» **Original Article** «

Influencing Factors for Abdominal Aortic Aneurysm Sac Shrinkage and Enlargement after EVAR: Clinical Reviews before Introduction of Preoperative Coil Embolization

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Background: We previously reported effectiveness of coil embolization (CE) to aortic branched vessels before endovascular aortic repair (EVAR) for abdominal aortic aneurysm (AAA) because of significant shrinkage of aneurysmal sac. In this study, we investigated EVAR cases to clarify influential factors of aneurysmal shrinkage and enlargement.

Methods: 148 consecutive cases before the introduction of CE were retrospectively reviewed based on the presence of PT2EL (persistent type 2 endoleak) and change in sac diameter after EVAR by multivariate analysis.

Results: (A) PT2EL risk factors were patent inferior mesenteric artery (IMA) and thinner mural thrombus inside aneurysmal sac. (B) Sac enlargement risk factors were antiplatelet intake, PT2EL, and female gender. (C) Sac shrinkage predictive factors were the absences of thoracic aortic aneurysm, antiplatelet intake, PT2EL, and coronary artery disease.

Conclusion: CE to IMA was considered to be effective because patent IMA and antiplatelet intake were significant risk factors for sac enlargement. So, more meticulous therapeutic strategy, including treatment priority (AAA first or CAD first) and choice of treatment (EVAR vs. AAA) based on anatomical features of AAA was required to improve late outcomes.

Keywords: EVAR, endoleak, sac enlargement and shrinkage, coil embolization

Introduction

Endovascular aortic repair (EVAR) is an established procedure for the treatment of abdominal aortic aneurysm (AAA), and has significantly altered the therapeutic strategy for AAA because of less invasiveness, low perioperative morbidity and mortality, and shorter hospital stay.^{1–3)} Although EVAR offers immediate

advantages over open surgical repair, close lifelong surveillance is required due to specific possible complications such as endoleaks, graft migration, and aneurysmal sac enlargement.⁴⁾ Of these complications, persistent type 2 endoleaks (PT2, present >6 months after EVAR) have been associated with an increased incidence of adverse outcomes, including aneurysmal sac growth, repeated endovascular intervention rate, late open conversion, and rupture.⁵⁾ Also, Jouhannet, et al. demonstrated endovascular reinterventions for PT2 associated with an enlargement of the aneurysmal sac after EVAR had resulted in little effectiveness on the stabilization of the diameter of the AAA.⁶⁾ So, focusing on the clinical significance of persistent type 2 endoleak, as of the beginning of June, 2011, we introduced preoperative coil embolization to aortic branched vessels, including the inferior mesenteric

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artery (IMA) and lumbar arteries (LAs) prior to EVAR to reduce the rate of PT2EL. This strategy was reported to be effective because approximately 50% of cases in this series showed significant shrinkage of the aneurysmal sac at 6 months after EVAR.⁷⁾ In this study, we retrospectively reviewed the influencing factors of aneurysmal sac shrinkage and enlargement after EVAR for consecutive EVAR cases before the introduction of preoperative coil embolization and evaluated whether or not coil embolization to aortic branched vessels can be effective therapeutic strategy to improve clinical outcomes of EVAR.

Methods

Data collection

From the beginning of May 2006 to the end of December 2013, 340 consecutive patients underwent elective EVAR for infrarenal AAA at our institute. Except for 3 cases complicated with type 1 or 3 endoleaks, the 148 patients who underwent EVAR prior to June 2011 before the introduction of preoperative coil embolization were reviewed in this study. All preoperative and postoperative computed tomography (CT) scans were reviewed by the attending vascular surgeons and the attending radiologists. Patients underwent preoperative CT imaging with 1.0-mm cuts. Preoperative anatomic variables included the patency of the IMA, the number of patent LAs, maximum aneurysm outer diameter (MAOD), maximum aneurysm luminal diameter (MALD), ΔD calculated as $MAOD - MALD$, and % mural thrombus simply calculated as $\Delta D / MAOD \times 100$. Preoperative patient backgrounds included age, gender, oral antiplatelet intake, oral Coumadin intake, and chronic obstructive pulmonary disease (COPD). All patients in this study received a follow-up CT scans with intravenous contrast at the time of before discharge and at the interval of every 6 months after EVAR. The presence of PT2EL was determined by the attending radiologists and the attending vascular surgeons. The patients were initially divided into two groups based on the presence of PT2EL; Group A cases with PT2EL (+) and Group B those with PT2EL (-). The risk factors of PT2EL were then analyzed between both groups. Secondly, they were divided into three sub-groups based on the prognosis of the aneurysmal sac; Group E cases with aneurysmal sac enlargement, Group S those with aneurysmal sac shrinkage, and Group N

Fig. 1 Persistent type 2 endoleak (PT2EL). Group A: Endovascular aortic repair (EVAR) cases with the presence of PT2EL. Group B: EVAR cases with the absence of PT2EL.

those with no changes in aneurysmal sac diameters. Thereafter the risk factors for sac enlargement and the influencing factors for sac shrinkage were retrospectively reviewed.

Statistical analysis

Continuous data was presented as mean $\pm$ standard deviation and analyzed using 2-tailed t-tests or compared with a Mann-Whitney U-test for independent data as appropriate. Categorical variables are given as a count and percentage of patients and compared using χ^2 or Fisher's exact test. Risk factors for sac enlargement and influencing factors for sac shrinkage were assessed with multivariable Cox proportional hazards model. Univariate analysis was also performed on all variables to detect potential risk factors for PT2EL and sac enlargement and influencing factors for sac shrinkage. The univariate predictors with a $P < 0.1$ were selected by the stepwise method and entered into the multivariate analysis. A $P < 0.05$ was statistically considered significant. All data were analyzed using the Statistical Analysis Systems software JMP 9.0 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Patient demographics

In this study, as shown in **Fig. 1**, there were 36 (24.3%) cases in Group A and 112 (75.7%) in Group B, respectively. There were significant differences in preoperative anatomic variables, including the IMA patency, MALD, and % mural thrombus between both groups (**Table 1**). Also, the number of cases was 45 (30.4%) in Group S, 21 (14.2%) in Group E, and 82 (55.4%) in Group N (**Fig. 2**).

Table 1 Comparison of preoperative data between with and without endoleak

	Group A : PT2EL (+) (n = 36)	Group B : PT2EL (-) (n = 112)	P value
Age	79.3 ± 6.8	76.9 ± 8.5	0.1258
Female	7 (19.4%)	16 (14.3%)	0.4398
Antiplatelet	11 (30.6%)	28 (25.0%)	0.5200
Coumadin	7 (19.4%)	20 (17.9%)	0.8080
COPD	3 (8.3%)	19 (17.0%)	0.2844
Patent IMA	33 (91.7%)	77 (68.8%)	0.0075
Patent LA	1.9 ± 1.2	1.7 ± 1.4	0.4293
MAOD (mm)	47.5 ± 9.1	47.7 ± 10.6	0.9284
MALD (mm)	38.0 ± 10.1	33.9 ± 9.9	0.0338
ΔD (mm)	9.8 ± 6.8	13.7 ± 9.9	0.0367
% mural thrombus	28.6 ± 20.8	47.1 ± 39.9	0.0198

PT2EL: persistent type 2 endoleak; COPD: chronic obstructive pulmonary disease; IMA: inferior mesenteric artery; LA: lumbar artery; MAOD: maximum aneurysm outer diameter; MALD: maximum aneurysm luminal diameter

Fig. 2 Aneurysmal sac behavior. Group S: Endovascular aortic repair (EVAR) cases with aneurysmal sac shrinkage. Group E: EVAR cases with aneurysmal sac enlargement. Group N: EVAR cases with no change in aneurysmal sac diameter.

Risk factors for PT2EL after EVAR

Of 148 patients, PT2EL (Group A) was identified in 36 cases (24.3%). According to univariate analysis, patent IMA, $\Delta D < 15.0$ mm, and % mural thrombus $< 57.7\%$ were detected as possible risk factors for PT2EL after EVAR. Multivariate analysis revealed patent IMA (OR: 5.2, 95%CI: 1.7–23.0, $P = 0.0019$), % mural thrombus $< 57.7\%$ (OR: 6.9, 95%CI: 1.4–52.0, $P = 0.0179$) as significant risk factors for PT2EL after EVAR (Table 2).

Risk factors for sac enlargement after EVAR

Among the total of 148 patients in this study, sac enlargement (Group E) was found in 21 cases (14.2%). By univariate analysis, female gender, antiplatelet intake, patent IMA, and PT2EL were isolated as possible risk factors for sac enlargement after EVAR.

Multivariate analysis demonstrated female gender (OR: 3.6, 95%CI: 1.0–12.2, $P = 0.0441$), antiplatelet intake (OR: 3.2, 95%CI: 1.1–9.6, $P = 0.0341$), and PT2EL (OR: 6.7, 95%CI: 2.3–20.5, $P = 0.0004$) as significant risk factors for sac enlargement after EVAR (Table 3).

Influencing factors for sac shrinkage after EVAR

Forty-five cases (30.4%) in Group S showed significant sac shrinkage after EVAR. Univariate analysis revealed absence of coronary artery disease (CAD), thoracic aortic aneurysm (TAA), antiplatelet intake, and PT2EL as possible influencing factors for sac shrinkage after EVAR. Also, by multivariate analysis, absence of TAA (OR: 4.0, 95%CI: 1.2–18.3, $P = 0.0202$), antiplatelet intake (OR: 4.1, 95%CI: 1.0–19.3, $P = 0.0469$), and PT2EL (OR: 3.9, 95%CI: 1.5–12.7, $P = 0.0055$) were detected as significant influencing factors for sac shrinkage after EVAR (Table 4).

Discussion

Continued pressurization of an aneurysmal sac due to persistent endoleak remains a serious complication after EVAR. It is needless to say that secondary re-intervention is indispensable to type 1 or 3 endoleaks. However, its indication for persistent type 2 endoleak (PT2EL) is still controversial. Rayt, et al. demonstrated that a policy of regular surveillance for PT2EL was not associated with any adverse outcomes after

Table 2 Preoperative risk factors for PT2EL after EVAR

	Univariate analysis		Multivariate analysis	
	OR (CI)	P value	Adjusted OR (CI)	P value
Patent IMA (+)	5.0 (1.6–21.8)	0.0030	5.2 (1.7–23.0)	0.0031
$\Delta D < 15$ mm	2.8 (1.2–7.1)	0.0137	1.2 (0.4–3.9)	0.7043
% mural thrombus <57.7%	8.1 (2.3–51.3)	0.0004	6.9 (1.4–52.0)	0.0179

PT2EL: persistent type 2 endoleak; EVAR: endovascular aortic repair; OR: odds ratio; CI: confidence interval; IMA: inferior mesenteric artery

Table 3 Preoperative risk factors for sac enlargement after EVAR

	Univariate analysis		Multivariate analysis	
	OR (CI)	P value	Adjusted OR (CI)	P value
Female	3.5 (1.2–9.8)	0.0262	3.6 (1.0–12.2)	0.0441
Antiplatelet (+)	3.1 (1.2–8.0)	0.0230	3.2 (1.1–9.6)	0.0341
Patent IMA (+)	3.8 (1.0–24.3)	0.0463	2.0 (0.5–13.6)	0.3797
PT2EL (+)	7.3 (2.8–20.6)	<0.0001	6.7 (2.3–20.5)	0.0004

PT2EL: persistent type 2 endoleak; EVAR: endovascular aortic repair; OR: odds ratio; CI: confidence interval; IMA: inferior mesenteric artery

Table 4 Influencing factors for sac shrinkage after EVAR

	Univariate analysis		Multivariate analysis	
	OR (CI)	P value	Adjusted OR (CI)	P value
CAD (–)	3.3 (1.4–8.7)	0.0050	1.3 (0.4–4.8)	0.6355
TAA (–)	3.8 (1.2–16.7)	0.0186	4.0 (1.2–18.3)	0.0202
Antiplatelet (–)	5.3 (1.9–18.6)	0.0006	4.1 (1.0–19.3)	0.0469
PT2EL (–)	3.4 (1.3–10.7)	0.0090	3.9 (1.5–12.7)	0.0055

EVAR: endovascular aortic repair; OR: odds ratio; CI: confidence interval; CAD: coronary artery disease; TAA: thoracic aortic aneurysm; PT2EL: persistent type 2 endoleak

EVAR⁸⁾ because there were no ruptured aneurysms or aneurysm-related death and no patients requiring late open conversion.⁸⁾ On the other hand, El Batti, et al. revealed not only persistent type 2 endoleak but recurrent type 2 endoleak can lead to life-threatening complications,⁹⁾ and aneurysmal sac enlargement in the presence of PT2 was reported to be an aggressive indication for reintervention, including coil embolization to aortic branch vessels and intrasac injection of prothrombotic material.^{4,10)} With respect to midterm or late term success rate to treat PT2EL, Gallagher, et al. demonstrated that midterm success rate was comparatively low, considering most patients required multiple reinterventions to treat PT2EL in their series.¹¹⁾ Also, Timur, et al. evaluated the long-term success of embolization of type 2 endoleaks in preventing aneurysmal sac growth, and they pointed out that a significant number of patients who underwent embolization of a type 2 endoleak continued to experience sac enlargement.¹²⁾ Therefore, endovascular reinterventions for type 2 endoleaks associated with aneurysmal

sac enlargement after EVAR are considered to have little effectiveness on the stabilization of aneurysmal sac diameter. Recently, Ward, et al. have advocated the effectiveness of preoperative IMA embolization before EVAR as a preventative method of reducing the incidence of aneurysmal sac enlargement, PT2EL, and repeated endovascular intervention.¹³⁾ Also, as stated above, we reported the clinical usefulness of embolization to aortic branched vessels before EVAR, and revealed approximately 50% of cases in this series showed significant shrinkage of the aneurysmal sac at 6 months after EVAR.⁷⁾ In addition, as previous studies have identified endoleak cavity volume (ECV) as a predictor of aneurysm enlargement,^{14,15)} reducing the ECV inside the aneurysmal sac as much as possible by performing coil embolization to patent aortic branched vessels prior to EVAR should prevent repeated endovascular interventions (EVT) derived from PT2EL which can lead to continuous aneurysmal sac growth. Multiple endovascular interventions (EVT), such as coil embolization to aortic branched

vessels and intrasac injection of prothrombotic material after EVAR have been reported to increase the risk of endograft infections.^{4,16,17} Hence, we consider EVAR should be a final and radical treatment for AAA, and additional EVT after EVAR should be avoided as much as possible, in consideration of the increased risk of endoprosthesis infection. Furthermore, a variety of indices have been advocated as predictors of AAA remodeling and aneurysmal sac behavior after EVAR. Sadek, et al. focused on preoperative CT variables to predict aneurysmal sac behavior, and identified that the proportion of thrombus inside the aneurysmal sac was significantly associated with sac shrinkage and enlargement after EVAR.¹⁸ In their series, aneurysms with a large thrombus burden are less likely to grow, compared with those with relatively little thrombus in their series. In the present study, we defined the proportion of thrombus inside the aneurysmal sac as % mural thrombus simply calculated by $(\text{MAOD} - \text{MALD}) / \text{MAOD} \times 100$, and multivariate analysis demonstrated that % mural thrombus <36.6%, and patent IMA on preoperative CT were significant predictors of PT2EL after EVAR. To be more precise, AAA with less thrombus burden as well as the patent IMA resulted in PT2EL after EVAR. In terms of risk factors for aneurysmal sac enlargement after EVAR, Joseph, et al. demonstrated warfarin therapy contributed to persistent sac expansion on their volumetric analysis.¹⁹ In our study, female gender, oral antiplatelet intake, PT2EL, and MALD >39.8 mm were significantly associated with aneurysmal enlargement after EVAR on multivariate analysis. That is, larger MALD not MAOD on preoperative CT complicated with PT2EL might place the patient at an increased risk for aneurysmal sac growth. In addition, it might be interesting to note gender differences were associated with aneurysmal sac behavior after EVAR. On the other hand, with regard to influencing factors for aneurysmal shrinkage after EVAR, univariate analysis showed the absences of CAD, TAA, oral antiplatelet intake, and PT2EL were associated with sac shrinkage. Of these factors, the absences of TAA, oral antiplatelet intake, and PT2EL were pointed out as significant influencing factors for sac shrinkage on multivariate analysis. Recently, it has been advocated that AAA is frequently associated with coronary artery disease (CAD) or peripheral artery disease (PAD) because systemic atherosclerosis can affect all arterial segments of the vascular system.^{20,21} Thus, the critical issue is

the priority order for treating patients with AAA plus CAD or PAD. As shown in the results of the current study, whether or not patients with AAA on antiplatelet intake were significantly associated with aneurysmal sac shrinkage or enlargement after EVAR. In other words, those who were on antiplatelet intake after catheter intervention for CAD or PAD may be at an increased risk of continued aneurysmal sac growth after EVAR. Accordingly, a more meticulous therapeutic strategy, including priority order (AAA first or CAD first) and appropriate choice of treatment (EVAR or open surgery) based on the anatomic variables on preoperative CT and a patient's medical backgrounds is necessary to improve late outcomes of EVAR.

Study limitations

Our study has several limitations. It is a retrospective analysis, and all the possible influencing factors for aneurysmal sac behavior after EVAR may not be cited. Also, follow-up durations after EVAR to determine the aneurysmal sac prognosis varied, depending on individual cases. Furthermore, one of the important anatomic variables used in this study—percentage of thrombus load inside the aneurysmal sac (% mural thrombus) may have to be measured using a much more precise measuring software instead of a simple index.

Conclusion

In this study, whether the presence of persistent type 2 endoleak (PT2EL) or not was significantly associated with aneurysmal sac behavior (enlargement or shrinkage). So, coil embolization to IMA was considered to contribute to the prevention of PT2EL, which could result in aneurysmal sac enlargement after EVAR. Also, in patients with AAA on antiplatelet intake due to CAD or PAD, treatment priority for these combined systemic atherosclerotic disorders and appropriate choice of treatment for AAA should be well considered for individual cases.

Disclosure Statement

The authors of this article do not have any conflicts of interest in this study.

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