European Radiology (2019) 29:6591–6599
https://doi.org/10.1007/s00330-019-06306-5

COMPUTED TOMOGRAPHY

New predictors of aneurysm sac behavior after endovascular aortic aneurysm repair

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Received: 11 March 2019 / Revised: 7 May 2019 / Accepted: 5 June 2019 / Published online: 27 June 2019

Abstract

Objectives This study aimed to identify new predictors of sac behavior after endovascular aortic aneurysm repair (EVAR) and to investigate whether sac behavior is associated with long-term clinical outcomes.

Methods A total of 168 patients undergoing successful EVAR for abdominal aortic aneurysms with CTA follow-up of at least 1 year were included. Predictors of aneurysm sac behavior and its impact on long-term clinical outcomes were retrospectively analyzed.

Results According to sac behavior, eligible patients were stratified into the sac regression group ($n = 79$, 47.0%) and the sac non-regression group ($n = 89$, 53.0%). Patients in the regression group were younger ($p = 0.036$) and more likely to take sarpogrelate hydrochloride postoperatively ($p = 0.011$) than those in the non-regression group. The incidence of postimplantation syndrome (PIS) was significantly higher in the regression group ($p = 0.005$). On multivariate analysis, sac regression was more likely to occur in those with PIS (hazard ratio [HR], 1.68; 95% confidence interval [CI], 1.07–2.64; $p = 0.023$) and less likely to occur in those with transient type II endoleaks (HR, 0.43; 95% CI, 0.20–0.95; $p = 0.037$) and higher thrombus density within the sac on follow-up CTA (HR, 0.97; 95% CI, 0.95–0.99; $p = 0.013$). Non-regression of the sac was associated with significantly higher rates of re-intervention during the follow-up period ($p = 0.001$).

Conclusions In addition to type II endoleaks, PIS and thrombus density are new predictors of aneurysm sac behavior, and sac regression is significantly associated with lower rates of re-intervention.

Key Points

- *After endovascular aortic aneurysm repair (EVAR), patients with sac regression were younger and more likely to take sarpogrelate hydrochloride postoperatively than those with sac non-regression.*
- *The incidence of postimplantation syndrome (PIS) was significantly higher in patients with sac regression.*
- *In our analysis, PIS and thrombus density within the sac were newly identified predictors of aneurysm sac behavior after EVAR.*

Keywords Aortic aneurysm, abdominal · Endovascular procedures · Treatment outcomes

Abbreviations

AAA	Abdominal aortic aneurysm
CI	Confidence interval
CRP	C-reactive protein
DUS	Duplex ultrasound
EVAR	Endovascular aortic aneurysm repair
HR	Hazard ratio
HU	Hounsfield unit

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00330-019-06306-5) contains supplementary material, which is available to authorized users.

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PIS Postimplantation syndrome
WBC White blood cell

Introduction

Endovascular aortic aneurysm repair (EVAR) has become the standard treatment for abdominal aortic aneurysms (AAAs) [1]. The goal of EVAR is to prevent aneurysm-related deaths due to rupture and other complications by removing the aneurysm from the circulation [2]. Successful treatment is achieved when follow-up imaging demonstrates shrinking or arrested expansion of the AAA sac [3]. Although controversy exists about the effect of aneurysm sac behavior on long-term clinical outcomes, it is generally accepted that sac regression indicates that no further intervention is required and that the risk of rupture is minimal during long-term follow-up. It is also accepted that sac expansion is, by itself, a marker of potential AAA progression and has led to indefinite periods of EVAR surveillance to detect potential complications, such as endoleaks, aneurysm rupture, and graft migration or dislocation [4, 5]. To improve the results of EVAR and simplify post-EVAR surveillance, it would be worthwhile to identify any predictive factors of sac regression [5].

In this study, we aimed to identify new predictors of aneurysm sac behavior and determine the association between sac behavior and long-term clinical outcomes in patients who had undergone elective EVAR of an AAA.

Materials and methods

Study design and patient population

This was a single-center, retrospective, observational study using data extracted from a prospectively recruiting AAA registry. The study protocol was approved by our hospital's institutional review board (2018–0288), which waived the need for informed consent because of the study's retrospective design. All methods were performed in accordance with the relevant guidelines and regulations.

We included 352 consecutive patients who underwent EVAR of an AAA at our institution between January 2008 and December 2015. Patients were eligible for inclusion if they had undergone an initial successful EVAR for asymptomatic, uncomplicated infrarenal AAAs with CTA follow-up of at least 1 year. Patients treated for thoraco-AAAs ($n = 1$), symptomatic or ruptured aneurysms ($n = 9$), or isolated iliac aneurysms ($n = 5$) were excluded. To limit confounding factors, patients were included only if they met the criteria of treatment success, defined as the absence of the following: lost to follow-up ($n = 15$), imaging and clinical follow-up at another institution ($n = 64$), less than 1 year of CTA follow-up data ($n = 24$) or post-EVAR surveillance with duplex ultrasound (DUS) imaging ($n = 36$), and type I or III endoleaks on initial post-EVAR angiography or follow-up CTA ($n = 30$). Even if follow-up CTA within 1 month of EVAR was obtained, post-EVAR surveillance with DUS imaging was excluded in our study. This ensured that only similarly performed CTA data were analyzed, considering the possibility of a discrepancy in the measurements of the maximum diameter between CTA and DUS images [6]. Finally, 168 patients (47.7%) were included in the analysis (Supplementary Figure 1).

Index procedure and follow-up

EVAR was indicated when the maximum AAA diameter was at least 50 mm or when an increase of at least 10 mm in the maximum diameter was observed over a period of 1 year [7]. EVAR procedures were performed under general or regional anesthesia, complying with the instructions for use and following a standard vascular protocol. Our routine surveillance program included CTA and plain radiography of the abdomen within 1 month of EVAR, 6 and 12 months after EVAR, and annually thereafter, to monitor aneurysm sac behavior if the evaluations showed no abnormalities [8]. CTA was performed with a 120-kVp protocol, a reference mA of 200 with an automated tube current modulation with respect to the body habitus, and a reconstructed slice thickness of 0.6 mm with a 0.4-mm increment on a Siemens CT scanner (Siemens, SOMATOM Definition AS+). Initial and follow-up CTA images were obtained after intravenous administration of 100-mL nonionic iodinated contrast agent (iomeprol) at a rate of 3.5 mL/s followed by a 50-mL normal saline flush at a rate of 3.5 mL/s. Image acquisition was automatically initiated once a selected threshold (100 Hounsfield units [HU]) was reached at the end of the descending thoracic aorta level. At our institution, to minimize radiation exposure by reducing the number of phases per follow-up CTA (biphasic CTAs) [9], we did not perform non-contrast CT for post-EVAR surveillance for any study patients. Thrombus density was measured in HU during the arterial phase of CTA. All medication adjustments were made according to each patient's atherosclerosis risk factors. The interval between the last follow-up visit and EVAR was taken to represent the follow-up duration for each patient.

Definitions and data collection

All CTA images for each patient were evaluated by dedicated board-certified radiologists specializing in vascular imaging and intervention, who were unaware of the patients' general health status, according to the Society for Vascular Surgery reporting standards [7].

The maximum aneurysm sac diameter was measured in the axial imaging plane on the selected aortic section by positioning 2 calipers (external to external) [6]. Aneurysm sac regression was defined as a decrease of at least 5 mm in the maximum aneurysm sac diameter from before EVAR to any post-EVAR CTA evaluation, and sac expansion was defined as an increase of at least 5 mm in the maximum sac diameter [7]. Patients with a change of < 5 mm in either direction in maximum sac diameter were defined as having a stable sac [2]. For each patient, the change of maximal sac diameter was calculated on follow-up CTA via the aforementioned method.

Intraoperative endoleaks were considered present if any occurrence of endoleak was observed upon completion during an angiogram in the operating room. Per definition [10], endoleaks were subdivided into 2 categories: spontaneously resolving transient endoleaks and new or persistent endoleaks [8]. Transient endoleaks were defined as spontaneously resolving endoleaks at the last CTA without re-intervention, whereas persistent endoleaks were defined as persisting or newly developed endoleaks at the last CTA.

The definition of postimplantation syndrome (PIS) was adapted in accordance with that of the systemic inflammatory response syndrome, as previously described [8]: a continuous temperature > 38 °C lasting for > 1 day and a white blood cell (WBC) count > 12,000/mm^3 despite antibiotic therapy and negative culture results. The density of the thrombus within the sac was calculated as the mean of 3 absolute thrombus HU values at maximal sac diameter level and each of 3 or 4 cuts above and below this level in the follow-up CTA within 1 month of EVAR. The mean absolute thrombus HU values at each level were calculated as the mean of 3 ROIs that were chosen at the midpoint of the aneurysm sac and the stent graft (Fig. 1). A 5 × 5 pixel grid was placed centrally within ROIs to measure the HU values. ROIs were chosen at the point without contrast leakage in patients with type II endoleaks, to prevent the problem of pseudoenhancement and the inaccurate classification of thrombus HU values. Thrombus HU values were quantified as described by Puig et al [11].

Eligible patients were stratified into 2 groups according to aneurysm sac behavior as follows: sac regression (regression group) and sac expansion or stable sac (non-regression group). We also conducted further analysis by dividing the non-regression group into stable sac and sac expansion subgroups. When we compared the clinical variables for sac behavior

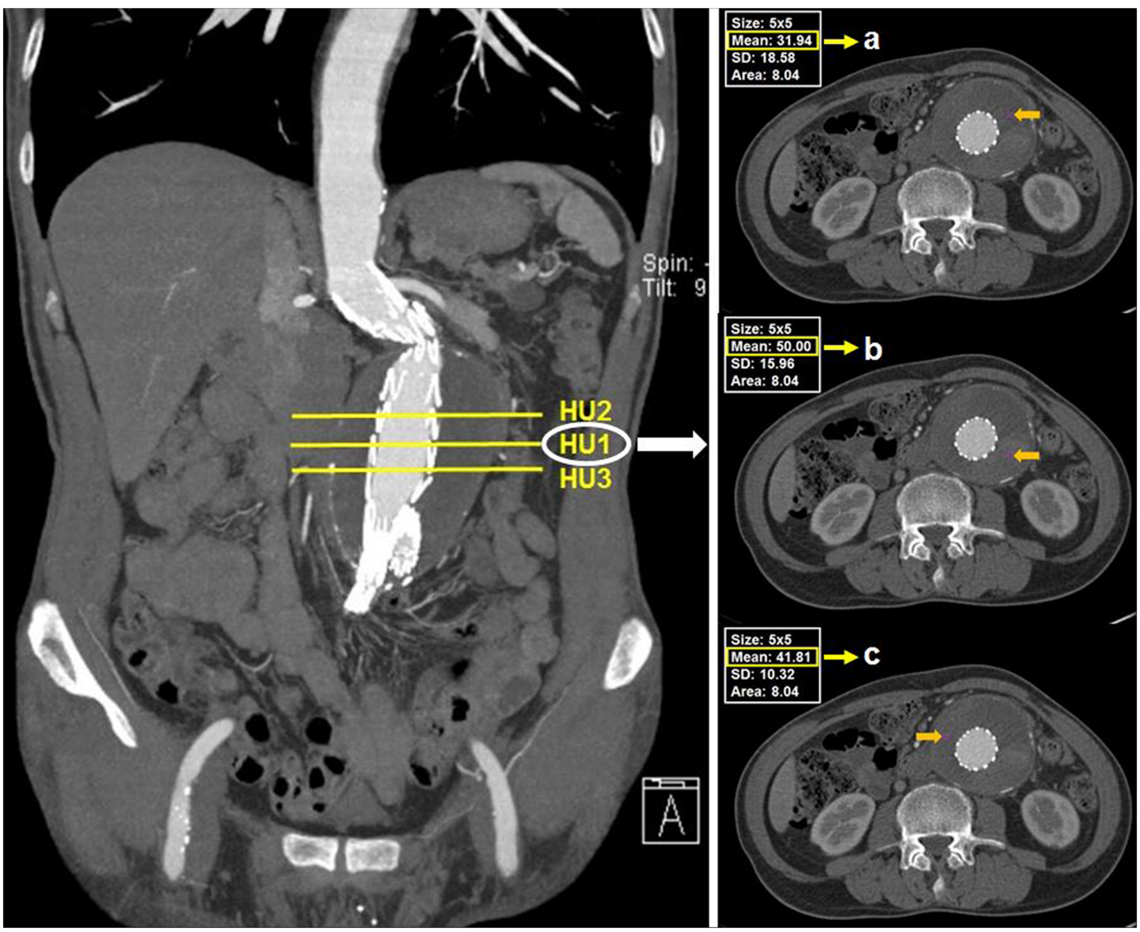

Fig. 1 Measurement of the mean absolute thrombus HU values. Thrombus Hounsfield unit (HU) values were obtained by calculating the mean of 3 absolute thrombus HU values at maximal diameter level (HU1) and each of 3 or 4 cuts above (HU2) and below (HU3) this level in follow-up CTA. The mean absolute thrombus HU values at each level were obtained by calculating the mean of 3 regions of interest (ROIs) that were chosen at the midpoint of the aneurysm sac and the stent graft. HU1 = (a + b + c) / 3; HU2 = (a' + b' + c') / 3; HU3 = (a" + b" + c") / 3; thrombus HU value = (HU1 + HU2 + HU3) / 3. SD, standard deviation

using the one-way ANOVA based on the 3 subgroups, there was a significant difference in thrombus HU values between the subgroups ($p = 0.003$) (Supplementary Table 1). Following this, post hoc analysis was performed, and there was a significant difference in HU values between sac regression and stable sac ($p = 0.001$) and between sac regression and sac expansion ($p = 0.034$); however, no significant difference was noted between stable sac and sac expansion ($p = 0.876$). In this analysis, we focused on the relationship between thrombus HU values and aneurysm sac behavior, and therefore, we used 2 groups: the sac regression and non-regression groups.

Body temperature, WBC and platelet counts, and serum C-reactive protein (CRP) concentrations were serially assessed 1 day before EVAR and during hospitalization, depending on the clinical status of the patient [8]. Clinical outcomes were defined as all-cause mortality, aneurysm-related mortality, re-intervention, late conversion to open surgery, and late rupture during the follow-up period.

Demographics, risk factors of interest, and other data—including clinical presentation, morphological characteristics of the aneurysm, and clinical outcomes—were recorded for each patient. All data were prospectively entered into an Excel database (Microsoft Corp.) for all consecutive patients and retrospectively analyzed.

Statistical analysis

The demographic and clinical characteristics of the patients are presented as counts and percentages for categorical variables and as means ± standard deviations for continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test, whereas continuous variables were compared using Student's t test. A Cox proportional hazards model was used to identify possible predictors of aneurysm sac regression. Because the dates of sac regression on follow-up CTA were not the same for all patients, we used a Cox proportional hazards model rather than logistical regression at a date point. Variables associated with sac regression that showed significance with a cutoff p value of 0.1 in univariate analysis were introduced into a multivariate analysis. Hazard ratios (HRs) and their 95% confidence intervals (CIs) are reported. A p value < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS version 21.0 (IBM Corp).

Results

A total of 168 consecutive patients who had undergone successful elective EVAR for AAAs, with at least 1 year of CTA follow-up, were included in this analysis. The mean patient age was 71 years (range, 50–91 years), and 91.7% of the patients were men. During the mean follow-up period of 44 months (range, 12–104 months), according to the aneurysm sac behavior evaluated using post-EVAR CTA images, eligible patients were stratified into the sac regression group ($n = 79$, 47.0%) and the sac non-regression group ($n = 89$, 53.0%). The regression rate in the present study was 47.0%. Within the sac non-regression group, there were 22 patients with sac expansion and 67 patients with a stable sac. The baseline characteristics of the patients, grouped according to aneurysm sac behavior, are given in Table 1. There were no significant differences between the sac regression and sac non-regression groups in terms of demographics, atherosclerotic risk factors, and anatomical parameters of the AAA, except that patients with sac regression were younger than those with sac non-regression (69.6 ± 6.6 vs. 71.8 ± 6.9 years, $p = 0.036$). Those with sac non-regression were found to be less likely to smoke (73.4% vs. 59.6%, $p = 0.058$) and to more frequently have a prior coronary artery disease (24.1% vs. 37.1%, $p = 0.068$). The following stent grafts were used in the sac regression group: Zenith (Cook Medical Inc.; $n = 45$, 57.0%), Endurant (Medtronic; $n = 15$, 19.0%), Excluder (W.L. Gore and Associates Inc.; $n = 13$, 16.5%), and others ($n = 6$, 7.6%). Endurant was the most commonly used stent graft ($n = 39$, 43.8%) for EVAR in the sac non-regression group, followed by Zenith ($n = 29$, 32.6%), Excluder ($n = 16$, 18.0%), and others ($n = 5$, 5.6%). Although patients in the sac regression group were more likely to receive Zenith stent grafts during EVAR (57.0% vs. 32.6%, $p = 0.003$), there was no significant difference in graft composition (woven polyester [$n = 66$, 83.5% vs. $n = 73$, 82.0%] vs. expanded polytetrafluoroethylene [$n = 13$, 16.5% vs. $n = 16$, 18.0%]) between the 2 groups ($p = 0.794$). The clinical parameters are presented in Table 2. Patients with sac regression were more likely to have the highest mean WBC count ($p = 0.010$) and CRP concentration ($p = 0.019$) after EVAR and during hospitalization, although there were no significant differences in the baseline WBC count and CRP concentration between the 2 groups. The incidence of PIS (46.8% vs. 25.8%, $p = 0.005$) and the proportion of patients taking sarpogrelate hydrochloride (HCl) (Anplag®, Yuhan Corporation) postoperatively (38.0% vs. 20.2%, $p = 0.011$) were significantly higher in the sac regression group than in the sac non-regression group.

Based on the follow-up CTA evaluations, the incidences of transient (8.9% vs. 27.0%, $p = 0.003$) and persistent (13.9% vs. 41.6%, $p < 0.001$) type II endoleaks were significantly lower in the sac regression group than in the sac non-regression group (Table 2). The density of the thrombus within the sac, measured using mean HU values, was significantly lower in the sac regression group than in the sac non-regression group (43.1 ± 9.6 vs. 48.9 ± 11.4, $p = 0.001$). During the follow-up period, all-cause mortality showed no significant difference between the 2 groups (19.0% vs. 20.2%, $p = 0.840$), and there was no aneurysm-related mortality. The rates of re-intervention were significantly lower in the sac regression group than in the sac non-regression group (0%

Table 1 Baseline characteristics of the study population stratified by aneurysm sac behavior

	Total	Regression group	Non-regression group	*p* value
No. of patients	168	79 (47.0)	89 (53.0)	
Mean age (years)	70.8 ± 6.8	69.6 ± 6.6	71.8 ± 6.9	0.036
Male sex	154 (91.7)	74 (93.7)	80 (89.9)	0.376
BMI (kg/m^2)	24.4 ± 3.5	24.0 ± 3.3	24.8 ± 3.6	0.147
Risk factor				
Smoking	111 (66.1)	58 (73.4)	53 (59.6)	0.058
Hypertension	117 (69.6)	56 (70.9)	61 (68.5)	0.741
Diabetes mellitus	26 (15.5)	13 (16.5)	13 (14.6)	0.741
Dyslipidemia	94 (56.0)	43 (54.4)	51 (57.3)	0.708
Comorbidities				
CKD	2 (1.2)	2 (2.5)	0 (0.0)	0.220
CAD	52 (31.0)	19 (24.1)	33 (37.1)	0.068
CVA	14 (8.3)	8 (10.1)	6 (6.7)	0.428
Malignancy	36 (21.4)	18 (22.8)	18 (20.2)	0.686
Anatomic parameter (mm)				
Neck diameter	23.2 ± 3.2	23.0 ± 3.2	23.3 ± 3.2	0.572
Neck length	35.3 ± 13.4	33.9 ± 11.9	36.6 ± 14.5	0.203
Maximal diameter	56.1 ± 9.6	55.7 ± 8.4	56.5 ± 10.6	0.615
Sac length	80.4 ± 25.4	79.5 ± 28.0	81.2 ± 22.9	0.664
Graft composition				0.794
Woven polyester	139 (82.7)	66 (83.5)	73 (82.0)	
Expanded PTFE	29 (17.3)	13 (16.5)	16 (18.0)	

Continuous data are presented as means ± standard deviations; categorical data are given as number (%)

BMI, body mass index; *CAD*, coronary artery disease; *CKD*, chronic kidney disease; *CVA*, cerebrovascular accident; *PTFE*, polytetrafluoroethylene

vs. 13.5%, $p = 0.001$); among the patients in the sac non-regression group, there were 4 re-interventions (6.0%) in the stable sac subgroup and 8 (36.4%) in the sac expansion subgroup. In our analysis, there was 1 late conversion to open surgery in the sac non-regression group but no late rupture in either group.

To investigate the independent predictors of aneurysm sac regression, clinical variables associated with sac regression were analyzed using univariate and multivariate Cox proportional hazards regression analyses (Table 3). On univariate analysis, transient (HR, 0.37; 95% CI, 0.17–0.80; $p = 0.012$) and persistent (HR, 0.29; 95% CI, 0.15–0.56; $p < 0.001$) type II endoleaks and higher-density thrombus within the sac (higher HU values) (HR, 0.96; 95% CI, 0.94–0.98; $p = 0.001$) were independent negative predictors of aneurysm sac regression, whereas the use of sarpogrelate HCl (HR, 1.89; 95% CI, 1.20–2.98; $p = 0.006$) and PIS (HR, 1.96; 95% CI, 1.26–3.05; $p = 0.003$) was independent positive predictors of aneurysm sac regression. After adjustment for confounding variables, multivariate analysis indicated that sac regression was more likely to occur in patients with PIS (HR, 1.68; 95% CI, 1.07–2.64; $p = 0.023$) and less likely to occur in those with transient type II endoleaks (HR, 0.43; 95% CI, 0.20–0.95; $p = 0.037$) and higher-density thrombi within the sac (higher HU values) (HR, 0.97; 95% CI, 0.95–0.99; $p = 0.013$). A higher thrombus density within the sac is a significant negative predictor of sac regression for post-EVAR surveillance. The use of sarpogrelate HCl postoperatively was associated with an increased frequency of sac regression, approaching statistical significance (HR, 1.60; 95% CI, 1.00–2.56; $p = 0.052$).

Discussion

Although type II endoleak is a well-known predictor of aneurysm sac behavior, the main findings of this study were that PIS is a significant positive predictor of sac regression whereas a higher thrombus density within the sac is a significant negative predictor of sac regression. The use of sarpogrelate HCl is associated with sac regression with clinical significance. Moreover, our analysis showed that sac non-regression is associated with significantly higher rates of re-intervention, and no patients with sac regression experienced re-intervention during the follow-up period.

PIS is considered a kind of acute systemic inflammatory response after EVAR [8]. Several studies have demonstrated a substantial incidence of PIS after EVAR; however, PIS has not

Table 2 Clinical characteristics of the study population stratified by aneurysm sac behavior

	Total	Regression group	Non-regression group	*p* value
No. of patients	168	79 (47.0)	89 (53.0)	
Time interval (month)[a]	12.5 ± 22.4	13.8 ± 23.5	17.0 ± 21.4	0.359
Laboratory data				
Baseline platelet (× 10^3/uL)	199.9 ± 55.6	195.7 ± 46.3	203.7 ± 62.8	0.348
Baseline WBC (× 10^3/uL)	6.7 ± 1.7	6.9 ± 1.8	6.5 ± 1.6	0.136
Baseline creatinine (mg/dL)	1.0 ± 0.9	1.1 ± 1.3	0.9 ± 0.2	0.086
Highest WBC (× 10^3/uL)[b]	11.8 ± 3.8	12.6 ± 4.2	11.1 ± 3.2	0.010
Highest CRP (mg/dL)[b]	11.7 ± 5.6	12.9 ± 5.4	10.7 ± 5.5	0.019
Medication at follow-up				
Statin	127 (75.6)	62 (78.5)	65 (73.0)	0.412
Single antiplatelet	58 (34.5)	28 (35.4)	30 (33.7)	0.813
Dual antiplatelet	52 (31.0)	26 (32.9)	26 (29.2)	0.605
Sarpogrelate hydrochloride	48 (28.6)	30 (38.0)	18 (20.2)	0.011
Anticoagulation	12 (7.1)	4 (5.1)	8 (9.0)	0.324
Postimplantation syndrome	60 (35.7)	37 (46.8)	23 (25.8)	0.005
Follow-up CTA				
Transient type II endoleak	31 (18.5)	7 (8.9)	24 (27.0)	0.003
Persistent type II endoleak	48 (28.6)	11 (13.9)	37 (41.6)	< 0.001
Thrombus HU values[c]	46.2 ± 10.9	43.1 ± 9.6	48.9 ± 11.4	0.001
Re-intervention	12 (7.1)	0 (0)	12 (13.5)	0.001
All-cause mortality	33 (19.6)	15 (19.0)	18 (20.2)	0.840

Continuous data are presented as means ± standard deviations; categorical data are given as number (%)

CRP, C-reactive protein; *HU*, Hounsfield unit; *WBC*, white blood cell

[a] Time interval between the diagnosis of AAA and EVAR

[b] The highest WBC count/CRP concentration after EVAR and during hospitalization

[c] Thrombus HU values within the sac obtained in follow-up CTA obtained within 1 month of EVAR

been associated with long-term clinical outcomes [8, 12]. Recently, PIS has been proposed to have a protective effect against the development of type II endoleaks after EVAR; an acute systemic inflammatory response, namely PIS, could result in a high rate of obliteration of relatively low-pressure small arteries, followed by a reduced risk of the development of type II endoleaks and rates of re-intervention during follow-up [8]. In our study, we found that PIS was a significant positive predictor of sac regression during follow-up. However, some authors have previously suggested that there is a statistical time-related association between CRP level increase and AAA sac expansion after EVAR in the absence of confirmed endoleaks, and chronic systemic inflammatory response was, therefore, a potential critical pathogenic pathway determining

Table 3 Factors associated with aneurysm sac regression after EVAR

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age	0.97 (0.94–1.01)	0.095	0.98 (0.95–1.01)	0.197
Smoking	1.46 (0.89–2.41)	0.136	NA	NA
Sarpogrelate hydrochloride	1.89 (1.20–2.98)	0.006	1.60 (1.00–2.56)	0.052
Statin	1.35 (0.77–2.37)	0.296	NA	NA
CKD	1.12 (0.96–1.31)	0.146	NA	NA
Transient type II endoleak	0.37 (0.17–0.80)	0.012	0.43 (0.20–0.95)	0.037
Persistent type II endoleak	0.29 (0.15–0.56)	< 0.001	NA	NA
Postimplantation syndrome	1.96 (1.26–3.05)	0.003	1.68 (1.07–2.64)	0.023
Thrombus HU values	0.96 (0.94–0.98)	0.001	0.97 (0.95–0.99)	0.013

CI, confidence interval; *CKD*, chronic kidney disease; *HR*, hazard ratio; *HU*, Hounsfield unit; *NA*, not applicable aneurysm progression [13, 14]. In our analysis, the highest WBC counts and CRP concentrations after EVAR and during hospitalization (but not the baseline values and the relative rate of increase of CRP concentration) were significantly higher in the sac regression group. Although a chronic systemic inflammatory response might be involved in the formation of degenerative aneurysms and sac expansion after EVAR [15], an acute systemic inflammatory response, namely PIS, could be a new predictor of aneurysm sac regression. The pathophysiologic mechanism underlying PIS, as an acute inflammatory response, is not well understood in relation to AAA sac behavior. It is suggested that the increased ^{18}FDG uptake on FDG-PET CT after EVAR is associated with circulating WBC activation, endothelial cell damage, and cytokine release from the thrombus during manipulation and may be considered as a landmark of sac behavior after EVAR [16]. In our analysis, we did not perform FDG-PET CT in our study population, and future studies are required for a better understanding of the effect of acute and chronic inflammatory response on aneurysm sac behavior after EVAR.

Several studies have demonstrated the prognostic value of the anatomical characteristics visualized on CTA for aneurysm sac regression after EVAR [17, 18]; however, little is known about the properties of the thrombus within the sac, which determine the success of sac regression in these patients. CTA detects thrombi in large arteries and provides information about thrombus composition based on HU values [19]. Based on other studies of acute ischemic stroke concerning thrombus density [11, 20], we hypothesized that low clot density (lower HU) within the sac on post-EVAR CTA images could indicate thrombi that are more resistant to spontaneous thrombolysis and a higher chance of successful sac regression after EVAR. In our analysis, we did not find an association between sac regression and any other anatomical characteristics; however, thrombus density, measured using HU values, was strongly predictive of successful sac regression after EVAR. However, we could not prove the exact mechanism of aneurysm sac behavior after EVAR in relation to thrombus density within the sac in the current human study. Furthermore, the factors contributing to the thrombus density remain unclear, even among patients without identifiable endoleaks. One possible explanation is that patients with higher thrombus density have increased graft porosity with endotension; however, we were unable to account for this issue in this analysis. There may also be patients with endoleaks not detected on follow-up CTA who had higher thrombus density and lower probability of sac regression, although the number of these patients may be extremely small.

Conflicting and limited data exist about the role of medication in aneurysm sac behavior after EVAR [2]. Although statin therapy did not affect AAA sac regression in our analysis, we found that the use of sarpogrelate HCl promoted sac regression with clinical significance. Sarpogrelate HCl, a 5-hydroxytryptamine$_{2A}$-selective inhibitor, has been used clinically as an antiplatelet drug for preventing thrombosis in patients with atherosclerotic diseases [21]. A recent study suggested that this drug improves endothelial function and vascular remodeling [21, 22]. Considering that matrix metalloproteinases have been shown to play a major role in progressive extracellular matrix degradation in the development of AAAs [23], and sarpogrelate HCl could stabilize vulnerable plaques by reducing the expression of enzymes that degrade the arterial extracellular matrix in animal models [21], sarpogrelate HCl might be helpful in preventing AAA progression. However, the detailed mechanism by which this may occur, and whether it has antiatherosclerotic action or not, is unknown [22]. Furthermore, in our analysis, the proportion of patients taking sarpogrelate HCl was relatively small (28.6%), and the effect on sac regression did not reach statistical significance; therefore, future multicenter prospective trials with larger cohorts are warranted for a better understanding of the effect of sarpogrelate HCl on aneurysm sac behavior after EVAR.

This study has several limitations. First, this was a retrospective analysis of a prospectively maintained database and thus is subject to selection and information biases; hence, the number of excluded patients was considerable. Furthermore, although there are several definitions and approaches related to measuring maximal AAA diameter [6], in this study, we used the axial imaging planes of the initial and serial follow-up CTAs to measure the maximal diameter and sac behavior. There may be angle issues that would confound or at least bias the measurements. Second, our current findings were obtained at a single center, resulting in a small sample size, which limits the overall generalizability of our results, and therefore, we could not provide the precise high or low HU values predicting sac behavior. Finally, although non-contrast CT may better characterize intra-luminal thrombi than enhanced CT [24–27], which was used in our study, we could not obtain post-EVAR, non-contrast CT images because of the issue of radiation exposure. CTA is the current standard method for monitoring post-EVAR patients due to its high reproducibility, high diagnostic accuracy, and wide availability. Post-EVAR patients require lifelong imaging surveillance to detect potential complications, such as endoleaks, aneurysm rupture, and graft migration or dislocation [9, 28, 29]. However, serial CTA monitoring exposes patients to cumulative doses of radiation. Concerns regarding radiation dose have led some investigators to consider the possibility, in the follow-up protocols, of reducing CT radiation exposure by using low-dose protocols [30–32], including other imaging modalities, such as magnetic resonance imaging or DUS, or eliminating portions of multiphasic CTA. In this study, we did not perform non-contrast CT for post-EVAR surveillance in a substantial number of patients to reduce the number of phases per follow-up CTA. Furthermore, the thrombus HU values at each level were calculated as the mean of 3 ROIs that were manually chosen at the midpoint of the aneurysm sac and the stent graft, and manual ROI placement may be subject to operator bias.

In addition to previously identified predictors of sac regression, we found PIS and thrombus density on follow-up CTA to be new predictors of aneurysm sac behavior after EVAR. In our analysis, PIS and lower thrombus density within the sac were significant positive predictors of successful sac regression. Considering that AAA sac behavior during follow-up imaging can predict treatment success after EVAR, our results might prove to be helpful in selecting EVAR patients who should be more rigorously followed.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this study is Yong-Pil Cho.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors (Min-Ju Kim) has significant statistical expertise.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained (2018–0288).

Methodology
- retrospective
- observational
- performed at one institution

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