related. **Conclusions:** This study showed that having 4 or more patent lumbar arteries is an important predictive factor for postoperative sac growth in patients undergoing EVAR.

Clinical Impact
This study strongly suggests that having 4 or more patent lumbar arteries should be included in preoperative counseling for EVAR, in conjunction to the instructions for use (IFU).

Keywords
abdominal aortic aneurysm, abdominal aortic aneurysm repair, aneurysm sac, EVAR, endovascular repair, complications

Article Highlights

Key Findings: Infrarenal neck angulation and ≥4 patent lumbar arteries are preoperative predictive factors for post-EVAR aneurysm growth.

Take Home Message: The threshold for extension of the EVAR follow-up scheme of patients with ≥4 patent lumbar arteries should be low and the higher risk of post-EVAR sac growth in case of ≥4 patent lumbar arteries should be included in preoperative counseling.

Introduction

Post-endovascular aneurysm repair (EVAR) aneurysm sac enlargement indicates therapy failure, as it reflects ongoing

pressure within the abdominal aortic aneurysm (AAA) and therefore rupture risk after intervention.[1,2]

While much is known about postoperative predictors for aneurysm sac growth,[3] robust preoperative predictive factors have yet not been established. These would be clinically more relevant to guide treatment decisions (viz. open vs endovascular repair) and risk-stratified surveillance. Contributing factors to this lack of consensus include analysis of heterogeneous small panels of parameters and a shortage of studies with preoperative predictive factors as their primary objective.

The study aim was therefore to determine which preoperative factors predict post-EVAR aneurysm sac growth. A systematic review was performed to identify preoperative factors predictive for post-EVAR aneurysm sac growth, complemented by an evaluation of an EVAR cohort of our institution.

Methods

This was a two-stage study: first, a systematic review was conducted to identify potential preoperative factors associated with post-EVAR aneurysm sac growth, and subsequently, these findings were validated in a retrospective cohort study.

Systematic Review of Potential Preoperative Predictive Factors for Post-EVAR Aneurysm Sac Growth

A systematic literature review was conducted according to the PRISMA guidelines. Studies were identified by searching PubMed and Embase. The search strategy (outlined in Supplement 1 [Systematic Review Protocol]) was based on 3 search themes, combined in the search by AND. The first theme was created for EVAR, the second theme included risk factor prediction components, and the third theme was created for aneurysm sac growth.

The search was most recently updated on December 30, 2021. First, 2 authors (L.E.B., J.L.) independently reviewed the titles and abstracts for eligibility. Thereafter, 44 full-text articles were assessed, of which 33 full-text articles were included in the systematic review.[3,4]

Retrospective Cohort Study

We conducted a retrospective review of prospectively gathered data from 284 patients undergoing elective EVAR repair at our institution between January 2009 and December 2019.

Preoperative anatomical parameters were derived from standard preoperative computed tomography angiography (CTA) scans. Measurements were performed by individuals blinded to the patients. All measurements obtained were consistent with the Society for Vascular Surgery Reporting Standards,[5] including the definition for aneurysm sac growth: diameter increase $\geq$ 5 mm. All diameter measurements were calculated perpendicular to the flow line of the vessel of interest. All length and angle measurements were made along the lumen centerline.

Follow-up data were based on a standard follow-up scheme after EVAR that consists of a CTA scan after 6 weeks, duplex ultrasound at 6 and 12 months, and from then on a yearly duplex or CTA. Post-EVAR sac growth on duplex was always confirmed by a CTA scan. Nonscheduled CTA scans were performed only in cases of postoperative events and complications.

The duration of follow-up was calculated from the time of the procedure until the last control radiological examination (either CTA or duplex). Exclusion criteria included intra-operative conversion to open repair, fenestrated and chimney EVARs, or an isolated iliac artery aneurysm without a concurrent AAA.

This study was performed with the approval of the regional medical ethics committee (METC Zuid West).

The statistical analysis was performed using SPSS Statistics, version 28.0 (SPSS IBM® Statistics, Armonk, New York, USA). Univariate and multivariate Cox regression analysis was performed to calculate the hazard ratios (HRs) with a 95% confidence interval (CI) for sac growth. Any variable with a p value <0.1 on univariate analysis was included in the multivariate analysis. Factors in the multivariate analysis with a p value <0.05 were considered significant.

Analysis of time-to-event occurrence of AAA sac enlargement was performed with the Kaplan-Meier method. The log-rank test was used to compare differences between these curves (p value <0.05 was considered significant).

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All observations were censored at the time of the patient's last radiological examination.

Results

Systematic Review of Potential Preoperative Predictive Factors for Post-EVAR Aneurysm Sac Growth

The search strategy identified 861 articles after removal of duplicates, 769 of which were considered of potential relevance (Figure 1). On exclusion of articles deemed not relevant for this study, 33 full-text articles were included for the qualitative synthesis. Exclusion criteria included not about factors influencing aneurysm sac growth, exclusive focus on subgroups (eg, patients with type 2 endoleak), exclusive focus on postoperative risk factors, no given odds ratios or HRs, exclusive focus on sac regression as opposed to sac growth, sac growth taken together as a variable with other adverse events or other definition of sac growth instead of growth defined as an increase in aneurysm diameter of ≥5mm, and review articles.

Results of the systematic review are summarized in Table 1. The incidence of sac growth in the selection of articles varied from 1.1% to 41.0%.

A total of 34.886 patients were included in the studies, which were all retrospective cohort studies. In total, 8958 (25.7%) cases of growth were reported.

Of note, the majority of the included studies were potentially impaired by selection bias. Furthermore, follow-up data were severely limited. Reason for loss to follow-up data was often unspecified.

The systematic review identified the following potential preoperative correlative factors for post-EVAR sac growth: patient factors (age, sex, use of anticoagulants, use of antiplatelets, renal insufficiency, anemia, low thrombocyte count, pulmonary comorbidities, familial form of AAA), AAA anatomical factors (aneurysm diameter, neck diameter, neck angle >60°, neck length, hypogastric coverage, percentage of intraluminal thrombus, aneurysm sac thrombus, aortic branches, common iliac artery diameter, iliac tortuosity index, iliac calcifications, accessory renal arteries, iliac artery length, iliac aneurysms, number of patent lumbar arteries, angle of proximal landing zone, endograft oversizing), urgent repair, and brachial-ankle pulse wave velocity.

Preoperative factors that were selected for univariate regression analysis included age, sex, use of anticoagulants, use of antiplatelets, renal insufficiency, anemia, low thrombocyte count, pulmonary comorbidities, aneurysm diameter, neck diameter, neck angle, neck length, configuration of intraluminal thrombus, common iliac artery diameter, and the number of patent lumbar arteries. Next to patent lumbar arteries, a patent inferior mesenteric artery can also be a source for aneurysm sac feeding. As this aspect was not identified in the systematic review, this factor was also included.

Other potential factors were excluded due to a variety of reasons, including unavailability of 3-dimensional and volumetric analysis in our institution (iliac tortuosity index and length, iliac calcifications and lumen/thrombus percentage) and no (standardized) assessment at our institution (brachial-ankle pulse wave velocity and familial AAA occurrence). Moreover, hypogastric coverage and prothesis oversizing were excluded, because these subgroups were too small in our cohort for adequate assessment. In our institution, in case of a concomitant common iliac artery aneurysm, the internal iliac artery is embolized or stented with a branched device to prevent a type II endoleak. Moreover, the prothesis oversizing standard is 10% in our institution.

Retrospective Cohort Study for Preoperative Predictive Factors of Post-EVAR Aneurysm Sac Growth

Included patient (N=247) characteristics are described in Table 2. A total of 37 patients were excluded due to a follow-up of less than 1 year. Twenty-three (62%) patients were lost to follow-up due to mortality within 1 year, of which 2 (9%) were related to AAA. Two patients moved to another city, and 12 patients were lost to follow-up with unknown cause. The median maximum AAA diameter was 57 mm (interquartile range [IQR] = 54–62), and the median postoperative follow-up time was 54 months (IQR = 34–79).

Post-EVAR Growth Incidence and Related Adverse Outcomes

The primary endpoint was post-EVAR aneurysm sac growth, defined as a total increase in size of 5 mm or more in aneurysm diameter as compared with the last measured preoperative aortic diameter at any time during follow-up.[5]

In our cohort, 23% (n=57) of the patients suffered from post-EVAR growth. In 5 of these patients, recurrent growth after endoleak treatment was found. The median time for post-EVAR growth was 37 months (IQR = 24–63); see Figure 2 for a visual representation of post-EVAR sac growth distribution. Post-EVAR growth before the first postoperative year was rare (n=2).

In 46 of the 57 post-EVAR growth cases (81%), an endoleak was observed, and in 65% (n=37) of the total

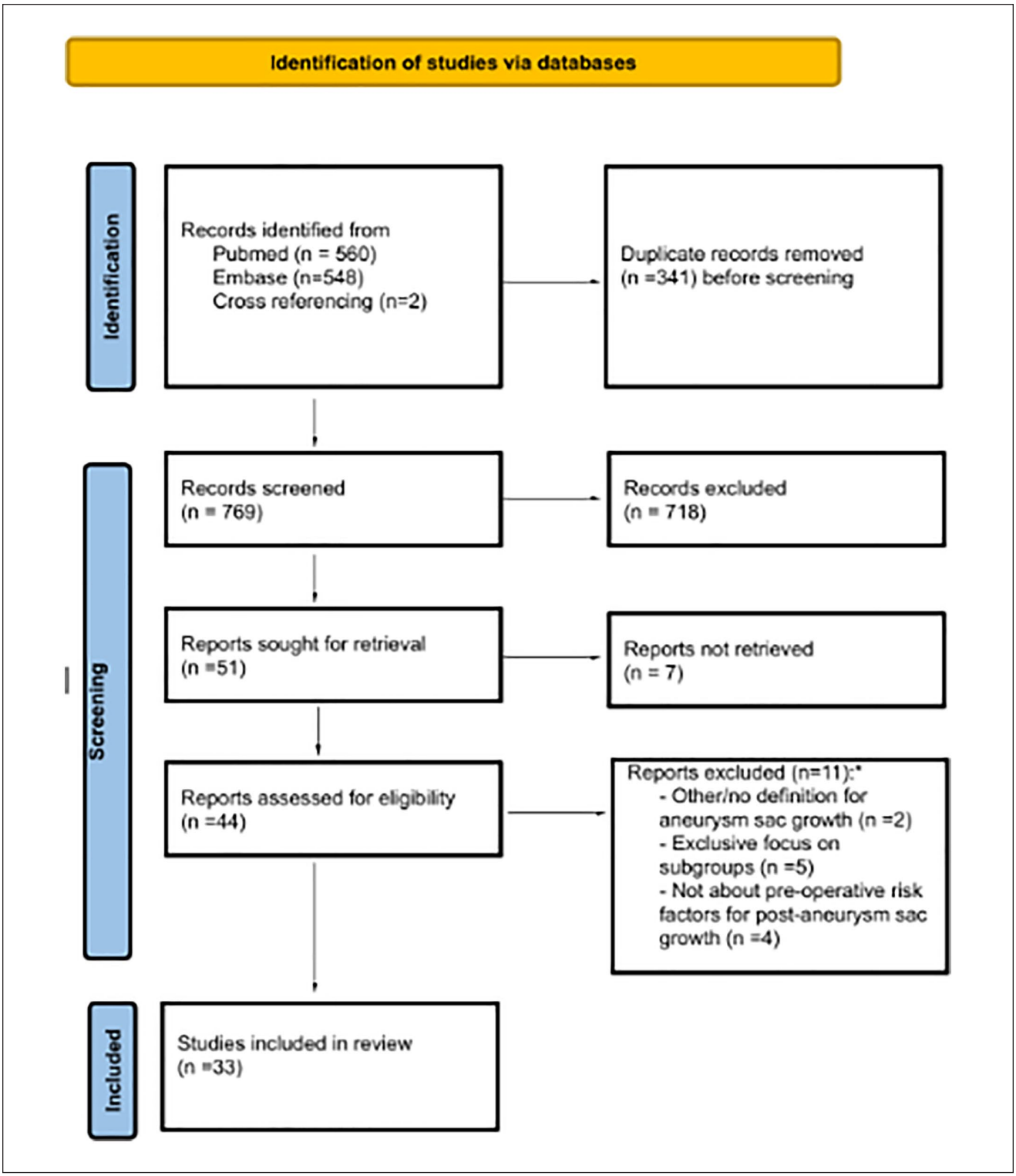

Figure 1. PRISMA diagram for selecting papers included in the systematic review.

Table 1. Systematic Review Results.

Study	Type of study	No. of included patients	No. of patients with sac growth (%)	Length of follow-up	Risk factors assessed	
					Significant correlation found	No significant correlation found
AbuRahma et al[4]	Cohort study	526	31 (6.6)	Mean = 30 months (range = 1–140 months)	Aneurysm neck angle >60°	Neck length < 10 mm Diameter > 31 mm ≥ 50% calcification ≥ 50% circumferential thrombus
AbuRahma et al[6]	Cohort study	688	33 (4.8)	For ≤31mm: mean = 25.2 months For >31mm: mean = 31.8 months	Large aneurysm neck diameter (>31 mm)	X
Bastos Gonçalves et al[7]	Cohort study	144	37 (26.1)	Maximum median of 3.34 years	Generation of implanted endoprosthesis Neck diameter Type I endoleak	Neck angulation
Beckerman et al[8]	Cohort study	566	66 (11.7)	Mean = 3.54 ± 2.65 years	X	Outside of IFU
Bryce et al[9]	Cohort study	125	28 (22.4)	Mean = 47.3 months (range = 12–91 months	X	Patients operated between 2004 and 2008 vs 2009 and 2013
Chikazawa et al[10]	Cohort study	148	21 (14.2)	Not stated	Antiplatelet intake Persistent type 2 endoleak Female sex	X
Choke et al[11]	Cohort study	147	7 (4.8)	Mean = 21.7 months	X	Hostile neck Type 2 endoleak
Deery et al[12]	Cohort study	1802	162 (9%)	1 year	Preoperative renal insufficiency Urgent repair Hypogastric coverage Type I/III or type II endoleak at follow-up.	Smoking status Aneurysm diameter
Ding et al[13]	Cohort study	184	7 (3.8)	Mean = 23.1 ± 18.0 months	X	Amount of intraluminal thrombus
Fairman et al[14]	Cohort study	351	6 (2.6; loss to follow-up included)	Not stated	Aneurysm diameter Endoleak at 24 months Relative neck thrombus/plaque	Age Aortic neck length Sex Patent inferior mesenteric artery Aortic neck shape Smoking status
Garbo et al[15]	Cohort study	91	9 (9.9)	Maximum median of 56.6 ± 36.6 months	Aneurysm diameter	X
Herman et al[16]	Cohort study	461	38 (8.1)	Mean = 2.1 ± 1.7 years	Violation of neck diameter	X
Hiraoka et al[17]	Cohort study	148	24 (16.2)	2.4 ± 1.4 years	Age Outer volume Percentage of intraluminal thrombus Type 2 endoleak	Aortic neck length Aortic neck angle Aneurysm diameter

(continued)

Table 1. (continued)

Study	Type of study	No. of included patients	No. of patients with sac growth (%)	Length of follow-up	Risk factors assessed	
					Significant correlation found	No significant correlation found
Hwang et al[18]	Cohort study	157	16 (10.2)	Median 32.5 months (interquartile range = 11.9–55.6)	Renal insufficiency Antithrombotics Endoleak	Hostile neck Age Sex Hypertension Diabetes mellitus Coronary artery disease Congestive heart failure Arrhythmia Cerebrovascular disease COPD Dyslipidemia Smoking status Malignancy
Ito et al[19]	Cohort study	157	32 (20.4)	Median = 23.6 months (range = 6–59)	Neck angulation Types I and II endoleak	Stroke Aneurysm wall thrombus Aneurysm wall enhancement
Iwakoshi et al[20]	Cohort study	127	19 (15.0)	Median = 43 months	Preoperative aneurysm sac diameter Angulated short proximal aortic neck	Age Sex Hypertension Diabetes mellitus Coronary artery disease Chronic renal failure Smoking status Anatomic features, except from aortic neck angulation and length
Kaladji et al[21]	Cohort study	213	51 (25.3)	Mean = 43.8 months ±22.1	Age Aneurysm sac thrombus Aortic branches Iliac tortuosity index Iliac calcifications	Aortic neck calcifications Aortic tortuosity index Aortic angle
Matsumoto et al[22]	Cohort study	106	3 (2.8)	Mean = 875 days	X	Off-label use of EVAR
Morisaki et al[23]	Cohort study	182	8 (8.4)	1 year	Antiplatelet therapy Anticoagulants therapy Aortic diameter Lack of posterior thrombus	X
Nakai et al[24]	Cohort study	143	22 (15.4)	Mean = 12 months (18.7 ± 1.08)	Endoleak Aneurysm diameter ≥60 mm Infrarenal neck angulation >60°	Sex Age Antiplatelet therapy IIA embolization Aortic proximal neck diameter and length

(continued)

Table 1. (continued)

Study	Type of study	No. of included patients	No. of patients with sac growth (%)	Length of follow-up	Risk factors assessed	
					Significant correlation found	No significant correlation found
O'Donnell et al[25]	Cohort study	14817	3732 (25)	1 year	Age Appearance of new endoleak Smaller aortic diameter Anemia Rupture	X
Okada et al[26]	Cohort study	589	112 (19)	Mean = 2.9 years ± 1.6 years	Low platelet count Persistent endoleak	History of previous abdominal surgery Outside instruction for use Procedure time Atrial fibrillation-atrial flutter Sex Aortic diameter Coronary artery disease Cerebrovascular disease Smoking status
Oliveira et al[27]	Cohort study	427	78 (18.3)	<30 mm neck diameter: median 3.1 years (1.2–4.7) ≥30 mm neck diameter/control: 4.1 years (2.7–5.6)	X	≥30 mm neck diameter
Png et al[28]	Cohort study	556	17 (3.1)	Median = 32.6 months	Age Pulmonary comorbidities Aortic neck diameter Iliac artery length Aortic and iliac aneurysms	Within instructions for use Sex Cardiac comorbidities Chronic renal disease Diabetes Hypertension Hypercholesterolemia Other anatomic parameters
Sadek et al[29]	Cohort study	136	21 (15.4)	11 months	Endoleak	Sex Device type Age AAA size Percent calcium
Schanzer et al[30]	Cohort study	10228	4193 (41)	Mean = 31 ± 18 months	Endoleak Age ≥80 years Aortic neck diameter ≥28 mm Aortic neck angle >60° Common iliac artery diameter >20 mm.	Sex Maximum AAA diameter ≥55 mm Aortic neck length Conical neck
Seike et al[31]	Cohort study	209	39 (18.7)	Mean 37 ± 12 months	Warfarin therapy Persistent type II endoleak	Number of patent lumbar arteries Patency of inferior mesenteric artery Oral antiplatelet
Seike et al[32]	Cohort study	194	24 (12)	Mean = 57 ± 23 months	The number of patent lumbar arteries	Patency of inferior mesenteric artery Aneurysm size Saccular aneurysm

(continued)

Table 1. (continued)

Study	Type of study	No. of included patients	No. of patients with sac growth (%)	Length of follow-up	Risk factors assessed	
					Significant correlation found	No significant correlation found
Seike et al[33]	Cohort study	159	37 (23)	Mean 48 ± 20 months	Angle of the proximal landing zone	AAA size Suprarenal angulation Terminal aorta diameter Distal landing zone Access route Embolization of bilateral internal iliac arteries were not identified
Sternbergh et al[34]	Cohort study	268	3 (1.1)	Not stated	Endograft oversizing of >30%	X
Ugajin et al[35]	Cohort study	175	28 (16)	Median 36 months	Brachial-ankle pulse wave velocity Age Persistent type II endoleak	Sex Tension Aneurysm size Outside instructions for use
Van de Luijtgaarden et al[36]	Cohort study	255	28 (11)	Median = 3.3 years	Familial form of AAA	X
Wild et al[37]	Cohort study	407	26 (6.4)	Median = 18 months	X	Warfarin therapy Antiplatelet therapy

Abbreviations: AAA, abdominal aortic aneurysm; COPD, chronic obstructive pulmonary disease; EVAR, endovascular aneurysm repair; IFU, instructions for use; X, not specified.

Table 2. Patient Characteristics (N=247).

General	
Age, median, y (Q1–Q3)	74 (68–79)
Sex, male, % (n)	82 (202)
Asymptomatic aneurysm, % (n)	91 (224)
Symptomatic aneurysm, % (n)	8 (20)
Inflammatory aneurysm, % (n)	1 (3)
Comorbidities	
Hypertension, % (n)	75 (185)
Diabetes mellitus, % (n)	22 (54)
Coronary artery disease,[a] % (n)	47 (115)
Peripheral arterial disease, % (n)	20 (50)
Chronic obstructive pulmonary disease, % (n)	28 (70)
Estimated glomerular filtration rate, median, ml/min/1.73 m^2 (Q1–Q3)	68 (58–81)
Renal insufficiency,[b] % (n)	3 (8)
Hemoglobin count, median, mmol/L (Q1–Q3)	8.7 (7.9–9.2)
Anemia, % (n)[c]	33 (82)
Thrombocyte count, median, $\times 10^9$/L (Q1–Q3)	230 (185–272)
Thrombocytopenia,[d] % (n)	8 (20)
Medication	
Antiplatelets, % (n)	65 (160)
Statins, % (n)	79 (196)
Angiotensin-converting enzyme inhibitors, % (n)	34 (83)
Angiotensin II receptor blockers, % (n)	28 (68)
Anticoagulants, % (n)	36 (90)
Anatomical parameters	
Maximum diameter AAA, median, mm (Q1–Q3)	57 (54–62)
Aortic neck diameter, median, mm (Q1–Q3)[e]	23 (21–25.6)
Aortic neck length, median, mm (Q1–Q3)[f]	38 (27–49)
Suprarenal neck angulation, median, degrees (Q1–Q3)[g]	19 (13–32)
Infrarenal neck angulation, median, degrees (Q1–Q3)[h]	34 (22–50)
Intraluminal thrombus configuration[i]	
No thrombus, % (n)	6 (16)
Anterior, % (n)	12 (31)
Posterior, % (n)	12 (30)
Circumferential, % (n)	70 (170)
Number of patent lumbar arteries, median, n (Q1–Q3)[j]	5 (3–6)
Patent inferior mesenteric artery, % (n)	74 (184)
Common iliac artery diameter, median, mm (Q1–Q3)[k]	14 (12–18)
Graft	
Cook, % (n)	64 (157)
Medtronic, % (n)	4 (10)
Cordis, % (n)	28 (69)
Gore, % (n)	4 (11)
Postoperative outcomes	
Post-EVAR growth, % (n)	23 (57)
No endoleak observed, % (n)	5 (11)
In presence of endoleak, % (n)	17 (46)
Endoleak type 1a	3.2 (8)
Endoleak type 1b	3.2 (8)
Endoleak type 1a+b	0.4 (1)
Endoleak type 2	6.5 (16)
Endoleak type 3	0.8 (2)
Endoleak type 2+3	0.8 (2)
Endoleak type 1+2	1.6 (4)
Endoleak type 1+3	0.8 (1)
Endoleak type 1+2+3	0.8 (2)
Endoleak type 1+2+3 and infection	0.4 (1)
Endoleak type 2+ infection	0.4 (1)
Conical neck anatomy in patients with endoleak, % (n)	40 (23)
Reinterventions, % (n)	15 (37)
Post-EVAR rupture, % (n)	2.4 (6)
Mortality, % (n)	24 (60)
AAA related[l]	4 (10)
Non-AAA related	20 (50)

Abbreviations: AAA, abdominal aortic aneurysm; Q1, first quartile; Q3, third quartile.

[a]Based on clinical manifestations of coronary artery disease, for example, myocardial infarction or angina pectoris.

[b]Renal insufficiency was defined as estimated glomerular filtration rate <30 ml/min/1.73 m^2.

[c]Anemia was defined as hemoglobin level for men <8.5 mmol/L, for women <7.5 mmol/L.

[d]Thrombocytopenia was defined as thrombocyte count $<150 \times 10^9$/L.

[e]Aortic neck diameter was defined as the aortic diameter at the lowest renal artery.

[f]Aortic neck length was defined as the distance between the lowest renal artery and the origin of the aneurysm, indicated by a 10% increase in diameter.

[g]The suprarenal neck angle was defined as the angle between the suprarenal aorta, the lowest renal artery, and the origin of the aneurysm.

[h]The infrarenal neck angle was defined as the angle between the lowest renal artery, the origin of the aneurysm, and the aortic bifurcation.

[i]For a description of the thrombus configuration classification, please appreciate Spanos et al.[38]

[j]All patent lumbar arteries between the lowest renal artery and the aortic bifurcation, including the median sacral artery, were registered. Lumbar arteries and the inferior mesenteric artery were registered as being patent when the ostium of the artery was visible in the aortic wall, with contrast being visible in the artery. If a pair of lumbar arteries had 1 ostium in the aortic wall, they were defined as being 2 patent arteries.

[k]The maximum diameter of the common iliac artery was measured. A diameter of ≥ 1.7 cm in men or ≥ 1.5 cm in women is considered aneurysmal.[39]

[l]Aneurysm-related mortality included aneurysm sac rupture post-EVAR (in some cases, due to endoleak), occlusion of EVAR leg prosthesis, occlusion of EVAR trunk prosthesis, bleeding after explantation EVAR, and aorto-enteric fistula.

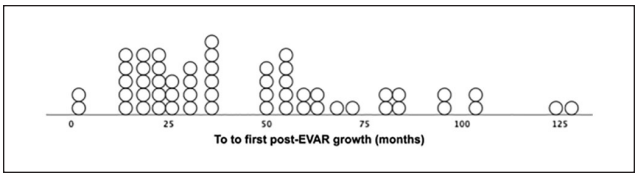

Figure 2. Timing of first post-EVAR (endovascular aneurysm repair) growth. Dot plot for a visual representation of the timing to the first post-EVAR growth (recurrent growth observed in 5 patients is not visualized). Every circle represents a case, on the x-axis months.

patent cohort, a reintervention was performed. In all, 2.4% (n=6) of the patients suffered from post-EVAR rupture. The total mortality in the cohort was 24% (n=60); 4% (n=10) was AAA related.

Preoperative Predictive Factors for Post-EVAR Growth

On univariate analysis (Table 3), the following patient characteristics were associated with an increased risk for AAA sac enlargement: age, chronic obstructive pulmonary disease (COPD), use of antiplatelets, infrarenal neck angulation, number of patent lumbar arteries, and patent inferior mesenteric artery. Multivariate analysis (Table 3) showed that infrarenal neck angulation (HR = 1.014; CI, 1.001–1.026; p=0.034) and the number of patent lumbar arteries (HR = 1.340; CI, 1.131–1.588; p <0.001) were associated with post-EVAR growth.

As the systematic review identified the presence of ≥4 patent lumbar arteries as a risk factor of post-EVAR growth, we also analyzed this cut-off in the multivariate analysis: a HR of 5.159 (CI, 1.979–13.448, p<0.001) was found.

Difference in estimated freedom from post-EVAR sac growth for patients with ≥4 patent lumbar arteries versus <4 patent lumbar arteries (Figure 3A) became clear after 2 years: 88.5% versus 100%, respectively (p<0.001). Of note, 31% of the patients (n=51) with ≥4 patent lumbar arteries (n=167) developed post-EVAR sac growth.

Subanalysis of infrarenal neck angulation outside instructions of use (>60°) showed no significant difference in freedom from post-EVAR sac growth (Figure 3B).

Discussion

This cohort study identified 2 preoperative predictive factors for post-EVAR aneurysm growth: infrarenal neck angulation and the number of patent lumbar arteries. These factors were identified in a preliminary systematic review, which also showed that robust and consistent data regarding preoperative predictive factors for post-EVAR sac growth is currently lacking.

Post-EVAR sac growth poses both significant morbidity as reintervention is often required, and potentially long-term mortality.[12] In 23% of our cohort, post-EVAR sac growth was found, which is in line with the current literature following our systematic review. In 2.4% of the patients, this led to a post-EVAR rupture. In 65% of post-EVAR growth cases, a reintervention was performed.

Having systematically evaluated pre-existent literature to guide potential risk factor selection, we identified several factors that potentially could have caused the wide variety and inconsistency of found risk factors. A first explanation is the various follow-up duration. In our cohort, post-EVAR sac growth was generally found after the first year in follow-up, implying that a minimal follow-up duration of 2 years should be practiced in studies aimed at identifying risk factors for post-EVAR sac growth. Furthermore, often a small spectrum of parameters was assessed, and this has probably impeded analysis for confounding factors. To overcome this problem, we included a broad range of potential predictive factors in univariate analysis. Indeed, multiple potential predictive factors in the univariate analysis resulted in 2 predictive factors in multivariate analysis: infrarenal neck angulation and the number of patent lumbar arteries.

The pathophysiological explanation for the association between patent lumbar arteries and aneurysm sac growth might be aneurysm sac pressurization due to arterial backflow. Previous studies have shown a strong correlation between the number of patent lumbar arteries and the development of a type 2 endoleak.[40,41] Furthermore, type 2 endoleak in itself is a strong predictor for growth, especially if it persists.[42] Despite the fact that a patent inferior mesenteric artery is also a possible source for a type 2 endoleak,[43] it did not appear as a significant predictive factor in the present study.

Although the treatment of type 2 endoleaks is controversial, recently evidence has emerged advocating a more aggressive reintervention strategy.[44,45] Some studies have evaluated endoleak occurrence and decrease of the aneurysm sac diameter after preoperative coil embolization of patent lumbar arteries and a patent inferior mesenteric artery.[46,47] These studies reported that coil embolization leads to a greater decrease in aneurysm sac diameter and less cases of type 2 endoleaks, especially in cases considered to be at high risk for type 2 endoleak based on the number of patent arteries.

However, this hypothesis is not all-encompassing because in our cohort, in 81% of the patients with post-EVAR sac growth, an endoleak was detected.

While infrarenal neck angulation is taken into account for treatment, the number of patent lumbar arteries is generally not considered in the decision to treat. The central question

Table 3. Univariate and Multivariate Analyses for Post-EVAR Growth.

	Univariate analysis			Multivariate analysis		
Variables	HR	95% CI	p value	HR	95% CI	p value
Age	1.050	1.012–1.089	0.01	1.036	0.996–1.077	0.08
Sex (men)	1.211	0.640–2.291	0.556			
COPD	0.547	0.283–1.058	0.073	0.697	0.354–1.371	0.295
Preoperative renal insufficiency	1.363	0.331–5.607	0.668			
Preoperative anemia	1.179	0.688–2.020	0.550			
Preoperative thrombocytopenia	0.638	0.199–2.046	0.450			
Use of antiplatelets	0.469	0.273–0.805	0.006	0.707	0.406–1.230	0.220
Use of anticoagulants	1.299	0.770–2.192	0.327			
Maximum diameter AAA	1.009	0.985–1.033	0.477			
Aortic neck diameter	0.989	0.910–1.075	0.801			
Aortic neck length	1.006	0.990–1.022	0.442			
Suprarenal neck angulation	1.008	0.990–1.026	0.363			
Infrarenal neck angulation	1.014	1.002–1.027	0.027	1.014	1.001–1.026	0.034*
Intraluminal thrombus configuration						
Anterior	0.313	0.084–1.169	0.313			
Posterior	0.778	0.265–2.287	0.778			
Circumferential	0.564	0.221–1.442	0.564			
Number of patent lumbar arteries	1.440	1.225–1.693	<0.001	1.340	1.131–1.588	<0.001**
				≥4 patent: 5.159	*1.979–13.448*	*<0.001***
Patent inferior mesenteric artery	1.744	0.902–3.372	0.098	1.159	0.562–2.389	0.689
Common iliac artery diameter	1.006	0.979–1.034	0.663			

Abbreviations: AAA, abdominal aortic aneurysm; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratios.
*$p<0.05$. **$p<0.001$ (2-tailed t test).

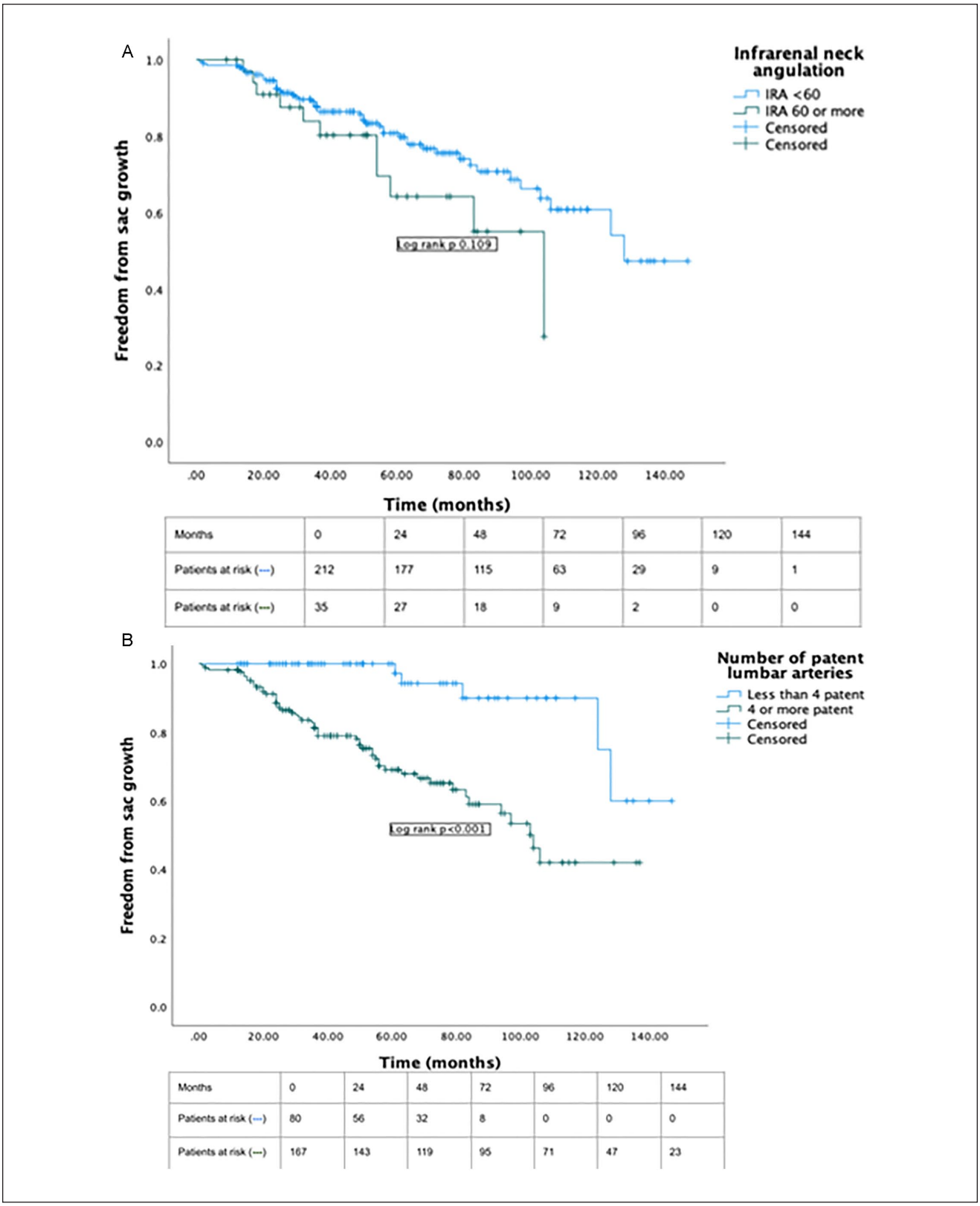

Figure 3. (A) Kaplan-Meier plot for freedom of post-EVAR (endovascular aneurysm repair) sac growth stratified by ≥4 or <4 patent lumbar arteries. (B) Kaplan-Meier plot for freedom of post-EVAR sac growth stratified by infrarenal neck angulation ≥60° or <60°. IRA, infrarenal angulation.

arising from this study is to what extent should this factor be implemented in clinical care. As 31% of the patients with ≥4 patent lumbar arteries developed post-EVAR sac growth, we suggest that standard pre-operative embolization for all EVAR endoprotheses is excessive. However, considering the potential ominous course of sac expansion and the effectiveness of coil embolization, we suggest that the threshold for extension of the frequency of follow-up in patients with ≥4 patent lumbar arteries should be low. Moreover, the higher risk of post-EVAR sac growth in case of ≥4 patent lumbar arteries should be included in preoperative counseling.

Limitations

This study included a relatively small patient sample. Furthermore, this study may carry selection bias, which is inherent to a retrospective review of a prospectively maintained database of nonrandomized patient cohorts, as individual surgeons drove patient selection to optimize outcomes. Patients with a follow-up less than 1 year were also excluded from analysis.

Regardless of these limitations, this study provides important insight into post-EVAR sac growth.

Conclusions

This study showed that having 4 or more patent lumbar arteries and infrarenal neck angulation are important predictive factors for postoperative sac growth in patients undergoing EVAR. This knowledge can be used in conjunction with the instructions for use (IFU) to assist in clinical decision making.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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