Aneurysm Sac Thrombus Volume Predicts Aneurysm Expansion with Type II Endoleak after Endovascular Aneurysm Repair

Takayuki Fujii MD, Hiroshi Banno MD, PhD, Akio Kodama MD, PhD, Masayuki Sugimoto MD, PhD, Naohiro Akita MD, Takuya Tsuruoka MD, Masashi Sakakibara MD, and Kimihiro Komori MD, PhD, FACS.

Division of Vascular Surgery, Department of Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

Correspondence: Takayuki Fujii, MD, Division of Vascular Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi, Japan

Tel.: +81-52-744-2224; Fax: +81-52-744-2226

Email: takayukifujii@med.nagoya-u.ac.jp

Abstract

Background: Several studies have analyzed risk factors that may influence the incidence of type II endoleak with sac expansion after endovascular aneurysm repair (EVAR). However, the impact of intraluminal thrombus volume on the incidence of sac expansion with type II endoleak requires further analysis. This study examined the correlation between preoperative intraluminal thrombus and the incidence of type II endoleak and late sac expansion by measuring the thrombus volume.

Methods: Between June 2007 and March 2014, 423 patients underwent EVAR at our institution. Two hundred eighty patients with preoperative and postoperative computed tomography angiography (CTA) were included in this study. Data were collected prospectively and supplemented with a retrospective review of the medical records and radiologic images, and demographic and clinical characteristic profiles were collected. Logistic regression and Cox regression analyses were used to assess each variable's association with the incidences of persistent or new endoleak and sac expansion.

Results: Of the 280 patients, 46.7% (131 patients) had persistent type II endoleak and 19.6% (55 patients) had persistent type II endoleak with significant sac expansion (≥5 mm). The mean follow-up duration was 60 months (interquartile range, 24 – 72 months). Cox regression analysis showed that older age (p = 0.001), intraluminal thrombus volume ratio (thrombus volume [*T* vol] / aortic aneurysm volume [*A* vol]) (p = 0.042) and IMA diameter (p = 0.004) were significant predictors of the incidence of sac expansion with persistent or new type II endoleak. The receiver operating characteristic curve analysis revealed a cutoff of 51% *T* vol / *A* vol (area under curve [AUC]: 0.59) and 2.9 mm (area under curve [AUC]: 0.60). The rate of freedom from sac expansion (≥5 mm) during follow-up was significantly higher in patients with ≥51% *T* vol / *A* vol than in those with a lower *T* vol / *A* vol (p = 0.010).

Conclusion: Preoperative sac thrombus volume, IMA diameter and older age predict the

incidence of aneurysm expansion with type II endoleak after EVAR.

Introduction

Endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) is a well-established procedure. Randomized trials have shown significantly lower early mortality rates after EVAR as compared with open repair. However, development of endoleaks after EVAR leads to high reintervention rates in the long term (10-29.6%).[1-4] Type II endoleak is a common complication after EVAR (11.7%).[5] This complication occasionally leads to sac expansion and eventual rupture.[6] The treatment efficacy for type II endoleak after EVAR is limited, with recurrence in one-third of patients following transarterial embolization and in approximately one-fifth of patients following translumbar embolization.[7] Many patients experience persistent sac expansion despite type II endoleak treatment (21.6%).[8] Several studies have reported that aortic side branch and/or sac embolization during EVAR helps prevent the development of type II endoleak.[9-11] However, not all type II endoleaks lead to sac expansion. Dijkstra ML et al reported a higher incidence of the sac growth in patients with a type II endoleak than in patients without a type II endoleak; however, the actual rate was only 21.9%.[12] Therefore, further investigation is required to determine the factors associated with sac expansion in the presence of type II endoleaks.

Previous studies have analyzed risk factors that may influence the incidence of type II endoleak after EVAR and have demonstrated a quantitative protective effect of intraluminal thrombus against type II endoleak. However, those studies assessed the proportion of intraluminal thrombus load indirectly through variables such as thrombus thickness, percentage of luminal circumference covered by the thrombus, and proportion of the sac area covered by the thrombus.[13, 14] Some reports have evaluated the association between the incidence of type II endoleak with sac expansion and the proportion of intraluminal thrombus volume by measuring the thrombus volume itself.[15-17] However, little information is available about the relationship between thrombus volume and the incidence of persistent type II

endoleak. Our study examined the correlation and impact of preoperative intraluminal thrombus volume and the incidence of persistent type II endoleak and late sac expansion.

Materials and Methods

Study population

Between June 2007 and March 2014, 423 patients underwent EVAR at our institution. Indications for EVAR were based on age, comorbidities, and patient preferences.[18] Ruptured, inflammatory, infected aneurysms and isolated iliac aneurysms were excluded. Patients who had not undergone preoperative or postoperative computed tomography angiography (CTA) with contrast medium or had not had ≥6 months of follow-up were also excluded (Fig 1). The cohort included 1 type Ia endoleak, 2 type Ib endoleaks and 2 type III endoleaks that were treated. Those patients had no type II endoleak at any point postoperatively. They underwent reintervention immediately, and we confirmed that those endoleaks were resolved by using contrast-enhanced CT. Therefore, they were included in this study. We did not include patients who had persistent type I or III endoleak.[19] No patients had undergone an embolization of the inferior mesenteric artery (IMA).

Type II endoleak is a well-known risk factor for sac increase; however, two-thirds of patients show sac diameter stabilization or decrease. Thus, we divided patients with sac expansion with type II endoleak into a malignant group and the others into a benign group. We compared the two groups to detect predictors of sac expansion with type II endoleak.

Procedures

Endovascular procedures were performed by vascular surgeons in a hybrid operating room via surgical femoral artery exposure. All patients in this study were treated using commercially available devices: Zenith (Cook Medical, Bloomington, IN), Endurant (Medtronic, Santa Rosa, CA), Excluder (W.L. Gore & Associates, Flagstaff, AZ), Powerlink

(Endologix, Hertogenbosch, the Netherlands), Talent (Medtronic Vascular, Santa Rosa, CA) and Incraft (Cordis, Vaughan, Ontario, Canada).

Study and follow-up protocol

Data were collected prospectively and supplemented with a retrospective review of the medical records and radiological images. Demographic and clinical characteristic profiles were collected. A standard follow-up protocol was applied at 30 days and 3, 6 and 12 months after surgery and annually thereafter. Patients underwent CTA at 3, 6, and 12 months and annually thereafter if renal function permitted. The method used for CTA with intravenous contrast medium was as follows. After intravenously injecting a bolus of nonionic contrast medium (3.5 mL/s), arterial phase images were obtained for all patients using a bolus-tracking technique. Delayed-phase images were obtained 90 s after the arterial-phase scan. The total volume of the contrast medium was 80 mL. The images were reconstructed from 1-mm-thick slices. CTA was evaluated using Aquarius iNtuition software (TeraRecon, Foster City, CA) to obtain the aneurysm sac and intraluminal thrombus volumes and other anatomical factors. Maximum aortic diameter was measured on the minor axis of the largest axial cut of the aneurysm on the 2-dimensional CTA. All measurements were performed by one investigator. To estimate interobserver variability, 90 patients were extracted at random, and their *T* vol / *A* vol were measured by another investigator.

Definitions

We measured aneurysm and thrombus volumes by the method reported by Muller-Wille et al.[16] Briefly, preoperative intraluminal thrombus volume (*T* vol) was calculated by subtracting the volume of the contrast-enhanced aortic lumen from the volume of the whole aortic aneurysm (*A* vol). *A* vol and *T* vol were calculated from the aneurysm's origin to the aortic bifurcation. The intraluminal thrombus volume ratio (*T* vol / *A* vol [%])

was defined as *T* vol / *A* vol (%) = (aortic aneurysm volume - luminal volume) / aortic aneurysm volume × 100.

A persistent type II endoleak was defined as a type II endoleak upon case completion and at ≥6 months at least once during follow-up. A new type II endoleak was defined as no endoleak detected with angiography at the end of the case by CTA before discharge, and an endoleak reported ≥6 months postoperatively. A vascular study group in New England demonstrated that persistent or new type II endoleak are risk factors for the incidence of type II endoleak with sac expansion.[20] A significant AAA sac expansion was defined as an increase of ≥5 mm in aortic aneurysm diameter.

Preoperative coronary artery disease (CAD) was defined as an abnormal result on a coronary angiogram and a history of myocardial infarction or open or percutaneous coronary artery revascularization. Lung disease was defined to include a history of chronic obstructive pulmonary disease, asthma, bacterial pneumonia or interstitial pneumonia. Hypertension, dyslipidemia, and diabetes were identified in patients undergoing active medical treatment or diet modification. Cerebrovascular disease (CVD) was defined as a history of stroke, transient ischemic attack, or carotid intervention. Smoking history included patients who ever smoked. Anticoagulation included warfarin and direct oral anticoagulants (DOAC).

Statistical analysis

We compared categorical variables between outcome subgroups using chi-square and Fisher's exact tests. Continuous variable means were compared using Student's t-test. Logistic regression and Cox regression analyses were used to assess each variable's association with the incidence of persistent type II endoleak and sac expansion with persistent type II endoleak. A ROC curve of the model's predicted probabilities was plotted, and the area under the curve (AUC) was used to assess the differentiation of the *T* vol / *A* vol with or without persistent type II endoleaks with sac expansion after EVAR. Freedom from aneurysm

sac expansion was assessed using Kaplan-Meier life-table analysis, and a log-rank test was used to compare subgroups. Statistical analysis was performed using SPSS software, version 24 (IBM Corp., Armonk, NY, USA). P values <.05 were considered statistically significant. To estimate interobserver variability, Bland-Altman plot analysis was performed. This retrospective observational study was approved by the Institutional Review Board.

Results

During the study period, 423 patients underwent EVAR at our institution. Two hundred eighty patients (82.5% male, mean age 77.4 ± 6.2 years) were included in the study according to our inclusion and exclusion criteria. Of the 280 patients, 131 (46.8%) showed persistent type II endoleak, and sac expansion with type II endoleak was detected in 55 of 280 patients (19.6%). The median follow-up duration was 60 months (interquartile range, 24 – 72 months). Table I describes the patients' demographic data, comorbidities, devices, and anatomical characteristics. The mean maximum aortic aneurysm diameter was 53.5 ± 8.1 mm, and the mean *T* vol / *A* vol was 48.6 ± 17.3%. Bland-Altman plot analysis revealed that 95% of the data points lay within ± 2S*D* of the mean difference. Two hundred six patients had patent IMAs (73.6%). The mean IMA diameter was 2.33 ± 1.6 mm.

Complications and reinterventions

Thirty-eight reinterventions occurred after EVAR. Causes of reintervention included type Ia endoleaks (n = 1), type Ib endoleaks (n = 2), type II endoleaks (n = 21), type III endoleaks (n = 2), limb migration (n = 1) and access problems (n = 11). Most type II endoleaks were treated at our institution if they had 5 mm or more of aortic sac growth after EVAR.

Twenty-six patients (12.3%) died during the study. Aneurysm-related mortality was 0.5% (1 patient). The patient, an 86-year-old woman, underwent EVAR for an AAA of 57 mm in

diameter. Type II endoleak was detected 3 months after EVAR and remained unresolved during follow-up; however, it was kept under observation because of a slight aneurysm enlargement. When the patient was found at home, she was already dead. Autopsy imaging revealed a retroperitoneal hematoma, and the cause of death was diagnosed as AAA rupture.

Risk factor analysis

Univariate analysis of persistent type II endoleak with or without sac expansion

During follow-up, 131 of 280 patients (46.7%) showed persistent or new type II endoleak, and 55 of 280 patients (19.6%) showed persistent or new type II endoleak with significant sac expansion (≥ 5 mm).

As shown in Table II, univariate analysis revealed that the incidence of persistent or new type II endoleak was significantly correlated with female sex (p = 0.003), smoking history (p = 0.002), Zenith use (p = 0.003), Excluder use (p < 0.001), Powerlink use (p = 0.018), intraluminal thrombus volume (p = 0.032), *T* vol / *A* vol (p = 0.004), patent IMA (p = 0.019), IMA diameter (p = 0.001) and the number of patent lumbar arteries (p = 0.004).

Similarly, univariate analysis showed that the incidence of sac expansion with persistent or new type II endoleak was significantly associated with patient age (p = 0.001), female sex (p < 0.001), Endurant use (p = 0.019), coronary artery disease (p = 0.033), *T* vol / *A* vol (p = 0.025), the number of patent lumbar arteries (p = 0.029), patent IMA (p = 0.028) and IMA diameter (p = 0.013) (Table III).

Multivariate analysis for persistent type II endoleak with or without sac expansion

Logistic regression analysis showed that Excluder use (odds ratio [OR] 0.32, 95% confidence interval [CI] 0.15–0.65; p = 0.02), *T* vol / *A* vol (OR 0.98, 95% CI 0.96–0.99; p = 0.011), IMA diameter (OR 1.35, 95% CI 1.12–1.62; p = 0.001) and the number of patent lumbar arteries (OR 1.25, 95% CI 1.07–1.47; p = 0.005) were associated with the incidence

of persistent or new type II endoleak. Cox regression analysis showed that older age (OR 1.09, 95% CI 1.04–1.15; p = 0.01), lower preoperative *T* vol / *A* vol (OR 0.982, 95% CI 0.96–0.99; p = 0.045) and IMA diameter (OR 1.32, 95% CI 1.09–1.59; p = 0.04) were significant predictors of the incidence of sac expansion with persistent or new type II endoleak (Table IV).

ROC curve analysis of *T* vol / *A* vol showed that the AUC for the predicted probabilities was 0.58 (95% CI: 0.50–0.67). At a cutoff value of 51%, the sensitivity of the minimum *T* vol / *A* vol for predicting persistent or new type II endoleak with sac expansion was 67.3% with 51.6% specificity. Pursuant to this result, patients in this study were divided into 2 groups based on the *T* vol / *A* vol. One hundred thirty-four patients had a *T* vol / *A* vol ≥ 51%. No significant differences were found in the baseline morphology or clinical characteristics between the two groups. The rate of freedom from sac expansion (≥ 5 mm) after EVAR during follow-up was significantly higher in patients with a *T* vol / *A* vol ≥51% than in those with a lower *T* vol / *A* vol (p = 0.010) (Fig 2).

Similarly, the ROC curve analysis for IMA diameter showed that the AUC for predictive probabilities was 0.60 (95% CI: 0.52–0.68). At a cut-off value of 2.9 mm, the sensitivity of the minimum IMA diameter for predicting sac expansion with persistent or new type II endoleak was 61.8%, with a 68.4% specificity.

Discussion

Type II endoleak is considered mostly benign. However, persistent type II endoleak is associated with adverse outcomes, including aneurysm expansion, the need for conversion to open repair, reintervention and rupture.[21] Furthermore, reintervention does not always lead to satisfactory results.[22] Therefore, we identified high-risk patients who developed sac expansion with type II endoleak. Piazza et al. reported that sac embolization during EVAR using fibrin and coils reduced type II endoleak and its complications during early and

midterm follow-up in patients considered high risk for developing type II endoleak.[10] (That team defined the high-risk group of developing type II endoleak based on IMA diameter and number of patent lumbar arteries.) Similar studies defined high-risk groups based on patent IMA and number of patent lumbar arteries.[9, 23] In the present study, we demonstrated that a lower preoperative *T* vol / *A* vol was associated with the incidence of persistent or new type II endoleak with sac expansion and a < 51% *T* vol / *A* vol predicted aneurysm expansion after EVAR. This finding may make it possible to accurately identify high-risk patients with type II endoleak leading to sac expansion.

In this study, a significant AAA sac expansion was defined as an increase of ≥5 mm maximum aortic aneurysm diameter. Sac volume change may reflect the sac behavior more accurately. However, we adopted the change in maximum minor axis of aneurysm sac because sac increase > 5mm is the most common and accepted definition of sac expansion.

The correlation between the incidence of type II endoleak with sac expansion and preoperative intraluminal sac thrombus volume has not been extensively described. In the natural history of preoperative AAA, a large intraluminal thrombus volume is a significant factor for predicting high expansion rates.[24] An intraluminal thrombus is the source of many pro-proteolytic processes that stimulate aortic wall degradation and increasing expansion, possibly because of the accumulation of harmful active peptides.[25] However, previous studies demonstrated a quantitative protective effect of intraluminal thrombus against type II endoleak after EVAR.[13, 14, 26] Our study similarly demonstrated that a lower preoperative *T* vol / *A* vol significantly predicts the incidence of persistent or new type II endoleak with sac expansion after EVAR. However, the mechanism by which a large proportion of the intraluminal thrombus volume prevents the incidence of type II endoleak with sac expansion remains unclear. To estimate the thrombus proportion in the sac, previous authors indirectly assessed the volume of the intraluminal thrombus with variables such as thrombus thickness, percentage of luminal circumference covered by the thrombus, and proportion of the sac area

covered by the thrombus. Some studies reported correlations between thrombus volume and type II endoleak with sac expansion using *T* vol / *A* vol.[15-17] However, these studies had some limitations such as low patient numbers and short follow-up durations. Our study included more patients and a longer follow-up duration than those of previous works. Lo et al. stated that persistent and new type II endoleak predicted aneurysm expansion after EVAR.[20] We considered that persistent and new type II endoleak should be used as a definition of type II endoleak when identifying predictors of type II endoleak with sac expansion. However, no study has examined an association between intraluminal thrombus volume and persistent and new type II endoleak with sac expansion. Therefore, our study was meaningful in detecting the cut-off point of *T* vol / *A* vol for predicting persistent or new type II endoleak with sac expansion.

In our study, univariate and multivariate analyses revealed that older age was a significant risk factor for persistent or new type II endoleak incidence with sac expansion. Van Marrewjik et al. similarly showed that patients with persistent type II endoleaks were 2 years older than those without endoleaks.[27] Our study also showed that a patient age of > 80 years predicted the incidence of persistent or new type II endoleak with sac expansion after EVAR. Older patients may have larger sacs, and aortic wall weakness may cause expansion of the aneurysm after EVAR.[28] However, an explanation for this trend remains to be proposed.

Univariate analysis showed that coronary artery disease was a significant risk factor for sac expansion with type II endoleak. However, there appears to be no good clinical explanation. This result may be a random statistical anomaly. As a result, in this study, multivariate analysis showed that coronary artery disease was not a significant factor in the incidence of sac expansion with type II endoleak.

Multivariate analysis showed that Excluder use was a significant risk factor for persistent or new type II endoleak incidence. Similarly, Liana et al. reported that the use of an

Excluder increases the prevalence of type II endoleak compared with other devices.[29] On the other hand, another study reported that the use of different devices does not lead to different results in terms of type II endoleak incidence.[30] In our analysis, Excluder use was not associated with the incidence of sac expansion with type II endoleak. However, this result may be due to a type II statistical error caused by a relatively small sample size. No consensus exists on the correlation between stentgraft type and the incidence of sac expansion with type II endoleak.

Larger IMA diameter is considered a risk factor for developing type II endoleak after EVAR, and IMA embolization is performed during EVAR to prevent type II endoleak at some institutions. Many studies have demonstrated that IMA embolization during EVAR decreases the incidence of type II endoleak after EVAR and determined that indication of IMA embolization depends on the IMA diameter.[11, 31, 32] However, the impact of IMA diameter on type II endoleak with sac expansion remains controversial. Several authors have stated that the number of patent lumber arteries is associated with the incidence of type II endoleak with aneurysm expansion. In this study, the number of lumber arteries was not associated with the incidence of sac expansion with persistent type II endoleak.

This study had some limitations. First, the study was retrospective and observational in nature. Although our study included more patients than did previous reports, the cohort was small nonetheless. Second, patients who had not undergone preoperative or postoperative CTA or had not had ≥6 months of follow-up were excluded. Most patients did not undergo preoperative or postoperative CTA because of chronic kidney disease. Although there is ample evidence of contrast-enhanced ultrasound (CEUS) as a valid method for detecting type II endoleaks after EVAR, contrast for ultrasonography is not reimbursed in Japan. When patients have an allergy to contrast media or severe renal impairment, we usually use Doppler ultrasound (DUS) for the assessment of endoleak after EVAR. Unfortunately, there were not

enough technicians in our hospital during the study period, and as an alternative, DUS was not routinely performed.

Thus, of the 423 patients, 143 were excluded. However, the excluded patients did not significantly differ from the included patients in anatomical factors and thrombus volume proportion.

CONCLUSION

Our study demonstrated that the predictors of developing persistent or new type II endoleak differed between patients with and without sac expansion after EVAR and that *T* vol / *A* vol, older age and IMA diameter could predict the incidence of sac expansion with persistent or new type II endoleak. We revealed the cutoff value of *T* vol / *A* vol for predicting the incidence of type II endoleak with sac expansion. Lower *T* vol / *A* vol may make it possible to predict high-risk patients with type II endoleak leading to sac expansion.

REFERENCES

1. 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(14):1535-42.

2. D'Oria M, Mastrorilli D, Ziani B. Natural History, Diagnosis, and Management of Type II Endoleaks after Endovascular Aortic Repair: Review and Update. Ann Vasc Surg. 2019.

3. Stather PW, Sidloff D, Dattani N, Choke E, Bown MJ, Sayers RD. Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm. Br J Surg. 2013;100(7):863-72.

4. De Rango P, Cao P. Long-term results of OVER: the dream of EVAR is not over. Eur J Vasc Endovasc Surg. 2013;45(4):313-4.

5. Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. Br J Surg. 2017;104(3):166-78.

6. 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(5):805-12.

7. Kumar L, Cowled P, Boult M, Howell S, Fitridge R. Type II Endoleak after Endovascular Aneurysm Repair: Natural History and Treatment Outcomes. Ann Vasc Surg. 2017;44:94-102.

8. Ultee KHJ, Buttner S, Huurman R, Bastos Goncalves F, Hoeks SE, Bramer WM, et al. Editor's Choice - Systematic Review and Meta-Analysis of the Outcome of Treatment for Type II Endoleak Following Endovascular Aneurysm Repair. Eur J Vasc Endovasc Surg. 2018;56(6):794-807.

9. Fabre D, Fadel E, Brenot P, Hamdi S, Gomez Caro A, Mussot S, et al. Type II endoleak prevention with coil embolization during endovascular aneurysm repair in high-risk patients. J Vasc Surg. 2015;62(1):1-7.

10. Piazza M, Squizzato F, Zavatta M, Menegolo M, Ricotta JJ, 2nd, Lepidi S, et al. Outcomes of endovascular aneurysm repair with contemporary volume-dependent sac embolization in patients at risk for type II endoleak. J Vasc Surg. 2016;63(1):32-8.

11. Samura M, Morikage N, Mizoguchi T, Takeuchi Y, Ueda K, Harada T, et al. Identification of Anatomical Risk Factors for Type II Endoleak to Guide Selective Inferior Mesenteric Artery Embolization. Ann Vasc Surg. 2018;48:166-73.

12. Dijkstra ML, Zeebregts CJ, Verhagen HJM, Teijink JAW, Power AH, Bockler D, et al. Incidence, natural course, and outcome of type II endoleaks in infrarenal endovascular aneurysm repair based on the ENGAGE registry data. J Vasc Surg. 2019.

13. Sampaio SM, Panneton JM, Mozes GI, Andrews JC, Bower TC, Kalra M, et al. Aneurysm sac thrombus load predicts type II endoleaks after endovascular aneurysm repair. Ann Vasc Surg. 2005;19(3):302-9.

14. AbuRahma AF, Mousa AY, Campbell JE, Stone PA, Hass SM, Nanjundappa A, et al. The relationship of preoperative thrombus load and location to the development of type II endoleak and sac regression. J Vasc Surg. 2011;53(6):1534-41.

15. Hiraoka A, Chikazawa G, Ishida A, Miyake K, Totsugawa T, Tamura K, et al. Impact of Age and Intraluminal Thrombus Volume on Abdominal Aortic Aneurysm Sac Enlargement after Endovascular Repair. Ann Vasc Surg. 2015;29(7):1440-6.

16. Muller-Wille R, Guntner O, Zeman F, Dollinger M, Halg C, Beyer LP, et al. The Influence of Preoperative Aneurysmal Thrombus Quantity and Distribution on the Development of Type II Endoleaks with Aneurysm Sac Enlargement After EVAR of AAA. Cardiovasc Intervent Radiol. 2016;39(8):1099-109.

17. Sadek M, Dexter DJ, Rockman CB, Hoang H, Mussa FF, Cayne NS, et al. Preoperative relative abdominal aortic aneurysm thrombus burden predicts endoleak and sac enlargement after endovascular anerysm repair. Ann Vasc Surg. 2013;27(8):1036-41.

18. Yamamoto K, Komori K, Banno H, Narita H, Kodama A, Sugimoto M. Validation of Patient Selection for Endovascular Aneurysm Repair or Open Repair of Abdominal Aortic Aneurysm - Single-Center Study. Circ J. 2015;79(8):1699-705.

19. Madigan MC, Singh MJ, Chaer RA, Al-Khoury GE, Makaroun MS. Occult type I or III endoleaks are a common cause of failure of type II endoleak treatment after endovascular aortic repair. J Vasc Surg. 2019;69(2):432-9.

20. 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(4):895-901.

21. Jouhannet C, Alsac JM, Julia P, Sapoval M, El Batti S, Di Primio M, et al. Reinterventions for type 2 endoleaks with enlargement of the aneurismal sac after

endovascular treatment of abdominal aortic aneurysms. Ann Vasc Surg. 2014;28(1):192-200.

22. Zhou W, Blay E, Jr., Varu V, Ali S, Jin MQ, Sun L, et al. Outcome and clinical significance of delayed endoleaks after endovascular aneurysm repair. J Vasc Surg. 2014;59(4):915-20.

23. Aoki A, Maruta K, Hosaka N, Omoto T, Masuda T, Gokan T. Evaluation and Coil Embolization of the Aortic Side Branches for Prevention of Type II Endoleak after Endovascular Repair of Abdominal Aortic Aneurysm. Ann Vasc Dis. 2017;10(4):351-8.

24. Groeneveld ME, Meekel JP, Rubinstein SM, Merkestein LR, Tangelder GJ, Wisselink W, et al. Systematic Review of Circulating, Biomechanical, and Genetic Markers for the Prediction of Abdominal Aortic Aneurysm Growth and Rupture. J Am Heart Assoc. 2018;7(13).

25. Behr-Rasmussen C, Lindholt JS, Urbonavicius S, Halekoh U, Jensen PS, Stubbe J, et al. Abdominal Aortic Aneurysms Growth Is Associated With High Concentrations of Plasma Proteins in the Intraluminal Thrombus and Diseased Arterial Tissue. Arterioscler Thromb Vasc Biol. 2018.

26. Ward TJ, Cohen S, Patel RS, Kim E, Fischman AM, Nowakowski FS, et al. Anatomic risk factors for type-2 endoleak following EVAR: a retrospective review of preoperative CT angiography in 326 patients. Cardiovasc Intervent Radiol. 2014;37(2):324-8.

27. van Marrewijk CJ, Fransen G, Laheij RJ, Harris PL, Buth J, Collaborators E. 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(2):128-37.

28. Abularrage CJ, Crawford RS, Conrad MF, Lee H, Kwolek CJ, Brewster DC, et al. Preoperative variables predict persistent type 2 endoleak after endovascular aneurysm repair. J Vasc Surg. 2010;52(1):19-24.

29. Dubois L, Novick TV, Harris JR, Derose G, Forbes TL. Outcomes after endovascular abdominal aortic aneurysm repair are equivalent between genders despite anatomic

differences in women. J Vasc Surg. 2013;57(2):382-9 e1.

30. Sirignano P, Capoccia L, Mansour W, Ronchey S, Accrocca F, Siani A, et al. Type 2 Endoleak Incidence and Fate After Endovascular Aneurysms Repair in a Multicentric Series: Different Results with Different Devices? Ann Vasc Surg. 2019;56:224-32.

31. Nevala T, Biancari F, Manninen H, Matsi P, Makinen K, Ylonen K, et al. Inferior mesenteric artery embolization before endovascular repair of an abdominal aortic aneurysm: effect on type II endoleak and aneurysm shrinkage. J Vasc Interv Radiol. 2010;21(2):181-5.

32. Ward TJ, Cohen S, Fischman AM, Kim E, Nowakowski FS, Ellozy SH, et al. Preoperative inferior mesenteric artery embolization before endovascular aneurysm repair: decreased incidence of type II endoleak and aneurysm sac enlargement with 24-month follow-up. J Vasc Interv Radiol. 2013;24(1):49-55.

Table I. Demographic characteristics and risk factors in 280 patients

Variable[a]	*All (n = 280)*
Age (years)	77.4 ± 6.2 (55–91)
Female sex	49 (17.5)
Hypertension	197 (70.4)
Dyslipidemia	122 (43.6)
Lung disease[b]	40 (14.3)
Cerebrovascular disease	42 (15.0)
Coronary artery disease	96 (34.3)
Dialysis	6 (2.1)
Diabetes	29 (10.4)
Antiplatelet	109 (38.9)
Anticoagulant[c]	22 (7.9)
Smoking history[d]	170 (60.7)
Zenith	107 (38.2)
Excluder	101 (36.1)
Endurant	51 (18.2)
Powerlink	10 (3.6)
Talent	3 (1.1)
Incraft	8 (2.9)
Maximum aneurysm diameter (mm)	53.5 ± 8.1 (32–89)
Luminal volume (cm^3)	79.6 ± 54.0 (14.6–366)
Intraluminal thrombus volume (cm^3)	74.4 ± 50.6 (5.7–380)
T *vol* / A *vol* (%)	48.6 ± 17.3 (11.9–85)
Proximal neck length (mm)	36.2 ± 14.3 (9–86)

Location posterior[e]	128 (45.7)
Patent IMA	206 (73.6)
IMA diameter (mm)	2.33 ± 1.6 (0–6.3)
Number of patent LAs	5.19 ± 1.8 (0–9)

T *vol* / A *vol*, thrombus volume / aneurysm volume; IMA, inferior mesenteric artery; LA, lumbar artery.

[a]Data are presented as the mean ± standard deviation and range or number (%).

[b]Includes chronic obstructive pulmonary disease, asthma and interstitial pneumonia.

[c]Includes warfarin potassium and direct oral anticoagulants (DOACs).

[d]Includes patients who ever smoked.

[e]Defined as thrombus in the posterior aortic wall with ≥ 5 mm thickness.

Table II. Univariate analysis of variables regarding incidence of persistent type II endoleak

Variable[a]	***Persistent/new type II endoleak (+) (n = 131)***	***Persistent/new type II endoleak (-) (n = 149)***	***p value***
Age (years)	77.7 ± 5.6	77.1 ± 6.6	.463
Female sex	33 (25.2)	16 (10.7)	.003
Hypertension	93 (71.0)	104 (69.8)	.380
Dyslipidemia	55 (42.0)	67 (45.0)	.552
Lung disease[b]	18 (13.7)	22 (14.8)	.621
Cerebrovascular disease	14 (10.7)	28 (18.8)	.102
Coronary artery disease	42 (32.1)	54 (36.2)	.476
Dialysis	2 (1.5)	4 (2.7)	.512
Diabetes	12 (9.2)	17 (11.4)	.333
Antiplatelet	43 (32.8)	66 (44.3)	.085
Anticoagulant[c]	10 (7.6)	12 (8.1)	.636
Smoking history[d]	78 (59.5)	92 (61.7)	.002
Zenith	38 (29.0)	69 (46.3)	.003
Excluder	66 (50.4)	35 (23.5)	.000
Endurant	20 (15.3)	31 (20.8)	.231
Powerlink	1 (0.7)	9 (6.0)	.018
Talent	0	3 (2.0)	.103
Incraft	6 (4.6)	2 (1.3)	.105
Maximum aneurysm diameter (mm)	53.1 ± 7.1	54.0 ± 8.9	.374
Luminal volume (cm^3)	81.3 ± 50.1	78.1 ± 57.1	.328

Intraluminal thrombus volume (cm^3)	67.4 ± 42.3	80.4 ± 56.2	.032
T *vol* / A *vol* (%)	46.5 ± 17.3	50.9 ± 17.1	.004
Proximal neck length (mm)	36.3 ± 13.6	36.1 ± 15.0	.880
Location posterior[e]	52 (39.7)	76 (51.0)	.058
Patent IMA	105 (80.2)	101 (67.8)	.019
IMA diameter (mm)	2.67 ± 1.5	2.02 ± 1.6	.001
Number of patent LAs	5.51± 1.5	4.91 ± 1.9	.004
IIA embolization	42 (32.1)	48 (32.2)	.869

T *vol* / A *vol*, thrombus volume / aneurysm volume; IMA, inferior mesenteric artery; LA, lumbar artery.

[a]Dates are presented as the mean ± standard deviation and range or number (%).

[b]Includes chronic obstructive pulmonary disease, asthma and interstitial pneumonia.

[c]Includes warfarin potassium and direct oral anticoagulants (DOACs).

[d]Includes patients who ever smoked.

[e]Defined as thrombus in the posterior aortic wall with ≥ 5 mm thickness.

Table III. Univariate analysis of variables regarding the incidence of sac expansion with persistent type II endoleak

Variable[a]	***Sac expansion persistent/new type II endoleak (+) (n = 55)***	***Others (n = 225)***	***p value***
Age (years)	79.4 ± 5.2	76.8 ± 6.3	.001
Female sex	17 (30.9)	32 (14.2)	.001
Hypertension	35 (63.6)	162 (72.0)	.447
Dyslipidemia	21 (38.2)	101 (44.9)	.132
Lung disease[b]	6 (10.9)	34 (15.1)	.886
Cerebrovascular disease	5 (9.1)	37 (16.4)	.231
Coronary artery disease	13 (23.6)	83 (36.9)	.033
Dialysis	2 (3.6)	4 (1.8)	.051
Diabetes	5 (9.1)	24 (10.7)	.451
Antiplatelet	15 (27.2)	94 (41.8)	.053
Anticoagulant[c]	5 (9.1)	17 (7.6)	.958
Smoking history[d]	31 (56.4)	139 (61.8)	.040
Zenith	22 (40.0)	85 (37.8)	.761
Excluder	26 (47.3)	75 (33.3)	.054
Endurant	4 (7.3)	47(20.9)	.019
Powerlink	1 (1.9)	9 (4.0)	.434
Talent	0	3 (1.3)	.389
Incraft	2 (3.6)	6 (2.7)	.669
Maximum aneurysm diameter (mm)	52.6 ± 7.2	53.8 ± 8.3	.430

Luminal volume (cm^3)	84.6 ± 56.8	78.3 ± 53.2	.312
Intraluminal thrombus volume (cm^3)	66.9 ± 43.1	76.2 ± 52.1	.232
T *vol* / A *vol* (%)	44.4 ± 17.4	49.7 ± 17.1	.025
Proximal neck length (mm)	36.3 ± 14.1	36.1 ± 14.4	.962
Location posterior[e]	21 (38.2)	107 (47.6)	.191
Patent IMA	46 (83.6)	160 (71.1)	.028
IMA diameter (mm)	2.81 ± 1.53	2.21 ± 1.58	.013
Number of patent LAs	5.73 ± 1.40	5.06 ± 1.85	.029
IIA embolization	20 (36.4)	69 (30.7)	.771

T *vol* / A *vol*, thrombus volume / aneurysm volume; IMA, inferior mesenteric artery; LA, lumbar artery.

[a]Dates are presented as the mean ± standard deviation and range or number (%).

[b]Includes chronic obstructive pulmonary disease, asthma and interstitial pneumonia.

[c]Includes warfarin potassium and direct oral anticoagulants (DOACs).

[d]Includes patients who ever smoked.

[e]Defined as thrombus in the posterior aortic wall with ≥ 5 mm thickness.

Table IV. Multivariate analyses of predictors of the incidence of sac expansion with or without persistent type II endoleak

	Persistent/new type II endoleak			***Sac expansion with persistent/new type II endoleak***		
Predictors	*OR*	*95% CI*	*p value*	*OR*	*95% CI*	*p value*
Age (years)	-	-	-	1.09	1.041–1.159	.001
Sex	1.69	0.727-3.907	.224	1.98	0.975–4.047	.059
Zenith	1.40	0.693-2.810	.351	-	-	-
Excluder	0.32	0.156-0.656	.002	-	-	-
Endurant	-	-	-	1.62	0.576-4.573	.360
Powerlink	8.74	1.000-76.50	.050	-	-	-
Smoking history	1.69	0.868-3.295	.122	0.73	0.374–1.449	.375
Coronary artery disease	-	-	-	1.61	0.826–3.139	.162
T *vol* / A *vol* (%)	0.98	0.965-0.995	.011	0.98	0.968–0.999	.045
IMA diameter (mm)	1.35	1.127-1.627	.001	1.32	1.095-1.594	.004
Number of patent LAs	1.25	1.071-1.477	.005	1.07	0.913–1.271	.379

T vol / *A* vol, thrombus volume / aneurysm volume; IMA, inferior mesenteric artery; LA, lumbar artery; OR, odds ratio; CI, confidence interval.

Blanks in this table indicate that those variables have no significance in either univariate analysis, and thus, they were not included when performing the multivariate analyses.

Figure legends

Fig 1.

Flowchart of the study population and method. Two hundred eighty patients who underwent EVAR were enrolled. All patients were followed up for ≥ 6 months. Others include patients who have sac expansion without type II endoleak, type II endoleak without sac expansion and no sac expansion and type II endoleak. AAA, abdominal aortic aneurysm; EVAR, endovascular aneurysm repair; CT, computed tomography.

Fig 2.

Kaplan-Meier estimates of freedom from sac expansion (≥ 5 mm) according to the *T* vol / *A* vol; standard error never exceeded 10 %.

Fig 3. (a) Preoperative CT imaging of aneurysm with T vol / A vol ≥51%. (b) Postoperative CT imaging showing that no endoleak was detected.

Fig 4. (a) Preoperative CT image showing AAA with T vol / A vol < 51%. (b) CT image performed 6 months after EVAR showing incidence of type II endoleak. (c) CT image performed 5years after EVAR showing persistent type II endoleak and sac increase.

Supplemental Fig 1. Bland-Altman plot of difference in T vol / A vol 2 minus T vol / A vol 2 against the mean of the two measurements

Figure 1

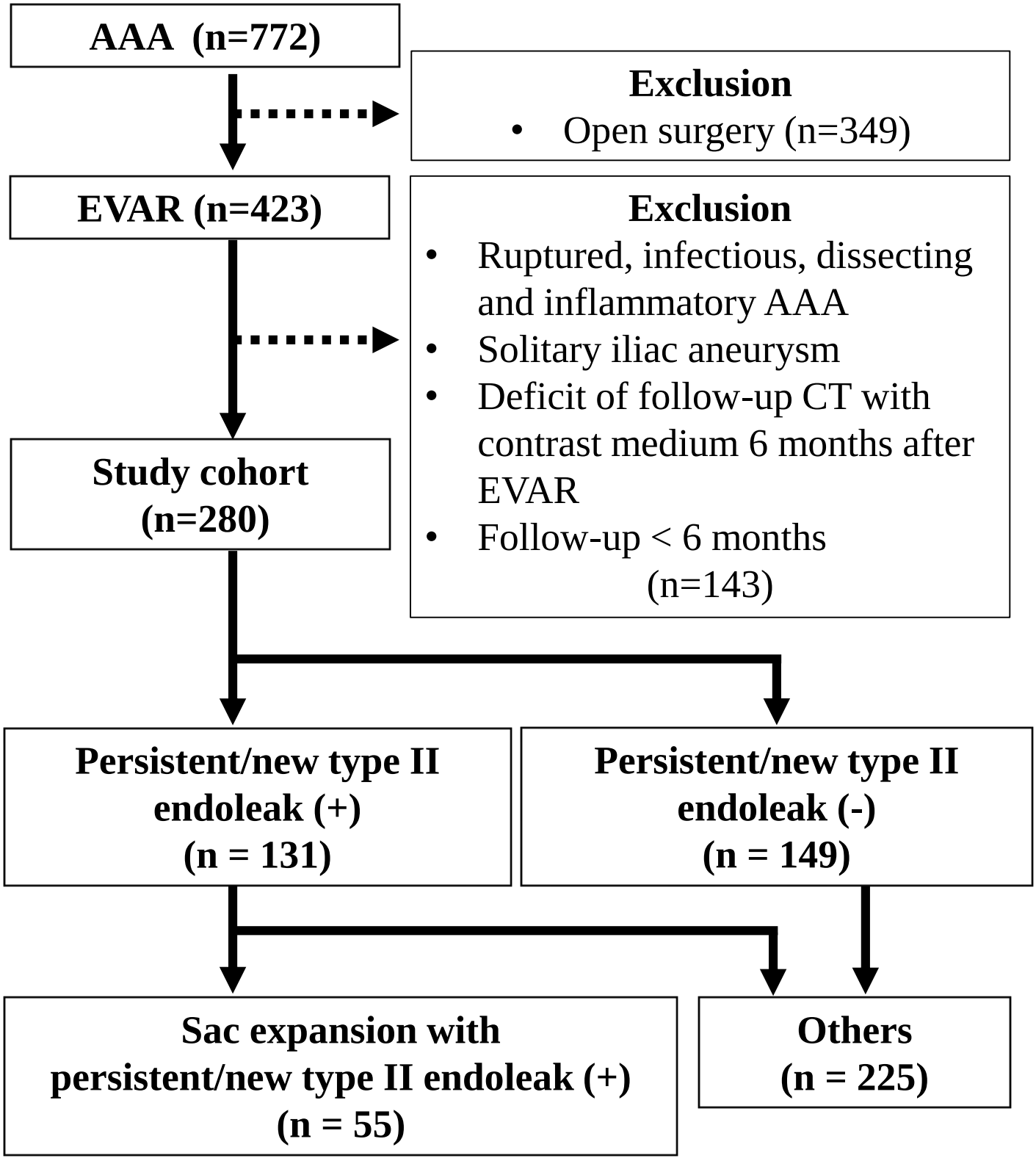
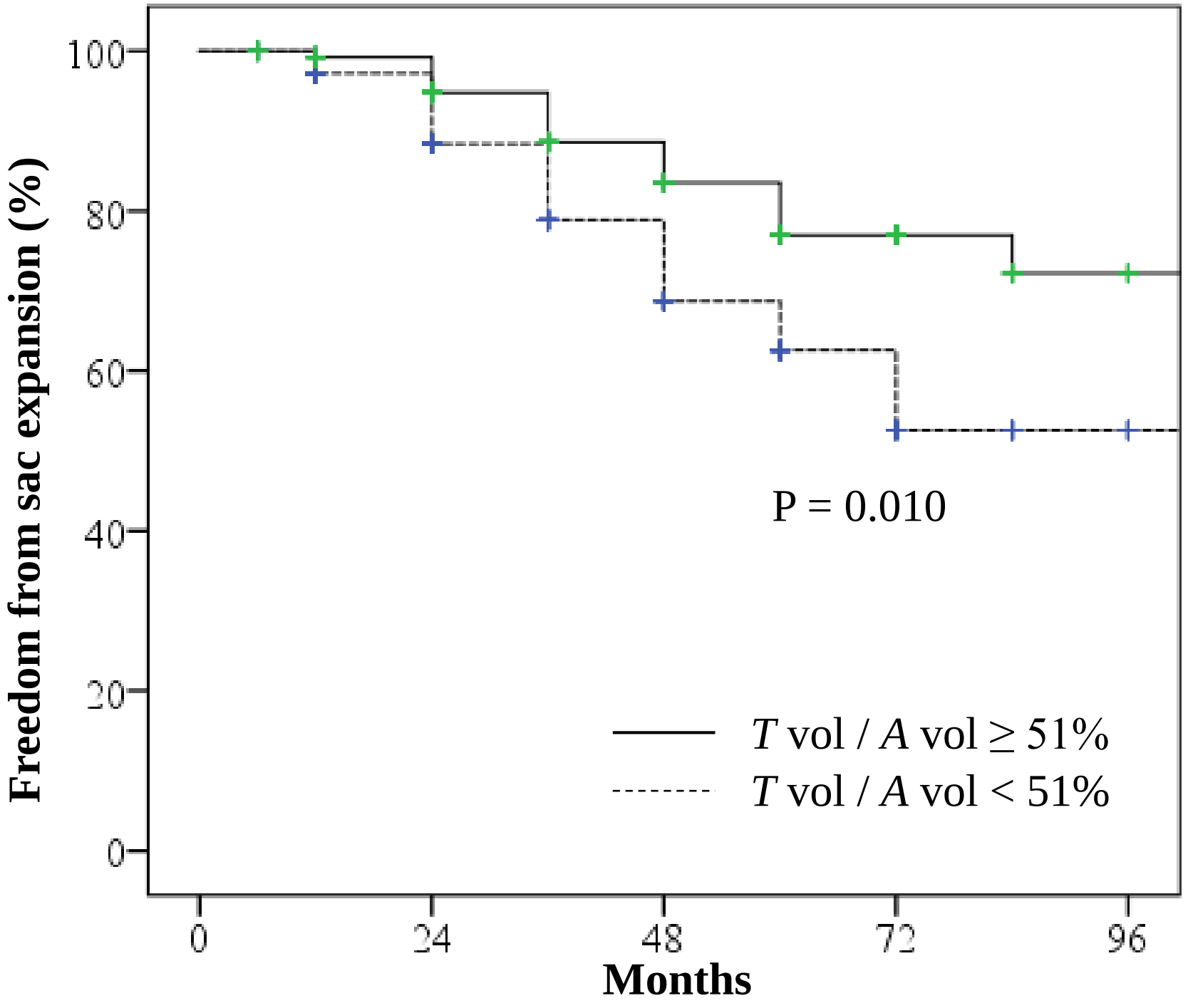

AAA (n=772)
Exclusion
• Open surgery (n=349)
EVAR (n=423)
Exclusion
• Ruptured, infectious, dissecting and inflammatory AAA
• Solitary iliac aneurysm
• Deficit of follow-up CT with contrast medium 6 months after EVAR
• Follow-up < 6 months
(n=143)
Study cohort (n=280)
Persistent/new type II endoleak (+) (n = 131)
Persistent/new type II endoleak (-) (n = 149)
Sac expansion with persistent/new type II endoleak (+) (n = 55)
Others (n = 225)

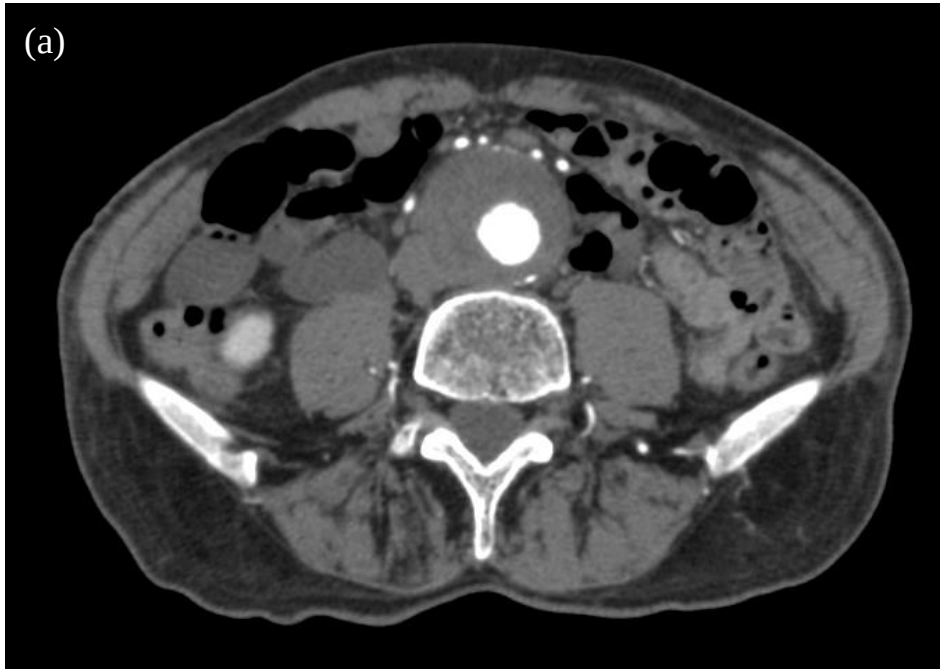
Figure 2



Number at risk

Months	0	24	48	72	96
≥ 51%	134	84	45	14	4
< 51%	146	92	51	16	4

Figure 3



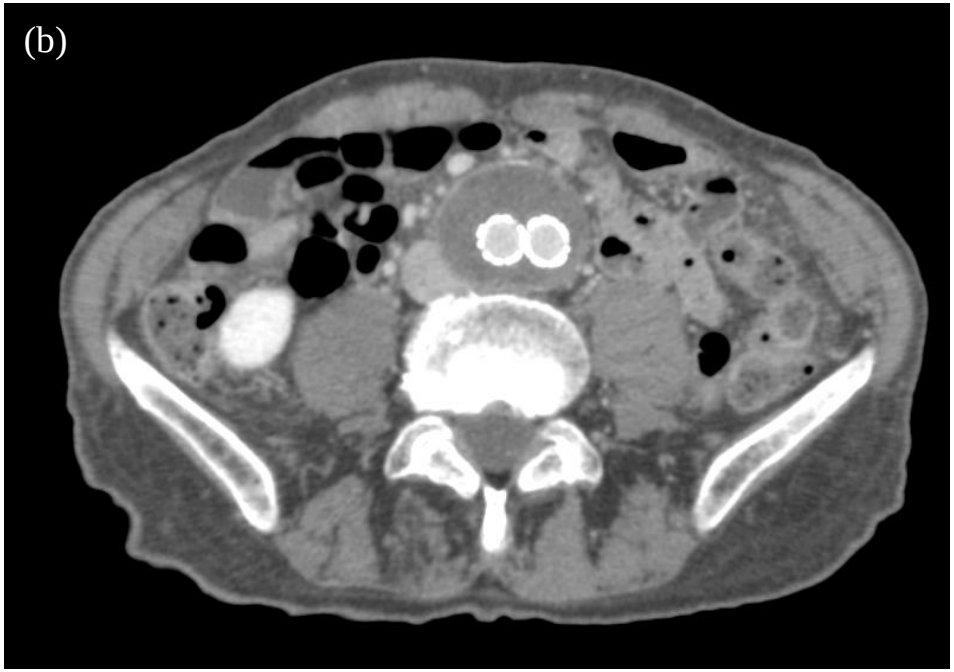
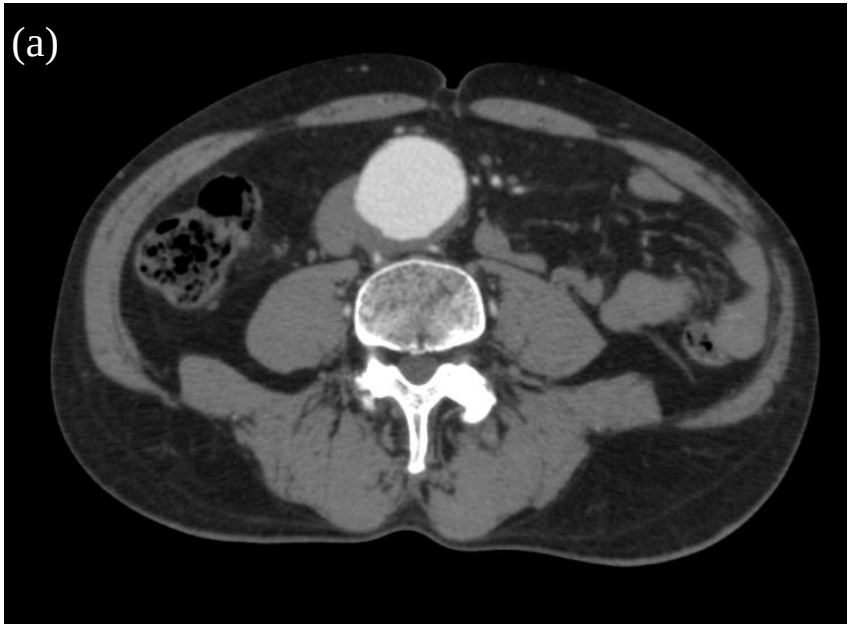
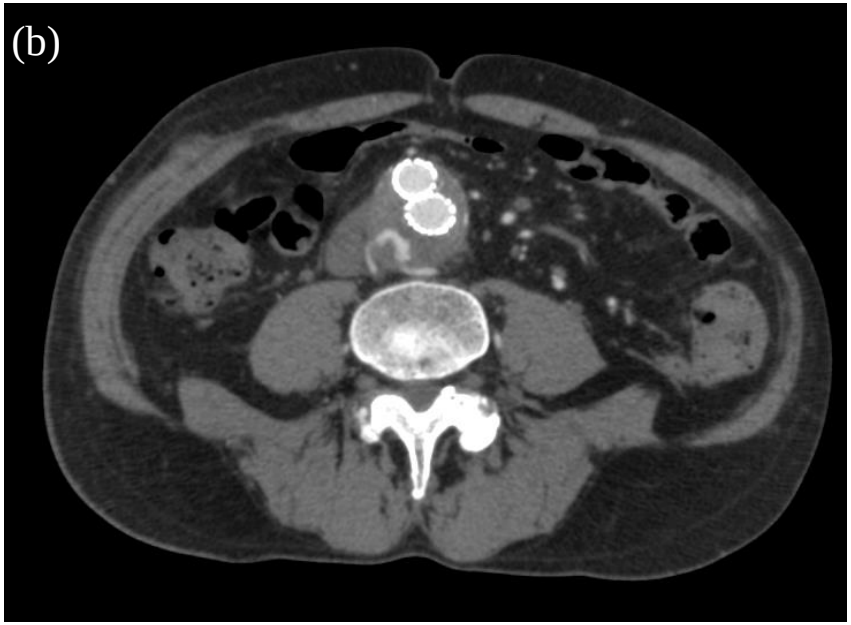
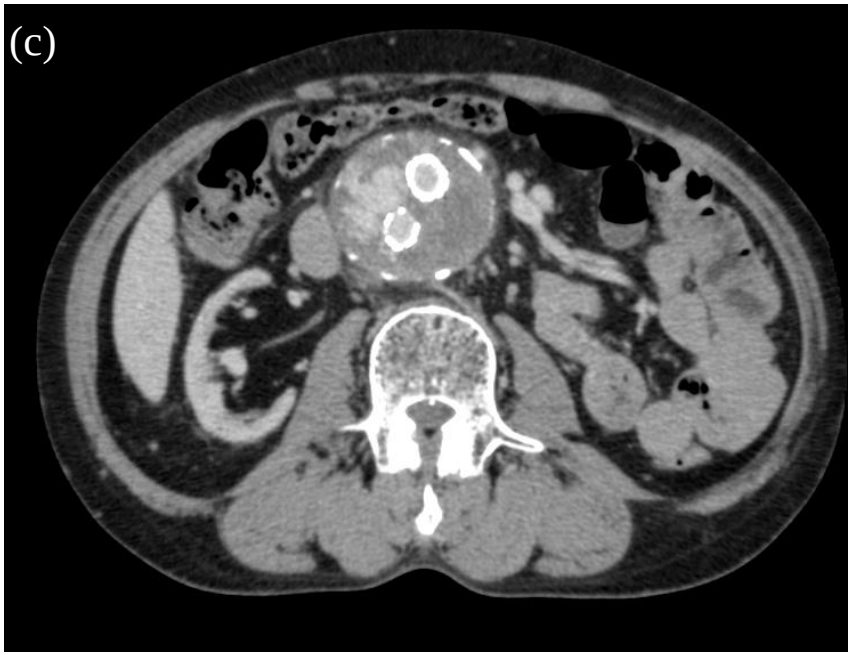


Figure 4







Supplement Figure