# CLINICAL RESEARCH STUDIES

From the Society for Vascular Surgery

# Familial abdominal aortic aneurysm is associated with more complications after endovascular aneurysm repair

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***Objective:*** **A familial predisposition to abdominal aortic aneurysms (AAAs) is present in approximately one-fifth of patients. Nevertheless, the clinical implications of a positive family history are not known. We investigated the risk of aneurysm-related complications after endovascular aneurysm repair (EVAR) for patients with and without a positive family history of AAA.**

***Methods:*** **Patients treated with EVAR for intact AAAs in the Erasmus University Medical Center between 2000 and 2012 were included in the study. Family history was obtained by written questionnaire. Familial AAA (fAAA) was defined as patients having at least one first-degree relative affected with aortic aneurysm. The remaining patients were considered sporadic AAA. Cardiovascular risk factors, aneurysm morphology (aneurysm neck, aneurysm sac, and iliac measurements), and follow-up were obtained prospectively. The primary end point was complications after EVAR, a composite of endoleaks, need for secondary interventions, aneurysm sac growth, acute limb ischemia, and postimplantation rupture. Secondary end points were specific components of the primary end point (presence of endoleak, need for secondary intervention, and aneurysm sac growth), aneurysm neck growth, and overall survival. Kaplan-Meier estimates for the primary end point were calculated and compared using log-rank (Mantel-Cox) test of equality. A Cox-regression model was used to calculate the independent risk of complications associated with fAAA.**

***Results:*** **A total of 255 patients were included in the study (88.6% men; age 72 ± 7 years, median follow-up 3.3 years; interquartile range, 2.2-6.1). A total of 51 patients (20.0%) were classified as fAAA. Patients with fAAA were younger (69 vs 72 years; $P = .015$) and were less likely to have ever smoked (58.8% vs 73.5%; $P = .039$). Preoperative aneurysm morphology was similar in both groups. Patients with fAAA had significantly more complications after EVAR (35.3% vs 19.1%; $P = .013$), with a twofold increased risk (adjusted hazard ratio, 2.1; 95% confidence interval, 1.2-3.7). Secondary interventions (39.2% vs 20.1%; $P = .004$) and aneurysm sac growth (20.8% vs 9.5%; $P = .030$) were the most important elements accounting for the difference. Furthermore, a trend toward more type I endoleaks during follow-up was observed (15.6% vs 7.4%; $P = .063$) and no difference in overall survival.**

***Conclusions:*** **The current study shows that patients with a familial form of AAA develop more aneurysm-related complications after EVAR, despite similar AAA morphology at baseline. These findings suggest that patients with fAAA form a specific subpopulation and create awareness for a possible increase in the risk of complications after EVAR. (J Vasc Surg 2014;59:275-82.)**

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Approximately 20% of the abdominal aortic aneurysm (AAA) patients have a positive family history for aneurysms, with a prevalence ranging largely from 6% to 35%, depending on ethnicity and method of data collection.[1-4] This suggests that in these families there is a genetic predisposition to AAA and that patients can be classified as familial AAA (fAAA), whereas patients without a clear inherited risk can be classified as sporadic AAA (spAAA). Despite the apparent familial tendency toward AAA formation and results from some genetic studies, the exact underlying genetic defects and their contribution to the development, growth, and severity of complications are unknown.[5] The molecular and clinical well-delineated genetic aortic aneurysm syndromes, including Marfan, Loeys-Dietz, the vascular Ehlers-Danlos syndrome, and defects in the smooth muscle cell genes *MYH11* and *ACTA2*, are mostly associated with thoracic aortic aneurysms, but occasionally

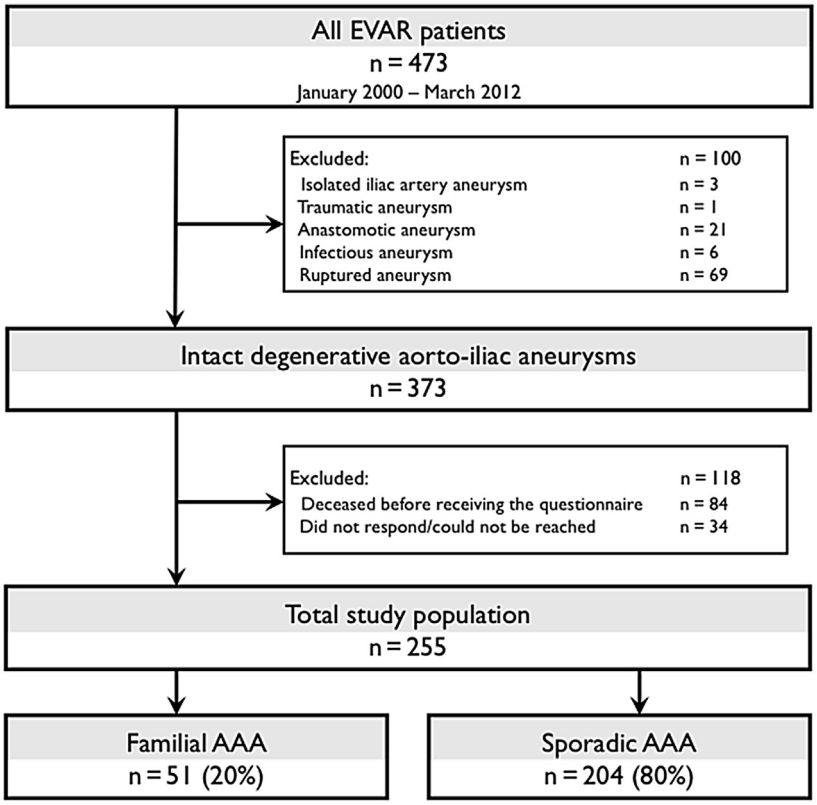



**Fig 1.** Flow diagram of patient inclusion. *AAA,* Abdominal aortic aneurysm; *EVAR,* endovascular aneurysm repair.

AAA may be observed in the affected families.[6-10] Like in most known syndromes, in AAA, there are recognized defects both in the connective tissue components and in cellular elements affecting all layers of the aortic wall.[5]

In the last decade, endovascular aneurysm repair (EVAR) has proven to be a valid treatment modality for AAA and the majority of elective patients are now treated endovascularly.[11] Generally, endovascular repair in patients with known genetic aortic aneurysm syndromes is not advised, since patients have a higher chance of complications.[12,13] At present, little is known on clinical outcome after EVAR for patients with an inherited risk for AAA, and no data on aneurysm morphology of this particular group are available to date. One may hypothesize that AAA patients with a positive family history may develop more seal and fixation problems, and also postimplantation sac growth because of inherited aortic wall defects. Furthermore, differences in aneurysm morphology for fAAA patients, if present, could also influence outcome. In the present study, we evaluated aneurysm-related complications after EVAR for patients with fAAA and spAAA and explored possible differences in aneurysm morphology in these groups.

## METHODS

The study population was derived from a prospective database including all EVAR procedures performed at the Erasmus University Medical Center in Rotterdam, The Netherlands. From January 2000 until March 2012, 473 patients were treated with EVAR at our institution. Exclusion criteria for this study were isolated iliac artery aneurysm, traumatic aneurysm, anastomotic aneurysm, infectious aneurysm, and ruptured aneurysm. Between 2009 and 2012, all AAA patients at our institution were contacted when visiting the outpatient clinic or by mail and asked to fill out a semistructured questionnaire to collect personal data and family histories. Patients who did not respond after one reminder were contacted and interviewed by telephone (K.V.). In families with multiple AAA patients, only one index patient (ie, first family member diagnosed with AAA) was included in the study. Patients previously diagnosed with a genetic aortic aneurysm syndrome (eg, Marfan, Loeys-Dietz, or vascular Ehlers-Danlos syndrome) were excluded, but no specific genetic testing was routinely performed. A flow diagram of patient inclusion is presented in Fig 1. The study complied with the declaration of Helsinki and was approved by the Institutional Review Board.

**Questionnaire and classification of familial AAA.** The questionnaire requested information on demographics and the medical history of the index patient. Furthermore, structured questions were included on the occurrence of aortic aneurysms and cardiovascular disease for all known relatives of the index patient. Patients were classified as

fAAA when at least one first-degree relative (parents, siblings, or children) was reported to have an aortic aneurysm.[1] Patients who did not report a first-degree relative affected with AAA were classified as spAAA. Patients reporting only second- or third-degree relatives were also classified as spAAA because the reporting of medical information of second- or third-degree relatives was considered less reliable.

**Image processing.** All patients were preoperatively assessed using computed tomography angiography (CTA) and entered the institutional surveillance protocol that included an early postoperative CTA (typically before hospital discharge), a CTA at 6 months and 1 year, and then CTA scans yearly after. Since 2007, the 6-month examination has been waived, and CTA surveillance replaced by duplex ultrasound (DUS) examinations in selected patients considered a lower risk according to the treating physician's experience in concurrence with Clinical Practice Guidelines of the European society for Vascular Surgery. Also, DUS examinations or noncontrast CT scans were performed as an alternative to CTA in patients with impaired renal function.

CTA was performed according to standardized institutional protocols. Morphologic analyses and measurements were performed using dedicated software with center lumen line (CLL) reconstruction (3Mensio, Vascular 4.2 software; 3Mensio Medical Imaging BV, Bilthoven, The Netherlands). CLLs were semiautomatically constructed and followed the center of the aortic and iliac permeable lumen.

The preoperative, early (<30 days) postoperative, and last follow-up CTA scans were analyzed in all patients. In patients with complications after EVAR, all CTA scans were analyzed.

Interobserver variability was previously assessed and agreement was high for AAA diameter ($R^2$ linear = 0.996), neck length ($R^2$ linear = 0.991), and neck diameter ($R^2$ linear = 0.935).[14]

**Definitions.** Aneurysm related definitions used in the study were derived from the reported standards for EVAR and/or were previously described.[11,14-17] Briefly, aneurysm and neck diameters were determined after CLL reconstructions. Aneurysm neck length was defined as the length of the lowermost renal artery to the level where the aortic diameter increases with at least 10%. Aneurysm angulation (suprarenal and infrarenal) were defined after CLL reconstruction. Aneurysm neck thrombus and calcification were defined as having more than 25% of the cross-sectional area of the neck being affected. Iliac stenosis was defined as having at least one focal stenosis in the one of the iliac arteries. Iliac tortuosity was defined as absent, minor, or major by one experienced observer (F.B.G.) using three-dimensional reconstruction. Iliac aneurysm was defined as having an iliac diameter over 3 cm measured after CLL reconstructions. Aneurysm sac behavior and proximal neck dilatation during follow-up were calculated for patients with at least two suitable imaging surveillance exams. Aneurysm neck growth was defined as an increase of ≥2 mm between the maximum neck diameter at first postoperative and last available CTA scan during follow-up. Aneurysm sac growth was defined as an increase of in diameter ≥5 mm and aneurysm sac shrinkage as a decrease in diameter ≥5 mm between the maximal aneurysm diameter at first postoperative and last available imaging (ie, two available CTA scans or two available DUS examinations) during follow-up.

**End points.** The primary study end point was freedom from complications after EVAR. Complications after EVAR was defined as a composite of one of the following: endoleak during follow-up (ie, type Ia, type Ib, type III, or undetermined type endoleaks on postoperative examinations), secondary intervention (ie, proximal stent/cuff, limb extension, coil/glue embolization, open ligation of collaterals, conversion to aorto-uni-iliac device, conversion to open repair and relining), aneurysm sac growth, acute limb ischemia, or postimplantation aneurysm rupture. Type II endoleak was not included as a complication after EVAR because we consider intervention for type II endoleak only when in combination with aneurysm sac growth, which is included as complication after EVAR.[11] In case the primary end point was met by multiple criteria, the date of the first event was considered for the purpose of survival analysis.

The secondary end points were individual components of the primary end point (endoleak during follow-up, secondary interventions, and aneurysm sac growth), aneurysm neck growth, and overall survival after EVAR.

**Clinical characteristics.** The medical histories of the patients were obtained from medical files. The demographic characteristics included sex and age. The cardiovascular comorbidities included ischemic heart disease (history of myocardial infarction, coronary revascularization, or pathologic Q-waves on the electrocardiogram), cerebrovascular disease (history of ischemic/hemorrhagic stroke or transient ischemic attack), and cardiac arrhythmia. The cardiovascular risk factors included kidney disease (estimated glomerular filtration rate <60 mL/min per 1.73 $m^2$), diabetes mellitus (fasting plasma glucose ≥7.0 mmol/L, nonfasting glucose ≥11.1 mmol/L, or use of antidiabetic medication), hypertension (blood pressure ≥140/90 mm Hg in nondiabetics, ≥130/80 mmHg in diabetics, or use of antihypertensive medication), and chronic obstructive pulmonary disease (history of chronic obstructive pulmonary disease or stage ≥1 according to the Global Initiative for Chronic Obstructive Lung Disease classification). Smoking status was obtained and included current smoking and ever smoking (ie, patients who are currently smoking OR patients with a history of smoking). Prescription medications were recorded and included the use of statins, beta-blockers, antiplatelets, and anticoagulant therapy.

**Statistical analysis.** Dichotomous data are described as counts and percentages. Continuous variables are described as mean (standard deviation) or median with interquartile range (IQR) when not normally distributed. Categorical data were analyzed with $\chi^2$ tests and continuous variables with analysis of variance or Kruskal-Wallis

**Table I.** Clinical characteristics at baseline

| *Variable*[a] | *Familial AAA (n = 51)* | *Sporadic AAA (n = 204)* | P *value* |
|---|---|---|---|
| Male sex | 44 (86.3) | 182 (89.2) | .554 |
| Age at diagnosis, years | 69.3 ± 8.1 | 72.1 ± 7.1 | .015 |
| Age ≤65 years at diagnosis | 14 (27.5) | 31 (15.2) | .040 |
| Cardiovascular comorbidities | | | |
| Ischemic heart disease | 20 (39.2) | 72 (35.3) | .619 |
| Cerebrovascular disease | 6 (11.8) | 25 (12.3) | .905 |
| Cardiac arrhythmia | 7 (13.7) | 17 (8.3) | .243 |
| Cardiovascular risk factors | | | |
| Kidney disease | 8 (15.7) | 51 (25.0) | .186 |
| Diabetes mellitus | 10 (19.6) | 39 (19.1) | .961 |
| Hypertension | 31 (60.8) | 138 (67.6) | .285 |
| COPD | 18 (35.3) | 83 (40.7) | .435 |
| Smoking – current | 17 (33.3) | 81 (39.7) | .403 |
| Smoking – ever | 30 (58.8) | 150 (73.5) | .039 |
| Medication | | | |
| Statins | 40 (78.4) | 148 (72.5) | .393 |
| Beta-blockers | 42 (82.4) | 152 (74.5) | .240 |
| Antiplatelets | 43 (84.3) | 150 (73.5) | .108 |
| Anticoagulants | 5 (9.8) | 27 (13.2) | .508 |

*COPD*, Chronic obstructive pulmonary disease.
[a]Continuous data are presented as the mean ± standard deviation and categorical data as number (%).

**Table II.** Aneurysm morphology at baseline

| *Variable*[a,b] | *Familial AAA (n = 51)* | *Sporadic AAA (n = 204)* | P *value* |
|---|---|---|---|
| Neck diameter, mm | 26.2 ± 4.2 | 25.4 ± 3.5 | .194 |
| Neck length, mm | 31.2 ± 17.5 | 31.5 ± 13.9 | .982 |
| AAA diameter, mm | 61.6 ± 12.8 | 60.3 ± 13.3 | .533 |
| Aneurysm angulation | | | |
| Suprarenal, degrees of angulation | 22.3 ± 17.7 | 24.0 ± 18.1 | .723 |
| Infrarenal, degrees of angulation | 37.5 ± 20.3 | 40.6 ± 24.8 | .415 |
| Neck thrombus | 14 (27.5) | 70 (34.3) | .263 |
| Neck calcification | 11 (21.6) | 50 (24.5) | .558 |
| Iliac stenosis | 8 (15.7) | 38 (18.6) | .553 |
| Iliac tortuosity | 28 (54.9) | 110 (53.9) | .985 |
| Iliac aneurysms | 15 (29.4) | 65 (31.9) | .736 |

*AAA*, Abdominal aortic aneurysm; *CTA*, computed tomography angiography
[a]Continuous data are presented as the mean ± standard deviation and categorical data as number (%).
[b]Preoperative CTA scans were available for 242 patients.

tests, as appropriate. A multivariable Cox regression was used to assess the hazard ratio (HR), along with the 95% confidence interval, for complications after EVAR between fAAA and spAAA. Variables entered into the multivariate Cox regression model were selected on basis of univariable significant differences at baseline between fAAA and spAAA (ie, age and ever smoking). Kaplan-Meier estimates were calculated for freedom from complications after EVAR. Estimates for fAAA and spAAA were compared using log-rank (Mantel-Cox) test of equality. To assess a possible selection bias, we tested for differences in complications after EVAR, for included and excluded patients of the complete EVAR database, using $\chi^2$ tests. For all tests, a $P$ value <.05 (two-sided) was considered significant. All analyses were performed using IBM SPSS Statistics v. 20.0 (SPSS Inc, Chicago, Ill).

## RESULTS

A total of 373 patients were treated with EVAR for intact degenerative aorto-iliac aneurysms (Fig 1). Since 84 patients died before receiving the questionnaire and 34 patients did not respond to the questionnaire and could not be reached, the total study population consisted of 255 patients. No patients were identified with a genetic aortic aneurysm syndrome. The mean age of the population was 71.5 (±7.4) years and 226 patients (88.6%) were of male sex.

**Clinical characteristics and aneurysm morphology at baseline.** Of the 255 included patients, 51 (20.0%) had at least one affected first-degree relative and were classified as fAAA. The remaining 204 patients (80.0%) had no affected first-degree relative and were classified as spAAA. All clinical characteristics at baseline are presented in Table I. Patients with fAAA were younger compared with spAAA patients (69 vs 72 years; $P = .015$) and were less likely to have ever smoked (58.8% vs 73.5%; $P = .039$). There were no differences in aneurysm morphology between the two groups (Table II). Preoperative neck and aneurysm diameter were similar, as well as the presence of iliac stenosis, iliac tortuosity, and iliac aneurysms.

**Complications after EVAR.** The median duration of follow-up was similar for fAAA and spAAA patients (3.9 years [IQR, 2.4-6.9] and 3.3 years [IQR, 2.1-5.5]; $P = .163$). During this period, a total of 57 patients (22.4%) had complications after EVAR; 18 fAAA patients and 39 spAAA patients (35.3% vs 19.1%; $P = .013$; Table III). Kaplan-Meier estimates for freedom of complications after EVAR were significantly different between both groups, with a 5-year estimate of 51% in fAAA and 74% in spAAA ($P = .007$; Fig 2).

A total of 19 patients (37.3% of fAAA) had two or more affected relatives. Patients with two or more affected relatives had more complications after EVAR compared with those with only one affected relative (42.1% vs 31.2%, respectively), although it did not reach statistical significance ($P = .443$)

Patients with fAAA had a 2.1-fold increased risk of complications after EVAR compared with spAAA patients after adjustment for age and ever smoking (HR, 2.1; 95% confidence interval [CI], 1.2-3.7; Table IV). Age (HR, 0.99; 95% CI, 0.95-1.02; $P = .405$) and ever smoking (HR, 0.84; 95% CI, 0.49-1.45; $P = .538$) did not predict for complications after EVAR in the multivariable model.

**Endoleaks during follow-up.** Patients with fAAA had more endoleaks during follow-up (15.7% vs 8.8%), although it did not reach statistical significance ($P = .147$). The difference appeared to be caused mainly by more type Ia and Ib endoleaks (15.6% vs 7.4%; $P = .063$).

**Table III.** Complications after endovascular aneurysm repair (*EVAR*)

| *Variable*[a] | *Familial AAA (n = 51)* | *Sporadic AAA (n = 204)* | P *value* |
|---|---|---|---|
| Complications after EVAR, patients | 18 (35.3) | 39 (19.1) | .013 |
| Endoleak during follow-up, events | 8 (15.7) | 18 (8.8) | .147 |
| Type Ia | 5 | 9 | |
| Type Ib | 3 | 6 | |
| Type III | 0 | 1 | |
| Type undetermined | 0 | 2 | |
| Secondary intervention | 20 (39.2) | 41 (20.1) | .004 |
| Proximal stent/cuff | 4 | 10 | |
| Limb extension | 5 | 18 | |
| Coil/glue embolization | 2 | 2 | |
| Open ligation of collaterals | 3 | 4 | |
| Conversion to AUI | 1 | 0 | |
| Conversion to open repair | 2 | 5 | |
| Relining | 3 | 2 | |
| Aneurysm sac growth[b] | 10 (20.8) | 18 (9.5) | .030 |
| Acute limb ischemia | 0 | 4 | .313 |
| Postimplantation aneurysm rupture | 0 | 0 | … |

*AAA,* Abdominal aortic aneurysm; *AUI,* aorto-uni-iliac device; *CTA,* computed tomography angiography; *DUS,* duplex ultrasound.
[a]Categorical data are presented as number (%).
[b]Aneurysm sac measurements were available for 237 patients with ≥ two postoperative imaging examinations (ie, two CTA scans or two DUS examinations).

**Secondary interventions during follow-up.** Patients with fAAA had a significantly higher secondary intervention rate after EVAR than spAAA patients (39.2% vs 20.1%; $P = .004$). Proximal stent/cuff, coil/glue embolization, open ligation of collaterals, and relining were more common in patients with fAAA. Detailed data regarding elements of secondary interventions are presented in Table III.

**Aneurysm sac behavior and proximal neck dilatation during follow-up.** Aneurysm sac growth was more common in patients with fAAA than those with spAAA (20.8% vs 9.5%; $P = .030$; Table V). Notably, this was independent of type II endoleaks, which occurred in 13.7% of the fAAA patients and 11.8% of the spAAA patients ($P = .713$). Patients with fAAA also tended to have less aneurysm sac shrinkage (47.9% vs 63.0%; $P = .057$). There was no difference in aneurysm neck growth, which occurred in 59.5% of the fAAA patients and 63.2% in patients with spAAA ($P = .662$).

**Overall long-term survival.** During follow-up, 41 patients died; seven (13.7%) in the fAAA group and 34 (16.7%) in the spAAA group ($P = .609$).

**Assessment of selection bias.** As mentioned above, no difference in survival was observed between the two groups. However, we observed a difference in complications after EVAR for patients included and excluded from analysis (22.4% vs 15.1%, respectively; $P = .046$).

## DISCUSSION

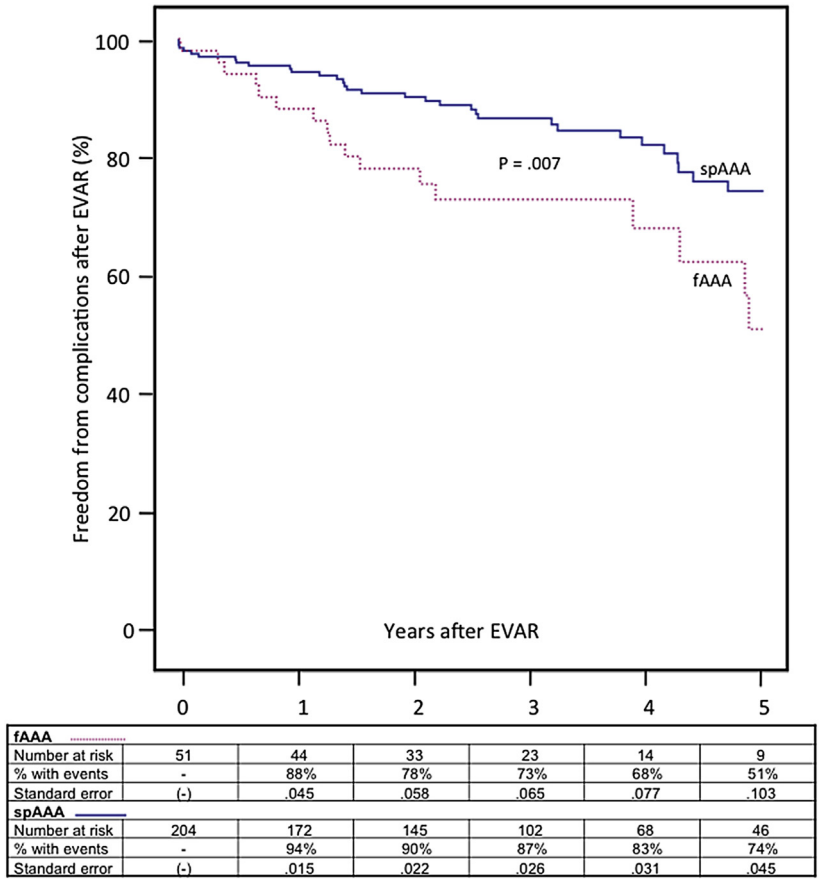
The main finding of the study was that patients with fAAA have a twofold higher risk of developing aneurysm-related complications after EVAR than patients with spAAA, despite similar AAA morphology. Although Brewster et al showed several years ago a trend toward more aneurysm-related mortality in patients with a history of aneurysmal disease,[18] this is the first report focusing on the association between family history and complications after EVAR.

In this study, we chose not to include patients with isolated iliac, traumatic, anastomotic, or infectious aneurysms because they either have different EVAR related complication risk or have other pathophysiological mechanisms leading to aneurysm formation compared with "typical" AAA. In addition, we excluded the ruptured aneurysms because they have a high rate of nonresponders because of high mortality, which could be an important source of bias. Also, the purpose of this study was primarily to determine the contribution of family history to preoperative risk assessment and modification, which is essentially directed at elective (preventive) situations. For ruptured aneurysms, family history of AAA is most likely not going to change the immediate attitude, which is to offer a life-saving procedure.

We found that 20% of our AAA population had a positive family history, which is similar to other studies reporting on the prevalence of fAAA.[1,19-21] Furthermore, patients with fAAA were younger and were less likely to have a history of smoking compared with patients with spAAA in our population. Previous studies similarly suggested that fAAA patients are slightly younger but studies on the effect of smoking are scarce.[1,20,22]

Since it is well known that adverse AAA morphology may result in increased number of adjunctive procedures,[23] and it is also known that some genetic aortic aneurysm syndromes are associated with specific anatomic features like arterial elongation and tortuosity,[24-26] we determined aneurysm morphology before stent implantation. Maximum AAA diameter and presence of iliac tortuosity or stenosis were comparable between the two groups. Similarly, aneurysm neck characteristics such as diameter, length, angulation as well as the presence of thrombus and calcification were not different for fAAA and spAAA patients. Consequently, the observed disparities in complications cannot be attributed to morphologic differences between the groups.

Secondary interventions and aneurysm sac growth were the most important elements accounting for the difference in the composite primary end point of complications after EVAR. Although patients with fAAA also tended to have more endoleaks, in particular proximal and distal type I endoleaks, this difference failed to reach statistical significance because of limited patient numbers in the two groups. Patients with fAAA displayed more aneurysm sac growth, independent of the presence of type II endoleaks and less aneurysm sac shrinkage than patients with spAAA. It may be hypothesized that an intrinsic weakness of the aortic wall results in more rapid progression of aneurysm disease and contributes to a higher need for secondary interventions in fAAA patients. These observations suggest

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|---|---|---|---|---|---|---|
| **fAAA** | | | | | | |
| Number at risk | 51 | 44 | 33 | 23 | 14 | 9 |
| % with events | - | 88% | 78% | 73% | 68% | 51% |
| Standard error | (-) | .045 | .058 | .065 | .077 | .103 |
| **spAAA** | | | | | | |
| Number at risk | 204 | 172 | 145 | 102 | 68 | 46 |
| % with events | - | 94% | 90% | 87% | 83% | 74% |
| Standard error | (-) | .015 | .022 | .026 | .031 | .045 |

**Fig 2.** Kaplan-Meier estimates are shown for complications after endovascular aneurysm repair (*EVAR*) between familial abdominal aortic aneurysm (*AAA*) (*dashed red line*) and sporadic AAA (*solid blue line*). *fAAA*, Familial AAA; *spAAA*, sporadic AAA.

**Table IV.** Uni- and multivariable analysis for complications after endovascular aneurysm repair (EVAR)-associated with familial abdominal aortic aneurysm (*AAA*)

| | *Univariable* | | | *Multivariable*[a] | | |
|---|---|---|---|---|---|---|
| | *HR* | *95% CI* | P *value* | *HR* | *95% CI* | P *value* |
| Sporadic AAA | Ref | | | Ref | | |
| Familial AAA | 2.15 | 1.22-3.81 | .008 | 2.05 | 1.15-3.66 | .015 |

*CI*, Confidence interval; *HR*, hazard ratio.
[a]Adjusted for age and ever smoking.

**Table V.** Aneurysm sac behavior and proximal neck dilatation during follow-up

| *Variable*[a] | *Familial AAA* | *Sporadic AAA* | P *value* |
|---|---|---|---|
| Aneurysm neck diameter[b] | | | |
| Growth | 25 (59.5) | 103 (63.2) | .662 |
| Aneurysm sac diameter[c] | | | |
| Growth | 10 (20.8) | 18 (9.5) | .030 |
| Stability | 15 (31.2) | 52 (27.5) | .608 |
| Shrinkage | 23 (47.9) | 119 (63.0) | .057 |

*AAA*, Abdominal aortic aneurysm; *CTA*, computed tomography angiography; *DUS*, duplex ultrasound.
[a]Categorical data are presented as number (%).
[b]Aneurysm neck measurements were available for 205 patients with ≥ two postoperative CTA scans.
[c]Aneurysm sac measurements were available for 237 patients with ≥ two postoperative imaging examinations (ie, two available CTA scans or two available DUS examinations).

that—as yet unknown—inherited connective tissue disorders may underlie aneurysm formation in patients with familial AAA.

Over the median follow-up period of 3 years, aneurysm neck growth was quite common (about 60%) in both groups. This high rate results from a low threshold definition and is comparable to other reports on contemporary stent grafts.[27,28]

In patients with known connective tissue disorders, endovascular therapies have been shown to result in much higher failure rates due to rapid dilatation or dissection of the aorta and are generally unadvised.[12,13]

Nevertheless, we still believe that EVAR is a valid treatment alternative over open repair in patients with a positive family history because most complications observed in our study in fAAA patients could be treated with minimally invasive techniques. Also, low morbidity and the early survival advantage of EVAR appears to be unchanged in the fAAA group. Although standard postoperative surveillance is still recommended, our study should create awareness for the fact that patients with fAAA may develop more complications after EVAR. New prospective studies are needed for clarification of our findings and should determine which postoperative surveillance program suits fAAA patients best. Apart from the surveillance program, all fAAA patients in our institute receive genetic counseling to provide information on the hereditary of aortic aneurysms and are offered screening for all first-degree relatives.

There are several limitations that need to be considered. First, the single-center nature of this study limits the generalization of the results. A second limitation is the classification of familial AAA based on self-reported family history alone. The chance of having affected relatives is lower in small families compared with large families. Also, since objective screening of relatives was not performed, under-reporting of fAAA is likely. Third, no systematic molecular screening was performed for the known genetic aortic aneurysm syndromes. However, since these syndromes are rare causes for AAAs and generally present at a younger age, their contribution to the study population is probably negligible. In addition, the relative short follow-up of 3.3 years should be taken into account because it is known that endoleaks may develop in a later stage. Long-term follow-up is therefore warranted. Lastly, our study is also limited by its retrospective design, therefore, we evaluated possible selection bias. The mortality of fAAA and spAAA patients was similar for both groups, which suggests homogeneity between the two included groups, but we observed small difference in complications after EVAR for included and excluded patients. This was probably explained by the fact that patients treated for ruptured aneurysms died more frequently in the perioperative period and consequently could not develop a complication. Also, patients with a small anastomotic aneurysm treated with a covered stent are less likely to develop an EVAR-related complication as defined in the study. Therefore, we believe that bias might be present due to the study design but was minimized by the chosen inclusion criteria and does not invalidate the main findings of the study.

In conclusion, the current study shows that patients with a familial form of AAA develop more aneurysm-related complications after EVAR, despite similar AAA morphology at baseline. Although the limitations of this study suggest caution in interpretation of the results, the twofold higher aneurysm-related complication rate after EVAR should create awareness for a possible incremental risk in this subgroup. Our findings emphasize the need for further research on genetic causes and underlying molecular mechanisms of AAA.

## AUTHOR CONTRIBUTIONS

Conception and design: KL, FB, DM, ER, RS, HV
Analysis and interpretation: KL, FB, SH
Data collection: KL, FB
Writing the article: KL, FB, SH
Critical revision of the article: DM, ER, RS, HV
Final approval of the article: KL, FB, SH, DM, ER, RS, HV
Statistical analysis: KL, FB, SH
Obtained funding: RS, HV
Overall responsibility: HV

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