Aneurysm sac expansion is independently associated with late mortality in patients treated with endovascular aneurysm repair

Sarah E. Deery, MD, MPH,[a] Emel A. Ergul, MS,[a] Marc L. Schermerhorn, MD,[b] Jeffrey J. Siracuse, MD,[c] Andres Schanzer, MD,[d] Philip P. Goodney, MD, MS,[e] Richard P. Cambria, MD,[a] *and* Virendra I. Patel, MD, MPH,[a] for the Vascular Study Group of New England, *Boston and Worcester, Mass; and Lebanon, NH*

ABSTRACT

Background: Patients undergoing endovascular aneurysm repair (EVAR) for abdominal aortic aneurysms can exhibit variations in sac behavior ranging from complete regression to expansion. We evaluated the impact of sac behavior at 1-year follow-up on late survival.

Methods: We used the Vascular Study Group of New England (VSGNE) registry from 2003 to 2011 to identify EVAR patients with 1-year computed tomography follow-up. Aneurysm sac enlargement ≥5 mm (sac expansion) and decrease ≥5 mm (sac regression) were defined per Society for Vascular Surgery guidelines. Predictors of change in sac diameter and impact of sac behavior on long-term mortality were assessed by multivariable methods.

Results: Of 2437 patients who underwent EVAR, 1802 (74%) had complete 1-year follow-up data and were included in the study. At 1 year, 162 (9%) experienced sac expansion, 709 (39%) had a stable sac, and 931 (52%) experienced sac regression. Sac expansion was associated with preoperative renal insufficiency (odds ratio [OR], 3.4; 95% confidence interval [CI], 1.5-8.0; $P < .01$), urgent repair (OR, 2.7; 95% CI, 1.4-5.1; $P < .01$), hypogastric coverage (OR, 1.7; 95% CI, 1.1-2.7; $P = .02$), and type I/III (OR, 16.8; 95% CI, 7.3-39.0; $P < .001$) or type II (OR, 2.9; 95% CI, 2.0-4.3; $P < .001$) endoleak at follow-up, and sac expansion was inversely associated with smoking (OR, 0.6; 95% CI, 0.4-0.96; $P = .03$) and baseline aneurysm diameter (OR, 0.7; 95% CI, 0.6-0.9; $P < .001$). Sac regression (vs expansion or stable sac) was associated with female gender (OR, 1.8; 95% CI, 1.4-2.4; $P < .001$) and larger baseline aneurysm diameter (OR, 1.4; 95% CI, 1.2-1.5; $P < .001$) and inversely associated with type I/III (OR, 0.2; 95% CI, 0.1-0.5; $P < .01$) or type II endoleak at follow-up (OR, 0.2; 95% CI, 0.2-0.3; $P < .001$). After risk-adjusted Cox regression, sac expansion was independently associated with late mortality (hazard ratio, 1.5; 95% CI, 1.1-2.0; $P = .01$), even with adjustment for reinterventions and endoleak during follow-up. Sac regression was associated with lower late mortality (hazard ratio, 0.6; 95% CI, 0.5-0.7; $P < .001$). Long-term survival was lower (log-rank, $P < .001$) in patients with sac expansion (98% 1-year and 68% 5-year survival) compared with all others (99% 1-year and 83% 5-year survival).

Conclusions: These data suggest that an abdominal aortic aneurysm sac diameter increase of at least 5 mm at 1 year, although infrequent, is independently associated with late mortality regardless of the presence or absence of endoleak and warrants close observation and perhaps early intervention. (J Vasc Surg 2018;67:157-64.)

Since the introduction of endovascular aneurysm repair (EVAR) by Juan Parodi in 1991,[1] EVAR has become the dominant approach to management of abdominal aortic aneurysms (AAAs).[2-4] Although there is a clear early survival benefit of EVAR, randomized controlled trials and large studies of Medicare beneficiaries show lower late survival in EVAR patients compared with open repair.[5-8] Late complications from EVAR include a need for reinterventions, conversion to open repair, and rupture.

Many of the reinterventions after EVAR are performed for endoleaks.[6] Whereas type I and type III endoleaks are generally considered to be procedural complications that necessitate intervention, type II endoleaks have

From the Division of Vascular and Endovascular Surgery, Massachusetts General Hospital,[a] and Division of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center,[b] Harvard Medical School, and the Division of Vascular and Endovascular Surgery, Boston University School of Medicine,[c] Boston; the Division of Vascular Surgery, University of Massachusetts Medical Center, Worcester[d]; and the Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon.[e]

Author conflict of interest: M.L.S. is a consultant for Endologix. V.I.P. is a proctor for Cook.

Presented at the 2013 Vascular Annual Meeting of the Society for Vascular Surgery, San Francisco, Calif, May 30-June 1, 2013.

Correspondence: Virendra I. Patel, MD, MPH, Columbia University Medical Center, Columbia University College of Physicians and Surgeons, Herbert Irving Pavilion, 161 Fort Washington Ave, 5th Flr, Rm 532, New York, NY 10032. (e-mail: vp2385@cumc.columbia.edu; virendraipatel23@gmail.com).

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

http://dx.doi.org/10.1016/j.jvs.2017.06.075

previously been thought to be more benign. Several studies have shown that persistent type II endoleaks independently predict aneurysm sac enlargement, which is often sufficient justification for reintervention.[9-12] However, not all patients with type II endoleaks develop sac enlargement, and the predictors of sac behavior after EVAR are less well known. In addition, the impact of aneurysm sac behavior on long-term survival after EVAR is unknown. Therefore, we aimed to identify predictors of AAA sac size enlargement or regression and to evaluate the impact of change in sac size on long-term survival after EVAR.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective review of prospectively collected data of the Vascular Study Group of New England (VSGNE) registry
- **Take Home Message:** There was a 9% risk of sac expansion at 1 year after 1802 endovascular aortic aneurysm repairs. Sac expansion was independently associated with late mortality, regardless of the presence or absence of endoleak.
- **Recommendation:** Sac expansion after endovascular aneurysm repair warrants close observation and perhaps early intervention.

METHODS

The Massachusetts General Hospital Institutional Review Board approved this study and waived informed consent because of the use of deidentified data collected in conjunction with a regional quality improvement initiative.

Population. This is a retrospective cohort study evaluating outcomes of patients undergoing EVAR (2003-2011) using data from the Vascular Study Group of New England (VSGNE) registry. The VSGNE is a regional collaboration developed in 2002 that currently consists of 31 academic and community hospitals throughout six New England states. The registry includes prospectively collected data on commonly performed vascular procedures from each participating institution. Further details on this registry have been published and are available at www.vsgne.org.[13]

For this study, patients who underwent EVAR for rupture were excluded. Because the primary objective was to evaluate the relationship between sac behavior at 1-year follow-up and mortality, those patients with no 1-year follow-up imaging data were excluded (n = 635 [26%]). To evaluate sac behavior, maximum anteroposterior aortic diameter at 1-year follow-up, per the VSGNE definition, was compared with preoperative aortic diameter. Sac expansion was defined as an increase of at least 5 mm and sac regression was defined as a decrease of at least 5 mm per Society for Vascular Surgery guidelines.[14] Stable sac size was defined as a change <5 mm in either direction. Of note, imaging modality was not recorded within the Vascular Quality Initiative registry, but at a minimum, all patients had sufficient imaging to determine sac diameter (ie, computed tomography, magnetic resonance imaging, ultrasound, or arteriography) to be eligible for inclusion in this study.

Variables. Patient demographics, clinical features, and surgical procedure details including concomitant procedures and intraoperative endoleak were identified. Intraoperative endoleak, which was considered present if there was any endoleak noted at any point intraoperatively, includes type I, type II, type III, or indeterminate endoleaks; this variable is recorded at the end of the case. Endoleaks were also defined at 1-year follow-up as recorded by the attending surgeon on the basis of follow-up imaging. Preoperative renal insufficiency was defined as an estimated glomerular filtration rate <30 mL/min/1.73 m^2 from a single preoperative creatinine value using the Modification of Diet in Renal Disease study equation.[15] Prior aortic surgery was any prior operation on the abdominal aorta, including open complex or infrarenal AAA repair, aortoiliac or aortofemoral bypass, or EVAR. The procedure was defined as urgent rather than elective by the Vascular Quality Initiative if it was performed for a symptomatic aneurysm, within 24 hours of presentation with pain or tenderness but without rupture. Graft configuration was defined as aortoaortic tube grafts, aortouni-iliac grafts, or aortobi-iliac grafts. Graft types were deidentified in the registry but were categorized as 1 of 12 different numbered grafts. Long-term survival was established using linkage of VSGNE data to the Social Security Death Index Masterfile.

Statistical analysis. All ordinal data were presented as absolute number and percentage prevalence in the study population, and all continuous data were presented as median (interquartile range). Univariate analysis comparing sac expansion with stable sac or sac regression was performed using Fisher exact test for discrete variables and the Mann-Whitney *U* test for non-normally distributed continuous variables. Multivariable logistic regression modeling was used to identify variables associated with sac expansion and sac regression. Actuarial survival was evaluated using Kaplan-Meier life-table analysis, and log-rank testing was used to compare survival of those with sac expansion with survival of those with stable sac or sac regression. Risk-adjusted late mortality risk was determined using multivariable Cox proportional hazards modeling. All tests were two sided, and a *P* value of <.05 was considered significant. Statistical data analysis was performed using Stata version 14.1 software (StataCorp LP, College Station, Tex).

Table I. Univariate analysis of demographics and comorbidities comparing those with sac enlargement and those without

Variable	Sac expansion (n = 162)	Stable sac or sac regression (n = 1640)	*P* value
Female	26 (16)	328 (20)	.26
Age, years	76 (69-81)	74 (68-79)	.03
White race	155 (96)	1608 (98)	.08
Body mass index	28.4 (24.3-31.3)	27.5 (24.5-30.9)	.52
Smoking, ever	31 (19)	490 (30)	<.01
Comorbidities			
Hypertension	134 (83)	1371 (84)	.74
Congestive heart failure	14 (8.6)	146 (8.9)	1.0
Coronary artery disease	57 (35)	556 (34)	.79
COPD	55 (34)	561 (34)	1.0
Baseline eGFR <30	8 (5.0)	33 (2.0)	.03
Dialysis	1 (0.6)	14 (0.9)	1.0
Diabetes	29 (18)	318 (19)	.75
Prior aortic surgery	7 (4.3)	32 (2.0)	.08
Preoperative medications			
Beta blocker	125 (77)	1240 (76)	.70
Any antiplatelet	111 (69)	1217 (74)	.16
Statin	111 (69)	1135 (69)	.93

COPD, Chronic obstructive pulmonary disease; *eGFR*, estimated glomerular filtration rate.
Categorical variables are presented as number (%). Continuous variables are presented as median (interquartile range).

RESULTS

Demographics. Using the VSGNE registry, we identified 2437 patients undergoing EVAR during the study period, of whom 1802 (74%) had 1-year anatomic follow-up data and were included in the primary analysis. Of these, 162 (9%) had sac expansion, 709 (39%) had a stable sac, and 931 (52%) had sac regression. As shown in Table I, patients with sac expansion were older (76 vs 74; $P = .03$), more frequently had preoperative renal insufficiency (5.0% vs 2.0%; $P = .03$), and were less likely to smoke (19% vs 30%; $P < .01$). Those with sac expansion were found to have a trend toward more frequently having had prior aortic surgery (4.3% vs 2.0%; $P = .08$).

Operative details. There was no difference in preoperative aortic diameter in those with and without sac expansion (56 vs 55 mm; $P = .43$) or in the presence of concomitant iliac aneurysm (24% vs 22%; $P = .62$); however, among patients with iliac artery aneurysms, the maximum iliac artery diameter was greater in patients who eventually developed sac expansion (36.5 vs 25 mm; $P < .001$). Those with sac expansion were more likely to have had an urgent presentation (9.3% vs 4.5%; $P = .01$). Operative time, blood loss, graft configuration, and graft type were similar between groups (Table II). There was no difference between those with sac expansion and those without in overall occurrence of concomitant procedures (37% vs 37%; $P = 1.0$), including graft extension (sac increase, 8.0%; stable or decrease, 9.7%; $P = .66$), but those with sac expansion were more likely to have undergone hypogastric artery coiling or coverage (25% vs 17%; $P = .02$) and renal artery angioplasty and stenting (5.3% vs 2.5%; $P = .06$). Those with sac expansion were less likely to have undergone iliac artery angioplasty (1.3% vs 5.3%; $P = .03$). There was a trend toward higher rates of any completion endoleak in those who later developed sac expansion (32% vs 26%; $P = .08$). Whereas more patients who developed sac expansion had completion type I (3.7% vs 1.8%; $P = .13$) and type II (27% vs 22%; $P = .14$) endoleaks, these relationships were not statistically significant. Rates of type III endoleak were very low and no different between those with eventual sac expansion and those without (0% vs 0.4%; $P = 1.0$).

One-year outcomes. At 1-year follow-up, 81% of patients had no endoleak, 1.5% had type I endoleak, and 15% had type II endoleak. Patients with sac expansion were more likely to have endoleaks of each type than those with a stable aneurysm sac, who were more likely to have endoleaks than those with sac regression (expansion, 43%; stable, 26%; regression, 10%; $P < .001$; Table III). Of note, 57% of patients with sac expansion had no endoleak, and 26% of patients with type II endoleak had sac regression. By 1 year, 5.6% of patients underwent a secondary intervention, with higher reintervention rates among patients with sac expansion compared with those without (17% vs 4.6%; $P < .001$).

Predictors of sac behavior. After multivariable adjustment, independent predictors of sac expansion were preoperative renal insufficiency (odds ratio [OR], 3.4;

Table II. Operative characteristics comparing those with sac enlargement and those without

Variable	Sac expansion (n = 162)	Stable sac or sac regression (n = 1640)	*P* value
Urgent repair	15 (9.3)	73 (4.5)	.01
Aortic diameter, mm	56 (50-62)	55 (52-60)	.43
Iliac aneurysm	39 (24)	365 (22)	.62
Operative time, minutes	150 (120-198)	145 (115-192)	.20
Estimated blood loss >500 mL	23 (14)	214 (13)	.71
Any transfusion	9 (5.6)	86 (5.2)	.85
Graft configuration			.54
Aortoaortic	3 (1.9)	21 (1.3)	
Aortouni-iliac	5 (3.1)	73 (4.5)	
Aortobi-iliac	154 (95)	1,543 (94)	
Graft type (of 12 types)			.10
Concomitant procedures, any	11 (37)	98 (37)	1.0
Hypogastric coiled/embolized	26 (17)	133 (9.2)	<.01
Hypogastric covered	35 (22)	198 (12)	<.01
Graft extension used	12 (8.0)	140 (9.7)	.66
Femoral endarterectomy	6 (4.0)	65 (4.5)	1.0
Femoral-femoral bypass	4 (2.7)	43 (3.0)	1.0
Iliofemoral bypass	0 (0)	12 (0.8)	.62
Iliac angioplasty	2 (1.3)	77 (5.3)	.03
Renal angioplasty/stenting	8 (5.3)	36 (2.5)	.06
Completion endoleak, any	52 (32)	419 (26)	.08
Type I	6 (3.7)	30 (1.8)	.13
Type II	44 (27)	362 (22)	.14
Type III	0 (0)	6 (0.4)	1.0

Categorical variables are presented as number (%). Continuous variables are presented as median (interquartile range).

Table III. Relationship between sac behavior and endoleak and reinterventions at 1-year follow-up

	Sac regression, % (n = 931)	Stable sac, % (n = 709)	Sac expansion, % (n = 162)	*P* value
No endoleak	90	74	57	<.001
Any endoleak	10	26	43	
Type I	0.4	1.3	8.2	
Type II	7.8	22	29	
Type III	0.1	0	0	
Type IV	1.3	2.4	5.1	
Reintervention	3.3	6.2	17	<.001

95% confidence interval [CI], 1.5-8.0; $P < .01$), urgent repair (OR, 2.7; 95% CI, 1.4-5.1; $P < .01$), hypogastric coverage (OR, 1.7; 95% CI, 1.1-2.7; $P = .02$), type I/III endoleak (OR, 16.8; 95% CI, 7.3-39.0; $P < .001$), and type II endoleak (OR, 2.9; 95% CI, 2.0-4.3; $P < .001$). In addition, smokers were less likely to have sac expansion (OR, 0.6; 95% CI, 0.4-0.96; $P = .03$), as were those with a smaller preoperative aneurysm diameter (OR, 0.7; 95% CI, 0.6-0.9; $P < .001$; Table IV, *A*). Sac regression was more likely to occur in women (OR, 1.8; 95% CI, 1.4-2.3; $P < .001$) and those with larger aneurysm diameter (OR, 1.5; 95% CI, 1.2-1.9; $P < .001$) and less likely to occur in patients with type I/III (OR, 0.2; 95% CI, 0.1-0.5; $P < .01$) or type II endoleaks (OR, 0.2; 95% CI, 0.2-0.3; $P < .001$), as seen in Table IV, *B*.

Long-term survival. Long-term survival shown in the Fig was lower (log-rank, $P < .001$) in patients with sac expansion (98% 1-year and 68% 5-year survival) compared with all others (99% 1-year and 83% 5-year survival). After adjusting for age, sex, comorbidities known to affect survival, history of prior aortic surgery, concomitant procedures, presence of endoleak at 1 year, and reinterventions (Table V), sac expansion

Table IV. A, Multivariable predictors of sac enlargement ≥5 mm

	Sac expansion		
Variable	OR	95% CI	*P* value
Preoperative eGFR <30	3.4	1.5-8.0	<.01
Smoking	0.6	0.4-0.96	.03
Preoperative aneurysm diameter, by cm	0.7	0.6-0.9	<.001
Urgent repair	2.7	1.4-5.1	<.01
Hypogastric coverage	1.7	1.1-2.7	.02
Type I or III endoleak at 1-year follow-up	16.8	7.3-39.0	<.001
Type II endoleak at 1-year follow-up	2.9	2.0-4.3	<.001

CI, Confidence interval; *eGFR,* estimated glomerular filtration rate; *OR,* odds ratio.
OR >1 is a risk factor for enlargement; OR <1 is protective against enlargement.
Also adjusted for age and sex.

Table IV. B, Multivariable predictors of sac regression ≥5 mm

	Sac regression		
Variable	OR	95% CI	*P* value
Female sex	1.8	1.4-2.4	<.001
Preoperative aneurysm diameter, by cm	1.4	1.2-1.5	<.001
Type I or III endoleak at 1-year follow-up	0.2	0.1-0.5	<.01
Type II endoleak at 1-year follow-up	0.2	0.2-0.3	<.001

CI, Confidence interval; *OR,* odds ratio.
OR >1 is predictive of regression; OR <1 is a risk factor for nonregression.
Also adjusted for age, iliac aneurysm, and hypogastric artery coiling/coverage.

independently predicted late mortality (hazard ratio, 1.5; 95% CI, 1.1-2.0; $P = .01$). Conversely, sac regression predicted a decrease in late mortality (hazard ratio, 0.6; 95% CI, 0.5-0.8; $P < .001$).

DISCUSSION

Despite the early benefit of EVAR over traditional open AAA repair, randomized controlled trials and large, observational studies of Medicare beneficiaries have shown higher late mortality after EVAR compared with open repair, with high rates of secondary intervention and risk of late rupture as high as 5.4%.[7,8,16] The most common complication after EVAR, and one that frequently results in reintervention, is endoleak.[17-20] Type I and type III endoleaks have been associated with sac expansion and repressurization with subsequently worse aneurysm-related outcomes.[17,21] The management of type II endoleaks, once thought to be benign, is more controversial. Whereas several studies suggest that type II endoleaks are benign,[22] others show that in the setting of sac expansion, type II endoleaks warrant intervention, given higher aneurysm-related adverse outcomes, such as reintervention, rupture, and conversion to open repair.[9,12,18,23]

Among patients with 1-year follow-up data, we identified a 15% rate of type II endoleak, which is comparable to the 10% to 20% rates identified in the literature,[24-27] including a recent meta-analysis of >20,000 patients with a 10.2% rate of type II endoleak.[28] However, of the 1515 patients with type II endoleak, only 1% eventually experienced aneurysm rupture,[28] which again suggests that type II endoleak may be ominous only in certain clinical scenarios. In this cohort, we not surprisingly found that reintervention rate was significantly higher in patients with sac expansion compared with those without sac expansion.

Although sac expansion is often attributed to endoleak, not all patients with endoleak develop sac expansion, and not all patients with sac expansion have identifiable endoleak.[23,29] We also demonstrated this, as more than half of patients with sac expansion had no identifiable endoleak, and roughly one-quarter of patients with type II endoleak still had sac regression. Whereas our rate of no identifiable endoleak among patients with sac expansion was high at 57%, other centers have also shown high rates ranging from 22% to 43%.[30-32] The reason for the discrepancy in our rate and the rate of others is perhaps because sac expansion in our cohort could have been defined on the basis of ultrasound alone, and it is unclear whether these patients underwent imaging that could have identified an endoleak, whereas in other studies, all patients underwent computed tomography imaging. Other potential explanations include the possibility of a methodologic error inherent in the VSGNE data set in which endoleaks are self-reported by participating centers without any core imaging laboratory adjudication. Finally, detection of an endoleak is not always obvious and can depend on the timing of intravenous administration of the contrast agent or the technologist's experience if duplex ultrasound is used, or it may require multiple modalities for diagnosis.

The EVAR 1 trial identified sac expansion as an independent predictor of late rupture,[19] and other series have also suggested that when type II endoleak is associated with sac expansion, reintervention to prevent late rupture and other adverse outcomes may be warranted.[12,33] Candell et al[17] reported on a large, multicenter U.S. series with 10 years of follow-up. Of 15 patients with late rupture, 10 were known to have sac expansion preceding rupture. Conversely, sac regression is associated with treatment success. Houbballah et al[34] showed that significant sac regression >75% was associated with significantly lower rates of endoleak and reintervention, and no patients with significant sac regression experienced late aneurysm rupture.

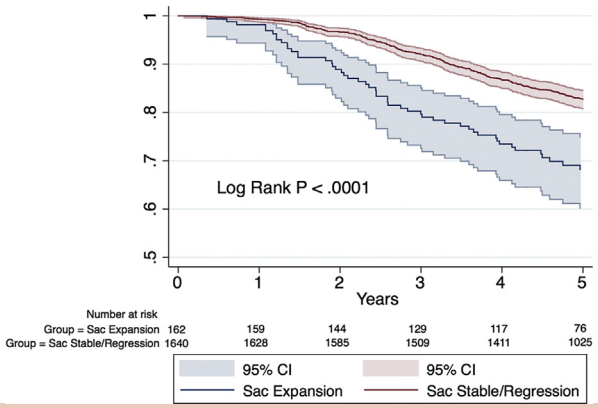

Fig. Kaplan-Meier survival estimates for the full cohort of patients, including those excluded from the remainder of the study because of missing long-term follow-up data. *CI,* Confidence interval.

Table V. Cox regression for long-term mortality

Variable	Death hazard ratio	95% CI	*P* value
Sac expansion	1.5	1.1-2.0	.01
Sac regression	0.6	0.5-0.8	<.001
Age, by decade	1.6	1.4-1.8	<.001
Congestive heart failure	1.4	1.1-2.0	.02
Chronic obstructive pulmonary disease	1.5	1.2-1.8	<.001
Concurrent iliofemoral bypass	3.1	1.5-6.7	<.01

CI, Confidence interval.
Hazard ratio >1 is a risk factor for mortality.
Also adjusted for patient sex, preoperative aneurysm diameter, history of prior aortic surgery, procedure urgency, concurrent hypogastric coverage, and any endoleak or reinterventions at 1-year follow-up.

We observed that the 5-year survival rate is markedly lower among patients with sac expansion (68% vs 83%). Notably, all patients who died within the first postoperative year (6.4% of the cohort) were excluded from this analysis, which compared patients on the basis of 1-year follow-up data. Sensitivity analyses by including these patients with the stable sac or sac regression cohorts showed similar results, leading to the same conclusions as presented. After adjusting for age, patient sex, comorbidities including renal insufficiency, history of prior aortic surgery, operative differences including urgency of repair, persistent endoleak, and reinterventions, sac expansion was associated with increased mortality, and sac regression was associated with lower mortality. The simultaneous observation of risk-adjusted lower survival in patients with sac expansion and higher survival associated with sac regression suggests that sac behavior is likely a surrogate for aneurysm-related mortality.

Notably, sac behavior was more predictive of mortality than presence of any type of endoleak or the need for reintervention. Many prior studies have suggested that the increased late mortality after EVAR compared with open repair in some patients is partly explained by graft complications, endoleak, late conversion to open, and late rupture[5-7,17]; however, no study to our knowledge has specifically associated sac behavior with late mortality. It appears that sac expansion, even in the absence of identifiable endoleak, is more strongly associated with late mortality than endoleak alone. This is further corroborated by the recent 15-year follow-up data from the EVAR 1 trial that showed higher rates of late aneurysm-related mortality attributable to late aneurysm rupture in EVAR patients, although that study did not directly report on sac expansion as a precursor to rupture.[35]

Given the impact of sac behavior on survival, we additionally sought to identify clinical and operative predictors of aneurysm sac enlargement and regression 1 year after EVAR. Although endoleak and sac expansion were not perfectly linked, we still demonstrated a correlation on univariate analysis ($P < .001$), and both type I/III and type II endoleaks were significant positive predictors of sac expansion and negative predictors of sac regression. Several studies have reported a positive correlation between type II endoleak and sac enlargement.[9,10,12]

The management of sac expansion in the absence of endoleak merits further investigation, although it is clear this is not a benign process. Even when controlling for patients who underwent reinterventions and for patients with expansion without endoleak, sac expansion is associated with lower survival. It is not clear what is contributing to the worse survival, even among patients without identifiable endoleak. One possible explanation is that these patients have increased graft porosity with endotension. We are unable to account for this in this analysis, but notably, adjusting for graft type did not mitigate this disparity. There also may be patients with endoleaks not captured on follow-up imaging. We anticipate that the number of these patients is small, as most vascular surgeons who identify sac expansion would likely pursue additional imaging. If endoleak was not identified even on computed tomography scan, those patients with sac expansion may then benefit from aortic angiography to identify endoleaks not found on routine imaging and intervention as necessary in appropriate-risk patients.

There are several limitations to this study, including those inherent to the clinical registry used for data collection, such as misclassification and missing data. As our primary objective was to evaluate the association between sac behavior 1 year postoperatively and long-term outcomes, all patients with missing 1-year follow-up data, including all those who died in the first year, were excluded. Whereas this leads to a clear selection bias, the nature of our study question necessitates exclusion of these patients, and sensitivity analysis showed no changes in conclusion. We are unable in this analysis to account for management of the inferior mesenteric artery, use of instructions for use,[11] or use of preoperative

or postoperative anticoagulation, as this information is not included in the VSGNE data set. Similarly, several anatomic parameters that may contribute to aneurysm sac behavior, such as aortic neck length, diameter, angle, and thrombus burden, are unfortunately not captured in the VSGNE data set. Endoleak at follow-up may also be underestimated as the imaging modality used to determine sac diameter may not have been adequate to detect endoleak. In addition, whereas we identified a cohort of patients who underwent reintervention, we do not know the indication for reintervention because of limitations of the registry. Finally, our primary end point of mortality was obtained by using the Social Security Death Index, which remains the most current data set available to researchers for ascertaining patient vital status, despite its recent limitations with selected states not releasing data immediately. Furthermore, cause of death is not reported in the Social Security Death Index, so only all-cause and not aneurysm-related mortality can be calculated. However, this study is unique in its evaluation of sac behavior among a large cohort of patients and showing that there is an independent association between sac behavior and patient mortality after EVAR.

CONCLUSIONS

This study demonstrated that AAA sac expansion >5 mm at 1 year, although infrequent, is an independent predictor of late mortality, even after adjusting for presence of endoleak and occurrence of secondary intervention. Even in the absence of identifiable endoleak, sac expansion is not a benign process, and it warrants close observation, potentially additional imaging, and intervention in good-risk patients to influence sac regression, which has survival benefit.

AUTHOR CONTRIBUTIONS

Conception and design: SD, RC, VP
Analysis and interpretation: SD, EE, MS, JS, AS, PG, RC, VP
Data collection: SD, RC, VP
Writing the article: SD, VP
Critical revision of the article: SD, EE, MS, JS, AS, PG, RC, VP
Final approval of the article: SD, EE, MS, JS, AS, PG, RC, VP
Statistical analysis: SD, VP
Obtained funding: Not applicable
Overall responsibility: VP

REFERENCES

1. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg 1991;5:491-9.
2. Brewster DC, Jones JE, Chung TK, Lamuraglia GM, Kwolek CJ, Watkins MT, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair: the first decade. Ann Surg 2006;244:426-38.
3. Giles KA, Pomposelli F, Hamdan A, Wyers M, Jhaveri A, Schermerhorn ML. Decrease in total aneurysm-related deaths in the era of endovascular aneurysm repair. J Vasc Surg 2009;49:543-50; discussion: 550-1.
4. Schwarze ML, Shen Y, Hemmerich J, Dale W. Age-related trends in utilization and outcome of open and endovascular repair for abdominal aortic aneurysm in the United States, 2001-2006. J Vasc Surg 2009;50:722-9.e2.
5. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT Jr, Matsumura JS, Kohler TR, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009;302:1535-42.
6. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. Lancet 2005;365:2179-86.
7. United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010;362:1863-71.
8. Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. N Engl J Med 2015;373:328-38.
9. El Batti S, Cochennec F, Roudot-Thoraval F, Becquemin JP. Type II endoleaks after endovascular repair of abdominal aortic aneurysm are not always a benign condition. J Vasc Surg 2013;57:1291-7.
10. Fairman RM, Nolte L, Snyder SA, Chuter TA, Greenberg RK; Zenith Investigators. Factors predictive of early or late aneurysm sac size change following endovascular repair. J Vasc Surg 2006;43:649-56.
11. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation 2011;123:2848-55.
12. Jones JE, Atkins MD, Brewster DC, Chung TK, Kwolek CJ, LaMuraglia GM, et al. Persistent type 2 endoleak after endovascular repair of abdominal aortic aneurysm is associated with adverse late outcomes. J Vasc Surg 2007;46:1-8.
13. Cronenwett JL, Likosky DS, Russell MT, Eldrup-Jorgensen J, Stanley AC, Nolan BW, et al. A regional registry for quality assurance and improvement: the Vascular Study Group of Northern New England (VSGNNE). J Vasc Surg 2007;46:1093-101; discussion: 1101-2.
14. Ahn SS, Rutherford RB, Johnston KW, May J, Veith FJ, Baker JD, et al. Reporting standards for infrarenal endovascular abdominal aortic aneurysm repair. Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/International Society for Cardiovascular Surgery. J Vasc Surg 1997;25:405-10.
15. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the Modification of Diet in Renal Disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145:247-54.
16. De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. N Engl J Med 2010;362:1881-9.

17. Candell L, Tucker LY, Goodney P, Walker J, Okuhn S, Hill B, et al. Early and delayed rupture after endovascular abdominal aortic aneurysm repair in a 10-year multicenter registry. J Vasc Surg 2014;60:1146-52.
18. Lo RC, Buck DB, Herrmann J, Hamdan AD, Wyers M, Patel VI, et al. Risk factors and consequences of persistent type II endoleaks. J Vasc Surg 2016;63:895-901.
19. Wyss TR, Brown LC, Powell JT, Greenhalgh RM. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: data from the EVAR trials. Ann Surg 2010;252:805-12.
20. Zarins CK, Crabtree T, Bloch DA, Arko FR, Ouriel K, White RA. Endovascular aneurysm repair at 5 years: does aneurysm diameter predict outcome? J Vasc Surg 2006;44:920-9; discussion: 929-31.
21. Fransen GA, Vallabhaneni SR Sr, van Marrewijk CJ, Laheij RJ, Harris PL, Buth J, et al. Rupture of infra-renal aortic aneurysm after endovascular repair: a series from EUROSTAR registry. Eur J Vasc Endovasc Surg 2003;26:487-93.
22. Walker J, Tucker LY, Goodney P, Candell L, Hua H, Okuhn S, et al. Type II endoleak with or without intervention after endovascular aortic aneurysm repair does not change aneurysm-related outcomes despite sac growth. J Vasc Surg 2015;62:551-61.
23. Harris PL, Vallabhaneni SR, Desgranges P, Becquemin JP, van Marrewijk C, Laheij RJ. Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: the EUROSTAR experience. European Collaborators on Stent/graft techniques for aortic aneurysm repair. J Vasc Surg 2000;32:739-49.
24. Cieri E, De Rango P, Isernia G, Simonte G, Ciucci A, Parlani G, et al. Type II endoleak is an enigmatic and unpredictable marker of worse outcome after endovascular aneurysm repair. J Vasc Surg 2014;59:930-7.
25. Sheehan MK, Ouriel K, Greenberg R, McCann R, Murphy M, Fillinger M, et al. Are type II endoleaks after endovascular aneurysm repair endograft dependent? J Vasc Surg 2006;43:657-61.
26. van Keulen JW, de Vries JP, Dekker H, Goncalves FB, Moll FL, Verhagen HJ, et al. One-year multicenter results of 100 abdominal aortic aneurysm patients treated with the Endurant stent graft. J Vasc Surg 2011;54:609-15.
27. Sidloff DA, Gokani V, Stather PW, Choke E, Bown MJ, Sayers RD. Type II endoleak: conservative management is a safe strategy. Eur J Vasc Endovasc Surg 2014;48:391-9.
28. Sidloff DA, Stather PW, Choke E, Bown MJ, Sayers RD. Type II endoleak after endovascular aneurysm repair. Br J Surg 2013;100:1262-70.
29. Gilling-Smith GL, Martin J, Sudhindran S, Gould DA, McWilliams RG, Bakran A, et al. Freedom from endoleak after endovascular aneurysm repair does not equal treatment success. Eur J Vasc Endovasc Surg 2000;19:421-5.
30. Dias NV, Ivancev K, Malina M, Resch T, Lindblad B, Sonesson B. Intra-aneurysm sac pressure measurements after endovascular aneurysm repair: differences between shrinking, unchanged, and expanding aneurysms with and without endoleaks. J Vasc Surg 2004;39:1229-35.
31. Holt PJ, Karthikesalingam A, Patterson BO, Ghatwary T, Hinchliffe RJ, Loftus IM, et al. Aortic rupture and sac expansion after endovascular repair of abdominal aortic aneurysm. Br J Surg 2012;99:1657-64.
32. Nakai M, Ikoma A, Sato H, Sato M, Nishimura Y, Okamura Y. Risk factors associated with late aneurysmal sac expansion after endovascular abdominal aortic aneurysm repair. Diagn Interv Radiol 2015;21:195-201.
33. van Marrewijk CJ, Fransen G, Laheij RJ, Harris PL, Buth J; EUROSTAR Collaborators. Is a type II endoleak after EVAR a harbinger of risk? Causes and outcome of open conversion and aneurysm rupture during follow-up. Eur J Vasc Endovasc Surg 2004;27:128-37.
34. Houbballah R, Majewski M, Becquemin JP. Significant sac retraction after endovascular aneurysm repair is a robust indicator of durable treatment success. J Vasc Surg 2010;52:878-83.
35. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. Lancet 2016;388:2366-74.

Submitted Feb 7, 2017; accepted Jun 7, 2017.

INVITED COMMENTARY

Glenn R. Jacobowitz, MD, *New York, NY*

The authors have demonstrated an association of aneurysm sac expansion with late mortality in patients treated with endovascular aneurysm repair. However, there are several important limitations of this large cohort study that bear noting.

The cause of death was unknown, and therefore a causal relationship between aneurysm sac expansion and late mortality can only be inferred. The authors have noted that sac expansion was more predictive of mortality than the presence of any type of endoleak or the need for reintervention. However, sac expansion could not be shown to be a precursor of rupture in this study.

In addition, the imaging modality used in the follow-up of patients in this study was unknown, so it is possible that endoleaks could have been underestimated. For example, if duplex ultrasound scanning was used instead of computed tomography or conventional angiography, an endoleak could have been missed. The authors noted that they anticipated the number of such patients would be small because most vascular surgeons would likely pursue additional imaging if sac expansion without endoleak was identified on duplex ultrasound alone.

Patients with sac expansion were still noted to have lower survival after adjusting for differences in age, patient sex, operative differences, comorbidities,