されている(**図5, 6**)[21]．症例は63歳男性で腹部大動脈の腫瘤性病変と息切れの精査のために受診，CT/MRIにて右冠動脈に最大径3.0×2.6 cmの腫瘍性病変が認められた．カテーテル検査においてこのmassのために右房が顕著に圧排されていることが判明した．冠動脈造影を施行したところ，右冠動脈の血流は維持されていたがこの腫瘍性組織内に造影剤が流入しており，pseudoaneurysmと考えられた．なお腹部では5.5 cm大のinfrarenalタイプの腹部大動脈瘤が確認された．血中の免疫グロブリン血中濃度は，IgG 1,054 mg/dl (820～1,740)，IgA 373 mg/dl (90～400)，IgM 93 mg/dl (31～200)であり，IgG4は456 mg/dlと著明な高値を呈していた．胸部腹部同時手術で左内胸動脈を左前下行枝の対角枝に，橈骨動脈グラフトを右冠動脈へ吻合し，右冠動脈のmassを摘出，その後，腹部大動脈瘤も人工血管置換がなされた．摘出された右冠動脈周囲のmassは4.1×2.6×2.5 cmの赤茶色を呈し，血管周囲に腫瘍性に肥厚が認められている．大動脈瘤の組織は内膜に軽度の動脈硬化性変化が認められた．さらに詳細に検討すると，リンパ球・形質細胞の顕著な侵潤と線維性肥厚が目立ち，特に中膜，外膜において顕著であった．リンパ系細胞には異形成はなく成熟リンパ球であった．大動脈瘤組織についても同様の変化を認めている．さらに免疫組織的にIgG4陽性細胞が多数認められることを併せて確認している．このことは大動脈周囲のみならず，他の動脈においても動脈周囲炎が生じて病態形成にかかわることを示唆している．われわれも最近，冠動脈壁が顕著に肥厚し，かつIgG4が相対的に高い症例を経験しており，それらから類推すると大動脈のみならず冠動脈のような中小径の動脈においても血管周囲炎が生じることがあり，それらの可能性を疑った場合には内腔のみを描出する冠動脈造影よりもむしろ冠動脈CT・MRIなどを実施して血管周囲を含めた血管構造の把握を行うとともに血中IgG4値の評価を行うことが望ましい．

おわりに

IgG4関連疾患については日進月歩でデータが集約されつつある．血管周囲の炎症が顕著な心血管疾患や心膜疾患などを診る場合，IgG4関連症候群の可能性を念頭に置き，必要であれば血液中のIgG4値の評価を実施するとともに，外科手術が考慮される場合には摘出組織において集簇した炎症細胞のcharacterizationやIgG4陽性形質細胞の存在などを確認することが望ましい．

文　献

1) Hamano H, Kawa S, Horiuchi A, et al: High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med 344: 732-738, 2001
2) Zen Y, Harada K, Sasaki M, et al: IgG4-related sclerosing cholangitis with and without hepatic inflammatory pseudotumor, and sclerosing pancreatitis-associated sclerosing cholangitis: do they belong to a spectrum of sclerosing pancreatitis? Am J Surg Pathol 28: 1193-1203, 2004
3) Kitagawa S, Zen Y, Harada K, et al: Abundant IgG4-positive plasma cell infiltration characterizes chronic sclerosing sialadenitis (Kuttner's tumor). Am J Surg Pathol 29: 783-791, 2005
4) Zen Y, Sawazaki A, Miyayama S, et al: A case of retroperitoneal and mediastinal fibrosis exhibiting elevated levels of IgG4 in the absence of sclerosing pancreatitis (autoimmune pancreatitis). Hum Pathol 37: 239-243, 2006
5) Zen Y, Kitagawa S, Minato H, et al: IgG4-positive plasma cells in inflammatory pseudotumor (plasma cell granuloma) of the lung. Hum Pathol 36: 710-717, 2005
6) Deshpande V, Chicano S, Finkelberg D, et al: Autoimmune pancreatitis: a systemic immune complex mediated disease. Am J Surg Pathol 30: 1537-1545, 2006
7) Hamano H, Kawa S, Ochi Y, et al: Hydronephrosis associated with retroperitoneal fibrosis and sclerosing pancreatitis. Lancet 359: 1403-1404, 2002
8) Comings DE, Skubi KB, Van Eyes J, Motulsky AG: Familial multifocal fibrosclerosis. Findings suggesting that retroperitoneal fibrosis, mediastinal fibrosis, sclerosing cholangitis, Riedel's thyroiditis, and pseudotumor of the orbit may be different manifestations of a single disease. Ann Intern Med 66: 884-892, 1967
9) Sakamoto A, Okamoto K, Ishizaka N, et al: 18F-Fluorodeoxyglucose positron emission tomography in a case of retroperitoneal fibrosis. Int Heart J 47: 645-650, 2006
10) Meyer S, Hausman R: Occlusive phlebitis in multifocal fibrosclerosis. Am J Clin Pathol 65: 273-284, 1976
11) Hellmann DB, Grand DJ, Freischlag JA: Inflammatory abdominal aortic aneurysm. JAMA 297: 395-400, 2007

12) Rasmussen TE, Hallett JW Jr: Inflammatory aortic aneurysms. A clinical review with new perspectives in pathogenesis. Ann Surg 225: 155-164, 1997
13) Kasashima S, Zen Y, Kawashima A, et al: Inflammatory abdominal aortic aneurysm: close relationship to IgG4-related periaortitis. Am J Surg Pathol 32: 197-204, 2008
14) Stone JH, Khosroshahi A, Deshpande V, Stone JR: IgG4-related systemic disease accounts for a significant proportion of thoracic lymphoplasmacytic aortitis cases. Arth Care Res 62: 316-322, 2010
15) Takahashi M, Shimizu T, Inajima T, et al: A case of localized IgG4-related thoracic periarteritis and recurrent nerve palsy. Am J Med Sci 341: 166-169, 2011
16) 武田憲文，平田恭信，永井良三：後腹膜線維症による心血管病変．呼と循 55: 441-447, 2007
17) Amiya E, Ishizaka N, Watanabe A, et al: Retroperitoneal fibrosis with periaortic and pericardial involvement. Circ J 69: 760-762, 2005
18) Hanley PC, Shub C, Lie JT: Constrictive pericarditis associated with combined idiopathic retroperitoneal and mediastinal fibrosis. Mayo Clin Proc 59: 300-304, 1984
19) Sassa H, Kondo J, Tsuboi H, et al: A case of idiopathic retroperitoneal fibrosis with chronic pericarditis. Intern Med 31: 414-417, 1992
20) Omura Y, Yoshioka K, Tsukamoto Y, et al: Multifocal fibrosclerosis combined with idiopathic retroperitoneal and pericardial fibrosis. Intern Med 45: 461-464, 2006
21) Matsumoto Y, Kasashima S, Kawashima A, et al: A case of multiple immunoglobulin G4-related periarteritis: a timorous lesion of the coronary artery and abdominal aortic aneurysm. Hum Pathol 39: 975-980, 2008

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Inverse association between the existence of coronary artery disease and progression of abdominal aortic aneurysm

Atsuko Nakayama[a], Hiroyuki Morita[b,*], Tetsuro Miyata[c], Jiro Ando[a], Hideo Fujita[d], Hiroshi Ohtsu[e], Takafumi Akai[c], Katsuyuki Hoshina[c], Masatoshi Nagayama[f], Shuichiro Takanashi[f], Tetsuya Sumiyoshi[f], Ryozo Nagai[a,*]

[a] Department of Cardiovascular Medicine, Graduate School of Medicine, The University of Tokyo, Japan
[b] Department of Translational Research for Healthcare and Clinical Science, Graduate School of Medicine, The University of Tokyo, Japan
[c] Division of Vascular Surgery, Graduate School of Medicine, The University of Tokyo, Japan
[d] Department of Ubiquitous Health Informatics, Graduate School of Medicine, The University of Tokyo, Japan
[e] Department of Clinical Trial Data Management, Graduate School of Medicine, The University of Tokyo, Japan
[f] Sakakibara Heart Institute, Tokyo, Japan

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ABSTRACT

Objectives: A strong degree of co-existence between coronary artery disease (CAD) and abdominal aortic aneurysm (AAA) is widely acknowledged, however, it remains to be elucidated whether the existence of CAD is associated with an accelerated expansion rate of AAA. Also, the relationship between preoperative CAD and postoperative major adverse cardiovascular events (MACE) has not been examined in Japanese patients. The aim of this study was to investigate the deleterious effects of CAD on the progression of AAA and the onset of postoperative MACE after elective AAA repair.
Methods and results: A retrospective cohort study of 665 consecutive Japanese patients who underwent elective surgical repair for infrarenal AAA at 2 high-volume Tokyo hospitals from 2003 through 2010 was performed. Preoperative CAD was shown to be a significant determinant of postoperative MACE (HR 2.29; 95%CI, 1.12–4.66; $p = 0.02$). In the analysis of 510 patients for whom there were at least 2 follow-up CT scans of the size of their AAA before repair, the existence of CAD was shown to be inversely associated with the accelerated expansion rate of AAA.
Conclusion: This study on the patients undergone elective repair for infrarenal AAA identified an inverse association between the existence of CAD and progression of AAA as well as the significant impact of preoperative CAD on the occurrence of postoperative MACE after elective AAA repair.

1. Introduction

Abdominal aortic aneurysm (AAA) is a common condition, occurring in 5% of older men [1] and 1% of older women [2]. Some AAAs remain quiescent with little growth or regress whereas others continue to expand and eventually rupture [3,4]. About half of the patients with a ruptured AAA die before they reach the hospital [5] and elective repair of AAA is known to confer a significantly lower in-hospital mortality rate than emergency repair [6–10]. When the maximum diameter of an AAA exceeds the threshold, the likelihood of a catastrophic rupture increases. Identification of the clinical characteristics related to AAA formation and/or expansion could contribute to the detection and/or follow-up for AAA, particularly at the asymptomatic stage, thereby improving the therapeutic effectiveness for this disease.

On the other hand, in Japan, there is no systematic population screening for AAA, thus, asymptomatic AAAs are most likely to be identified incidentally during an annual health check-up for "healthy" people or during an extensive clinical examination of patients with coronary artery disease (CAD). The high detection rate of AAA in patients presenting with CAD can be explained by the strong correlation between atherosclerosis and AAA [11,12]. How is the association between the AAA expansion rate and CAD? The risk factors for the AAA expansion, which are not necessarily identical to those for the AAA formation, have been investigated. Smoking [3,4] is well-known to be associated with the accelerated expansion rate for AAAs and diabetes [3,4] and peripheral arterial disease [4] were reported to be associated with the slowed AAA growth. However, it remains unclear whether the existence of CAD by itself is associated with the accelerated expansion rate of AAA.

* Corresponding authors at: Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Tel.: +81 3 5800 9170; fax: +81 3 5800 9171.
E-mail addresses: hmrt-tky@umin.net (H. Morita), nagai-tky@umin.ac.jp (R. Nagai).

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Patients with AAA have a higher prevalence of cardiovascular risk factors, therefore, even after successful AAA repair, they remain at increased risk for a major adverse cardiovascular event (MACE) [13,14]. However, there is a lack of data on preoperative clinical characteristics in Japanese patients that can be used to predict MACEs following AAA repair.

To address these issues, we performed a retrospective cohort study in Japanese patients who underwent elective AAA repair at 2 high-volume hospitals in Tokyo. The aim of this study was to clarify the relationships among the preoperative risks, expansion rate of AAA, and the long-term prognosis after AAA repair, with a special focus on the cardiovascular risks and events.

2. Methods

We conducted a retrospective cohort study of 676 consecutive patients who underwent elective surgical repair for an infrarenal AAA at the University of Tokyo Hospital or Sakakibara Heart Institute from 1 January 2003 through 31 March 2010. All study participants were of Japanese ancestry. This study was approved by the ethical committees of the University of Tokyo Hospital and the Sakakibara Heart Institute Hospital.

The indications for and management of AAA repair were determined according to the Japanese Circulation Society Guidelines (when an AAA was greater than 50 mm in diameter) [15] by the vascular surgery team at each hospital. The size of the AAA was evaluated by CT scanning before the surgery in all patients. AAAs which were diagnosed as being a direct consequence of a specific cause such as trauma ($n=2$), infection ($n=4$), inflammatory disease ($n=2$), or Marfan syndrome ($n=3$) were excluded from the study. After exclusion of these 11 patients, 665 elective repair cases for non-ruptured AAA were enrolled.

In the patients receiving elective repair, preoperative coronary angiography (CAG) were performed less than 3 months before AAA repair (only 6 cases had no preoperative CAG). In this study, a prior MI and prior PCI/CABG were considered to be a disease onset and procedure that had occurred more than 3 months before AAA repair. A patient with CAD was defined as one who had a prior MI, prior PCI/CABG, and/or coronary stenosis identified during a preoperative CAG. An indication of preoperative revascularization (PCI or CABG performed following preoperative CAG less than 3 months before AAA repair) was determined based on the condition of the individual patient by the cardiologists and vascular surgery team at each hospital. Prior to elective AAA repair, preoperative revascularization was performed in 118 patients (PCI in 65 and CABG in 53). In the 2 participating hospitals, follow-up CAG is routinely scheduled around 180 days after PCI and 1 year after CABG, however, it can be performed earlier if needed. Information about target lesions, PCI (e.g. device, technique), and the lesions at follow-up CAG were reviewed by more than 2 cardiologists blinded to the study protocol. All other treatment and medication decisions were made by the attending physicians based on the standard therapy according to up-to-date guidelines and recommendations, without any interventions by researchers.

The details of surgical management and patient clinical characteristics before and after the AAA repair were obtained from the medical records. ECG abnormalities were defined as the presence of abnormal Q wave, ischemic ST change, T wave inversion or complete left bundle branch block [16]. Ex-smokers and current smokers were defined according to whether or not they had stopped smoking more than 1 month before the initial CT scan. Hemoglobin, creatinine, C-reactive protein, and HbA1c were measured immediately before the surgery. For the comparison of baseline characteristics, serum levels of creatinine were calculated after the exclusion of the patients receiving hemodialysis.

Follow-up ended on 30 September 2010. Medical records and reports from the catheter laboratory were used to assess the outcomes. Major outcomes were death from any cause and the occurrence of MACEs, defined as a composite of cardiovascular death, non-fatal acute coronary syndrome (ACS; myocardial infarction or unstable angina), and non-fatal cerebral infarction. During the one month period following AAA repair, serum CK (creatine kinase)-MB isozyme was routinely measured in order to detect myocardial injury.

Next, the AAA expansion rate was determined in patients for whom data were available from at least 2 follow-up CT scans before elective AAA repair. Patients with a follow-up period <90 days were excluded. AAAs exhibiting a saccular morphology or those accompanying dissection were also excluded.

Statistical analysis was performed with SPSS version 18.0 for Windows. Baseline characteristics were compared by the t-test for continuous valuables and chi-square test for categorical valuables. Multiple logistic regression analysis was also performed to compare the groups. Kaplan–Meier survival analyses with log rank and proportional hazard model by Cox were performed to evaluate the probability of freedom from MACE. All tests were two-sided with a significance value of $p<0.05$.

3. Results

3.1. Study population and follow-up

We analyzed a total of 665 patients who underwent elective AAA repair at the University of Tokyo Hospital or Sakakibara Heart Institute Hospital from 2003 to 2010 after excluding 11 patients according to the criteria mentioned above. The baseline characteristics of the patients are summarized in Table 1. Mean AAA size at the time of elective repair was 53.5 ± 12.2 mm.

Among these 665 elective repair cases, 576 patients received open surgical repair (Y-shaped aortic prosthesis in 346 and aortoaortic tube in 230) and 89 underwent endovascular repair.

Average (±SD) follow-up duration for mortality and MACE was 800 ± 742 days. The follow-up rate was relatively good (88%).

3.2. Preoperative variables associated with postoperative MACEs following elective repair for AAA

In the present study, 33 post-operative deaths occurred among the 665 elective repair cases. The 30-day mortality rate was remarkably low (6 cases, 0.9%). Ten patients died of a cardiovascular cause after elective surgery during the follow-up period. Only 1 of these 10 cardiovascular deaths occurred within 30 days of the operation. There were 49 MACEs, one of which was a silent myocardial infarction detected by the elevation of serum CK-MB. In the analysis of clinical characteristics related to postoperative MACE, the preoperative existence of CAD as well as an ECG abnormality was found to be the only preoperative variables associated with the occurrence of a MACE after elective AAA repair (HR 2.29; 95%CI, 1.12–4.66; $p=0.02$) (Fig. 1). In multivariable analysis, after adjusting for age > 65 years, gender, BMI > 25, hypertension, dyslipidemia, diabetes, current smoking, and hemodialysis, the preoperative existence of CAD remained significantly associated with the postoperative occurrence of a MACE (HR 2.91; 95%CI, 1.87–4.54; $p<0.001$). The HRs (and 95%CIs) for age > 65 years, male gender, BMI > 25, hypertension, dyslipidemia, diabetes, current smoking, and hemodialysis were as follows: 1.12 (0.66–1.86), 0.68 (0.41–1.12), 0.92 (0.58–1.45), 1.04 (0.67–1.60), 0.82 (0.54–1.25), 1.28 (0.83–1.98), 1.64 (1.08–2.49), and 4.18 (1.94–9.00), respectively. Postoperative MACEs were significantly more frequent in the

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Table 1
Baseline characteristics of the study population.

	Total (n = 665)	CAD (+) (n = 342)	CAD (−) (n = 323)	p value (CAD(+) vs. CAD(−))
Age (years)	73.3 ± 7.8	73.1 ± 8.0	73.4 ± 8.1	0.61
Male	550 (83%)	301 (88%)	249 (77%)	<0.01
BMI (kg/m^2)	23.0 ± 3.4	23.3 ± 3.5	22.7 ± 3.3	0.02
Hypertension	465 (70%)	250 (73%)	215 (67%)	0.07
Dyslipidemia	316 (48%)	190 (56%)	126 (39%)	<0.01
Diabetes	161 (24%)	95 (28%)	66 (20%)	0.03
Current or ex-smoking	433 (65%)	238 (70%)	195 (60%)	0.01
Hemodialysis	16 (2%)	12 (4%)	4 (1%)	0.06
Family history of AAA	44 (7%)	22 (6%)	22 (7%)	0.84
Family history of CAD	88 (13%)	55 (16%)	33 (10%)	0.03
Previous myocardial infarction	22 (3%)	22 (6%)	0 (0%)	–
Previous PCI	96 (14%)	96 (28%)	0 (0%)	–
Previous CABG	61 (9%)	61 (18%)	0 (0%)	–
Existence of preoperative CAD	342 (51%)	342 (100%)	0 (0%)	–
Ischemic changes on resting ECG	307 (46%)	192 (56%)	115 (36%)	<0.01
History of cerebral artery disease	86 (13%)	63 (18%)	23 (7%)	<0.01
History of COPD	138 (21%)	71 (21%)	67 (21%)	0.99
β, αβ-blocker	179 (27%)	114 (33%)	65 (20%)	<0.01
ACE inhibitor	63 (10%)	42 (12%)	21 (7%)	0.01
ARB	227 (34%)	123 (36%)	104 (32%)	0.31
Calcium channel blocker	335 (50%)	179 (52%)	156 (48%)	<0.01
All statins	185 (28%)	122 (36%)	63 (20%)	<0.01
Strong statins[a]	113 (17%)	79 (23%)	34 (11%)	<0.01
Hemoglobin (g/dL)	12.6 ± 1.6	12.6 ± 1.6	12.6 ± 1.6	0.77
Creatinine (mg/dL)[b]	1.0 ± 0.5	1.0 ± 0.6	0.9 ± 0.4	0.08
hsCRP (mg/dL)	0.6 ± 1.7	0.6 ± 1.5	0.6 ± 1.9	0.92
HbA1c (NGSP) (%)	5.9 ± 0.6	5.9 ± 0.7	5.8 ± 0.6	0.17
AAA diameter at operation (mm)	53.5 ± 12.2	54.3 ± 11.4	53.6 ± 13.0	0.08
Saccular morphology	29 (4%)	14 (4%)	15 (5%)	0.73
Dissection	38 (6%)	8 (2%)	30 (9%)	<0.01

[a] Strong statins; atorvastatin, rosuvastatin and pitavastatin.
[b] Serum creatinine levels were calculated after excluding the patients receiving hemodialysis.

patients with preoperative CAD than in those without preoperative CAD (Suppl Figure 1).

3.3. *Variables associated with the expansion rate of AAA*

From among the 665 cases described above, 510 cases for which there were at least 2 follow-up CT scans of the size of their AAA available. The clinical manifestations of these 510 cases were similar to those of the 665 cases above. Preoperative CAD was significantly related to the postoperative MACE also in these 510 cases.

Evaluation of the variables significantly associated with an expansion rate >5 mm/year revealed that the existence of CAD was inversely associated with an accelerated expansion rate (p < 0.01) (Fig. 2). In multivariable analysis, after adjusting for age > 65 years, gender, BMI > 25, hypertension, dyslipidemia, diabetes, current smoking, and hemodialysis, the existence of CAD remained inversely associated with an accelerated expansion rate >5 mm/year (HR 0.55; 95%CI, 0.32–0.94; p = 0.03). The HRs (and 95%CIs) for age > 65 years, male gender, BMI > 25, hypertension, dyslipidemia, diabetes, current smoking, and hemodialysis were as follows: 0.84 (0.38–1.85), 1.88 (0.89–3.96), 0.82 (0.45–1.50), 0.97 (0.52–1.81), 1.02 (0.58–1.80), 0.88 (0.49–1.58), 1.77 (0.97–3.22), and 1.85 (0.48–7.20), respectively. Although the administration of statins was also inversely associated with an accelerated expansion rate, that was not statistically significant after adjusting for the existence of CAD. The expansion rates between the CAD group and non-CAD group were compared for each 5 mm interval range of the absolute AAA diameter (Fig. 3). There was no significant difference in the follow-up duration or frequency of CT scans between these 2 groups. The expansion rate of AAAs which were more than 40 mm in diameter was significantly greater in the non-CAD group than in the CAD group.

4. Discussion

In this study, we performed a retrospective cohort study in 665 well-characterized Japanese patients who underwent elective surgical repair for infrarenal AAA at 2 high-volume hospitals and demonstrated an inverse association between the existence of CAD and an accelerated AAA expansion rate. In addition, preoperative CAD was found to be associated with postoperative MACE following elective AAA repair.

Since a strong co-existence of CAD and AAA [11,12] is well-known, the existence of CAD makes it necessary for clinicians to examine the abdominal aorta. However, it is unclear whether the existence of CAD by itself is potentially associated with an accelerated rate of expansion of an AAA. We investigated the relationship between the AAA expansion rate and the existence of CAD in 510 elective repair cases for which at least 2 follow-up CT scans of AAA were available. Remarkably, AAAs expanded significantly more rapidly in the patients without CAD than in those with CAD. AAA has been traditionally regarded as a consequence of atherosclerosis. Recent work lends support to the concept that AAAs grow through pathologic mechanisms that differ from those responsible for athero-occlusive disease [17–19]. In our study, the counterintuitive inverse association was observed between the existence of CAD and the expansion rate of AAA. A decrease in ABI, a measure of atherosclerotic burden [20], was previously reported to be associated with slower AAA growth [4], however, the present report is the first to demonstrate an inverse association between CAD by itself and AAA growth. The similarity and difference between atherosclerosis and aneurysm remain to be further investigated. Practically, in the very least, a lack of documented CAD should never be the rationale for exemption from AAA

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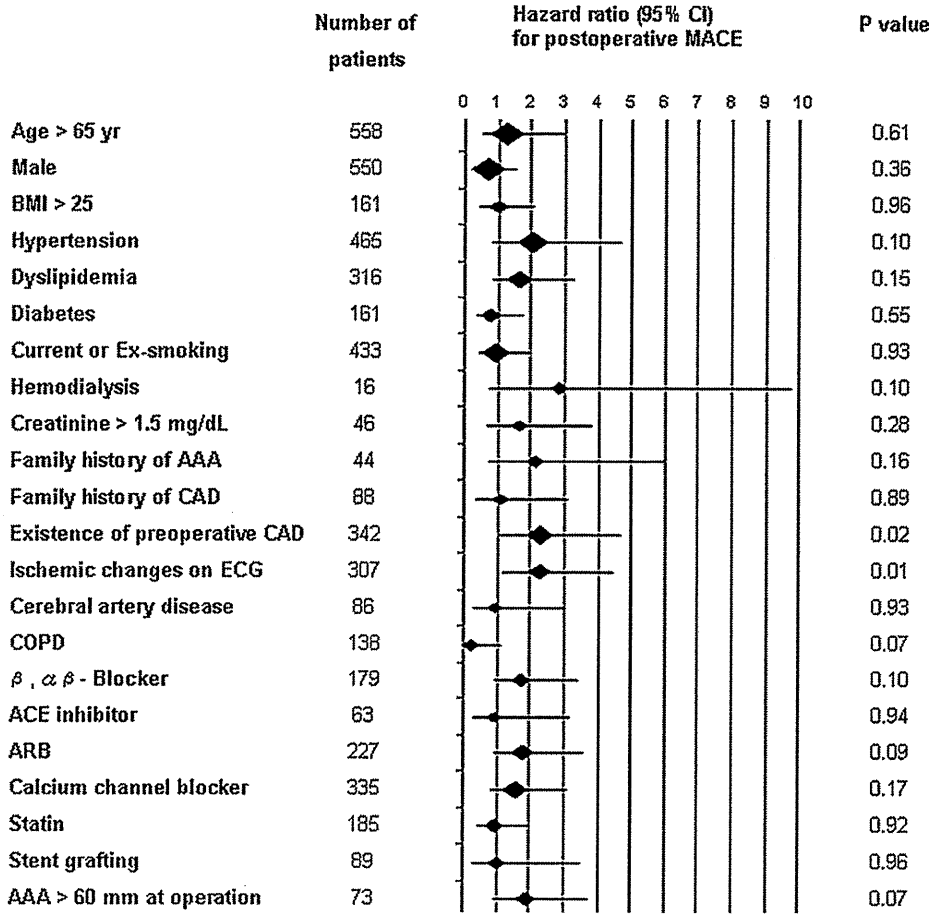

Fig. 1. Hazard ratio of postoperative MACE in prespecified subgroups.

screening. Ultimately, to reduce AAA-related mortality, population screening [21,22], with or without CAD, should also be recommended in Japan.

After adjustment for the existence of CAD, dyslipidemia and statin use were not significantly associated with the expansion rate. Smoking is well-known to be associated with the accelerated expansion rate for AAAs [3,4], leading to the recommendation for smoking cessation to reduce the risk of AAA growth [23]. The reason why smoking was not associated with expansion rate in our study is unknown. It might be because our study was a hospital-based retrospective study limited to the patients undergone elective AAA repair, not an epidemiological screening study. Although a lower prevalence of AAA as well as slowed AAA expansion in patients with diabetes has been reported in many epidemiological studies [3,4,24], in our analysis, diabetes was not inversely associated with the expansion rate. Judging from the HbA1c values in our study, the diabetic control was thought to be comparably good, therefore, the diagnosis as diabetes might not be related to the AAA expansion. The inverse association between peripheral arterial disease (PAD) and AAA expansion rate was reported [4]. As patients' data on the PAD could not be examined in our study, we could not investigate the association among CAD, PAD and AAA expansion. However, if possible, those data might profoundly imply the relationship between atherosclerosis and aneurysm growth. Here, statins, ACE inhibitors, ARBs, and β-blockers, whose effects remain controversial, had no significant effect.

Importantly, even patients who undergo successful elective AAA repair remain highly exposed to the risk for CAD, which is a predominant determinant of prognosis after AAA repair. Consistent with previous reports [6–10], in elective repair cases, postoperative mortality, particularly 30-day mortality, was comparably low, whereas postoperative MACEs were frequently observed. In our present study, preoperative CAD was shown to be an independent predictor for postoperative MACE, which is a novel finding at least in the Japanese patients. The adequate management of atherosclerotic risk factors is essential for reducing postoperative MACEs and improving the prognosis [25]. AAA repair should be recognized as a sort of important stimulus to beneficial lifestyle modification for reducing postoperative MACEs rather than a therapeutic goal [26].

Due to the inherent nature of retrospective studies, the possibility of bias and confounding variables could not be fully excluded from this study. As this study was limited to patients who had undergone AAA repair during the study period, patients who did not receive surgery due to the small size of their AAA with a slow expansion rate and patients who refused or were unfit for AAA repair were not included. Moreover, the 2 hospitals in our study are specialist centres located in metropolitan Tokyo. Therefore, the generalization of our results obtained at high-volume hospitals to other populations must be made with caution. In a recent large-scale study, the bimodal growth pattern for AAA was identified [3]. The fact that the expansion rate was fast and accelerated according to the AAA diameter in our study might be consistent with the study design limited to the patients who had undergone AAA repair. Indeed, small AAAs which remain quiescent could not be well recruited in such a hospital-based retrospective study like ours. In those subjects, the inverse association between the

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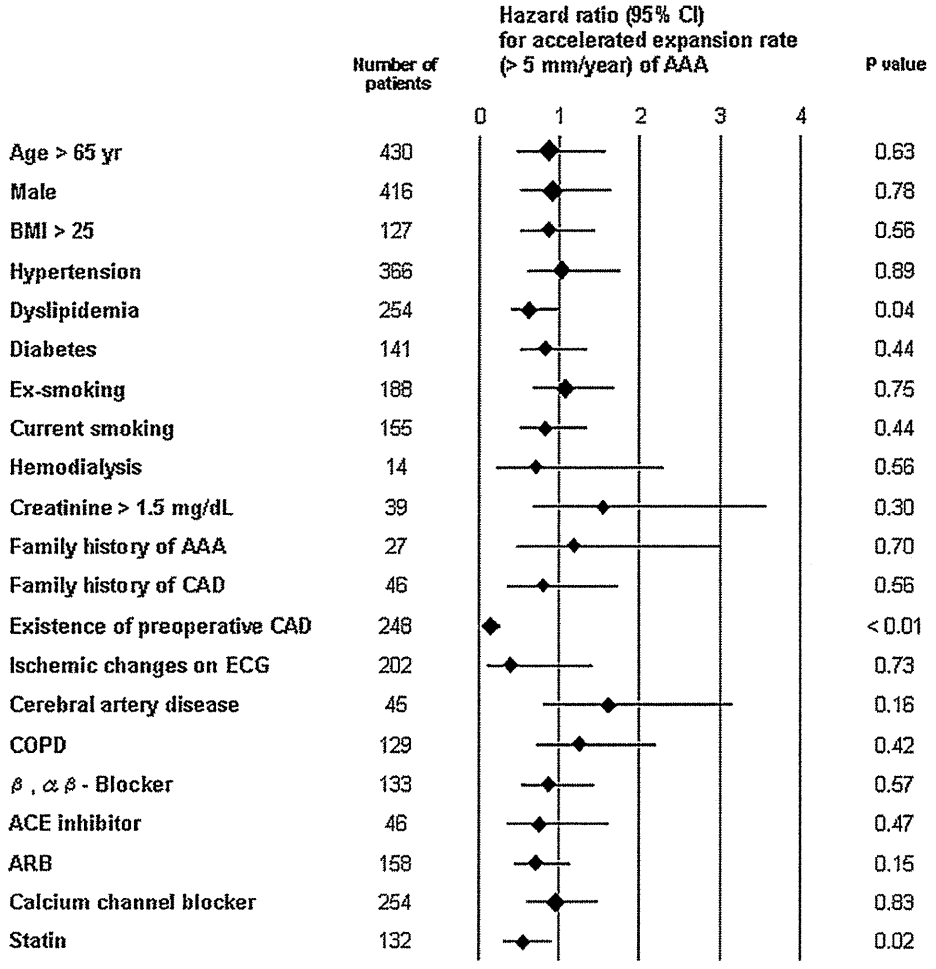

Fig. 2. Hazard ratio of accelerated expansion rate (>5 mm/year) of AAA in prespecified subgroups in the patients with at least 2 follow-up CT scans.

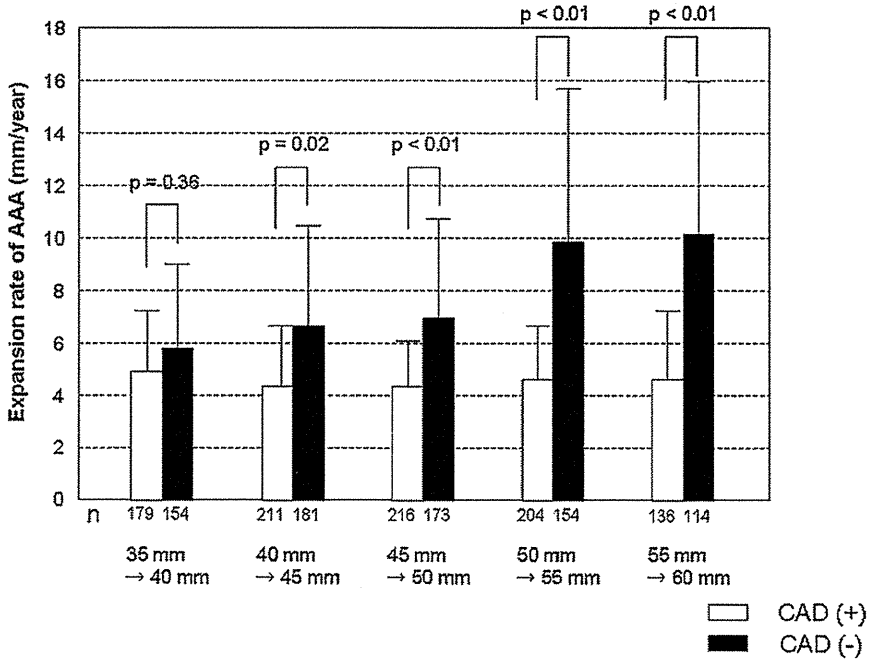

Fig. 3. Comparison of expansion rate of AAA between the patients with CAD and those without CAD in the patients with at least 2 follow-up CT scans. Open and solid bars represent the values in patients with CAD and those without CAD, respectively.

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existence of CAD and the progression of AAA might not be the case. In other words, our present findings could be applied only to the AAAs which continue to expand. When the evaluation of AAA diameter becomes routine in health check-ups in Japan, the relationship between the existence of CAD and the AAA expansion rate can be epidemiologically investigated. In addition, in accordance with Japanese Circulation Society Guidelines [15], the AAA repair was performed when an AAA was greater than 50 mm in diameter (mean diameter was 53.5 mm in this study), which might not be the case in western countries. Another major limitation is that there could be 2–3 years lag between the initial AAA evaluation and the preoperative CAG. In some cases, the findings of preoperative CAG could not necessarily indicate that CAD had already existed just while AAA was expanding.

We would like to discuss the several strengths of the present study. There were no differences in the preoperative work-up, indications for treatment of concurrent heart disease, or contraindications for AAA repair between the 2 participating hospitals. All AAAs in this study were measured by CT scan, which is an excellent modality for serially and accurately monitoring changes in AAA size.

In this retrospective cohort study in Japanese patients who underwent elective AAA repair, we unexpectedly demonstrated an inverse association between the existence of CAD and the progression of AAA. In addition, preoperative CAD was shown to be a significant determinant of postoperative MACE. Further investigations are warranted whether risk reduction for the prevention of CAD could improve the cardiovascular prognosis after elective AAA repair.

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.atherosclerosis.2012.02.031.

References

[1] Lederle FA, Johnson GR, Wilson SE, et al. The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med 2000;160:1425–30.
[2] Lederle FA, Johnson GR, Wilson SE, Aneurysm Detection and Management Veterans Affairs Cooperative Study. Abdominal aortic aneurysm in women. J Vasc Surg 2001;34:122–6.
[3] Thompson AR, Cooper JA, Ashton HA, Hafez H. Growth rates of small abdominal aortic aneurysms correlate with clinical events. Br J Surg 2010;97:37–44.
[4] Brady AR, Thompson SG, Fowkes FG, et al. Abdominal aortic aneurysm expansion: risk factors and time intervals for surveillance. Circulation 2004;110:16–21.
[5] Wilmink TB, Quick CR, Hubbard CS, Day NE. The influence of screening on the incidence of ruptured abdominal aortic aneurysms. J Vasc Surg 1999;30:203–8.
[6] Kniemeyer HW, Kessler T, Reber PU, et al. Treatment of ruptured abdominal aortic aneurysm, a permanent challenge or a waste of resources? Prediction of outcome using a multi-organ-dysfunction score. Eur J Vasc Endovasc Surg 2000;19:190–6.
[7] Hallin A, Bergqvist D, Holmberg L. Literature review of surgical management of abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2001;22:197–204.
[8] McPhee JT, Hill JS, Eslami MH. The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001–2004. J Vasc Surg 2007;45:891–9.
[9] The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. Lancet 1998;352:1649–55.
[10] Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002;360:1531–9.
[11] Singh K, Bønaa KH, Jacobsen BK, Bjørk L, Solberg S. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study. Am J Epidemiol 2001;154:236–44.
[12] Forsdahl SH, Singh K, Solberg S, Jacobsen BK. Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromsø Study, 1994–2001. Circulation 2009;119:2202–8.
[13] Johnston KW. Nonruptured abdominal aortic aneurysm: six-year follow-up results from the multicenter prospective Canadian aneurysm study. Canadian Society for Vascular Surgery Aneurysm Study Group. J Vasc Surg 1994;20:163–70.
[14] Koskas F, Kieffer E. Long-term survival after elective repair of infrarenal abdominal aortic aneurysm: results of a prospective multicentric study. Association for Academic Research in Vascular Surgery (AURC). Ann Vasc Surg 1997;11:473–81.
[15] Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection (JCS 2006). Circ J 2006;70(Suppl. IV):1569–646 [in Japanese].
[16] De Bacquer D, De Backer G, Kornitzer M, et al. Prognostic value of ischemic electrocardiographic findings for cardiovascular mortality in men and women. J Am Coll Cardiol 1998;32:680–5.
[17] Xu C, Zarins CK, Glagov S. Aneurysmal and occlusive atherosclerosis of the human abdominal aorta. J Vasc Surg 2001;33:91–6.
[18] Carrell TW, Burnand KG, Wells GM, Clements JM, Smith A. Stromelysin-1 (matrix metalloproteinase-3) and tissue inhibitor of metalloproteinase-3 are overexpressed in the wall of abdominal aortic aneurysms. Circulation 2002;105:477–82.
[19] Golledge J, Norman PE. Atherosclerosis and abdominal aortic aneurysm: cause, response, or common risk factors. Arterioscler Thromb Vasc Biol 2010;30:1075–7.
[20] Newman AB, Siscovick DS, Manolio TA, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study Cardiovascular Heart Study (CHS) Collaborative Research Group. Circulation 1993;88:837–45.
[21] US Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. Ann Intern Med 2005;142:198–202.
[22] Kim LGP, Scott RA, Ashton HA, Thompson SG, Multicentre Aneurysm Screening Study Group. A sustained mortality benefit from screening for abdominal aortic aneurysm. Ann Intern Med 2007;146:699–706.
[23] Chaikof EL, Brewster DC, Dalman RL, et al. The care of patients with an abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines. J Vasc Surg 2009;50:S2–49.
[24] Weiss JS, Sumpio BE. Review of prevalence and outcome of vascular disease in patients with diabetes mellitus. Eur J Vasc Endovasc Surg 2006;31:143–50.
[25] Newman AB, Arnold AM, Burke GL, O'Leary DH, Manolio TA. Cardiovascular disease and mortality in older adults with small abdominal aortic aneurysms detected by ultrasonography: the cardiovascular health study. Ann Intern Med 2001;134:182–90.
[26] United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. N Engl J Med 2002;346:1445–52.

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Outcomes after Open Surgery and Endovascular Aneurysm Repair for Abdominal Aortic Aneurysm in Patients with Massive Neck Atheroma

K. Hoshina [a,*], A. Hosaka [a], T. Takayama [b], M. Kato [b], N. Ohkubo [b], H. Okamoto [a], K. Shigematsu [a], T. Miyata [a]

[a] *Division of Vascular Surgery, Department of Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan*
[b] *Department of Cardiovascular Surgery, Morinomiya Hospital, Osaka, Japan*

WHAT THIS PAPER ADDS

- The article presents that endovascular surgery for abdominal aortic aneurysm (AAA) with massive neck atheroma tends to develop late-phase complication, compared to open surgery. This is the first report to analyse the complication after AAA operation in detail (grades and time course) and relate it to cholesterol crystal embolism. Our definition of massive neck atheroma should be acceptable under our conclusion, and it would be the springboard for the definition of the unclear term: 'shaggy aorta'. Also, this paper should influence the algorism of aortic aneurysm surgery, especially in case of shaggy aorta.

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ABSTRACT

Objective: We retrospectively analysed surgically treated abdominal aortic aneurysm (AAA) in patients with massive atheroma in the aneurysmal neck and compared the outcomes of endovascular aneurysm repair (EVAR) and open surgery (OS) to determine an appropriate strategy for massive neck atheroma cases.

Methods: A retrospective study was performed in 326 consecutive patients who underwent EVAR and in 247 patients who underwent OS. We defined massive neck atheromas if the following characteristics were observed: (1) thickness ≥ 5 mm; (2) the circumference of the infrarenal aorta ≥ 75%; and (3) length ≥ 5 mm. Twenty-eight patients (8.5%) in the EVAR group and 22 (8.9%) in the OS group met these criteria. We modified the previously published reporting standards on the basis of the selection of systemic and embolisation-related complications.

Results: Patients in the EVAR group had less intra-operative blood loss, shorter operation time, and shorter hospital stays after the operation ($P < 0.01$). No perioperative deaths were observed in either group. Major complications were categorised as early (in-hospital) or late (outpatient, within 6 months). Five and three patients in the OS and EVAR groups had early complications, but the difference was not statistically significant. In contrast, 7 patients in the EVAR group had late complications, compared to no patients in the OS group ($P = 0.01$). Kaplan–Meier analysis revealed a significantly higher survival rate in the OS group ($P = 0.011$). Two of the 4 patients with suprarenal clamping developed major complications. Mild eosinophilia was observed in 10 patients in the EVAR group. Proteinuria occurred or worsened in 5 EVAR patients and 1 OS patient.

Conclusion: Compared to OS patients, EVAR patients with massive neck atheroma tend to develop late-phase complications possibly related to cholesterol crystal embolisation. The clinical features of massive neck atheroma patients receiving EVAR should be carefully monitored even after hospital discharge.

Although shaggy aorta is considered to be an atheromatous aorta with a spiculated and irregular appearance, it has not been defined clearly.[1] Aortic surgery for shaggy aorta via the open or endovascular approach sometimes results in adverse events.[1,2] Open surgery (OS) for patients with abdominal aortic aneurysm

* Corresponding author. K. Hoshina, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Tel.: +81 3 5800 8653; fax: +81 3 3811 6822.
E-mail address: traruba@gmail.com (K. Hoshina).

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(AAA) has traditionally required considerable efforts such as the flushing of debris and suprarenal clamping to avoid atheromatous embolisation. At present, OS for AAA patients has been replaced by endovascular aneurysm repair (EVAR) after two large prospective studies published in 2004 demonstrated excellent short-term outcomes.[3,4] In this endovascular era, there has been an increase in the use of EVAR. However, we are concerned that this low-stress technique is being used without carefully considering atheromatous shower.

The infrarenal aneurysm neck is commonly the site at which occlusion balloons are used for touch-up in EVAR procedures. If the atheroma is squeezed and released from the neck, it can cause shower embolisation. In contrast to OS, EVAR is performed in a 'closed space' where atheromatous debris cannot be flushed out. Therefore, we focussed on massive neck atheroma and hypothesised that it is correlated to postoperative outcomes after EVAR.

In this study, we retrospectively analysed AAA surgical cases with massive atheroma in the aneurysmal neck and compared outcomes between groups of patients treated by EVAR and OS. In addition, we determined an appropriate strategy for massive neck atheroma.

Patients and Methods

Two institutes participated in this study. From December 2006 to December 2009, 326 patients underwent EVAR at Morinomiya Hospital (Osaka, Japan). Between January 2003 and November 2010, 247 consecutive patients underwent OS at The University of Tokyo Hospital (Tokyo, Japan). These institutions collaborate in data collection but have their own guidelines for procedure selection for AAA. Most patients who were admitted at Morinomiya Hospital underwent EVAR; the rate of EVAR among AAA operations was 95%. By contrast, at The University of Tokyo Hospital, conventional OS was the first-line treatment for several decades until the EVAR procedure was first introduced in 2008. Thus, long-term follow-up data were available retrospectively. The rate of the OS procedures was still approximately 90% in this hospital.

The aneurysmal neck is defined as an infrarenal aorta with a normal diameter; it is therefore a suitable location for the proximal landing of the stent graft. In this study, we included patients with a neck length more than 10 mm. The inclusion criteria for massive neck atheroma were as follows: (1) thickness ≥5 mm, (2) circumference of the infrarenal neck ≥75% and (3) length ≥5 mm (axial section). The exclusion criteria were as follows: (1) cases in which contrast computed tomography (CT) was not performed, (2) juxtarenal AAA cases requiring branch reconstruction and (3) cases in which rupture occurred. Twenty-eight patients (8.5%) who underwent EVAR at Morinomiya Hospital (EVAR group) and 22 patients (8.9%) who underwent OS at The University of Tokyo Hospital satisfied the inclusion criteria. Follow-up examinations were performed until March 2011 (EVAR group: 3–45 months (median, 22 months); OS group: 4–96 months (median, 62 months)).

To evaluate postoperative complications, we referred to the reporting standards of the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of the Society for Vascular Surgery/American Association for Vascular Surgery.[5] From the list of complications, we selected systemic and embolisation-related complications to evaluate the short-term results. The standards adopted three grades (1: mild, 2: moderate and 3: severe) for each complication.[5] We focussed on the major complications (grades 2 and 3) (Table 1).

Patient demographics, including age, sex, the maximal anteroposterior aneurysm diameter, statin use, aspirin use and the rates of massive atheroma in the thoracic aorta are shown in Table 2.

Table 1
Classification and grades of complication severity.

Complication	Grades
Deployment-related complication	
Peripheral embolization	1 Resolution with embolectomy without tissue loss
	2 Minor tissue loss, including toe or ray amputation
	3 Major amputation or significant tissue loss
Access site (wound) infection	1 Resolved with oral antibiotics
	2 Operative drainage, intravenous antibiotics
	3 Major debridement or drainage with laparotomy
Implant-related complication	
Graft infection	1 Apparently resolved or controlled with antibiotics
	2 Graft removal with extraanatomic or in situ repair
Limb occlusion	1 Resolved at primary procedure
	2 Limited retroperitonetal repair or thrombectomy
	3 Bypass or conversion
Buttock/leg claudication/ischaemia	1 Transient
	2 Persistent but not disabling
	3 Sufficiently disabling to necessitate intervention
Systemic complication	
Cardiac	1 Little or no haemodynamic consequence
	2 Symptomatic necessitating intravenous medication, percutaneous transluminal coronary angioplasty. Stent therapy
	3 Severe haemodynamic dysfunction necessitating resuscitation, cardiac arrest, or fatal outcome
Pulmonary	1 Prompt recovery with medical treatment
	2 Prolonged hospitalization or intravenous antibiotics
	3 Prolonged intubation, tracheostomy, deterioration in pulmonary dysfunction, O2 dependence
	4 or fatal outcome
Renal insufficiency	1 No dialysis
	2 Temporary dialysis, prolonged hospitalization, permanently reduced renal function
	3 Permanent dialysis, transplant, or fatal outcome
Cerebrovascular	1 Temporary deficit with recovery within 24 h
	2 Delayed recovery, infarct on CT or magnetic resonance, permanent deficit with mild impairment
	3 Severe impairment or fatal outcome
Deep vein thrombosis	1 Anticoagulation therapy, inferior vena cava filter
	2 Surgical or lytic therapy
Pulmonary embolism	1 Anticoagulation therapy, inferior vena cava filter
	2 Haemodynamic instability, endovascular or surgical therapy, or fatal outcome
Coagulopathy	1 Transfusion therapy
	2 Surgical intervention or fatal outcome
Bowel ischaemia	1 Recovered without invtervention
	2 Recovered with intravenous antibiotics or total parenteral nutirition
	3 Bowel resection, or fatal outcome
Spinal cord ischaemia	1 Resolution within 24 h
	2 Resolution within 1 month or minor permanent deficit, able to walk without support
	3 Major permanent deficit

Massive atheroma of the 'thoracic' aorta was defined as an atheroma with the following characteristics: (1) thickness ≥5 mm, (2) circumference of the thoracic aorta ≥75% and (3) length ≥100 mm.

Table 2
Basic demographics and preoperative characteristics of the EVAR and the OS groups.

Variables	EVAR ($n = 28$)	OS ($n = 22$)	P-value
Age	75.8 ± 6.3	74.7 ± 8.0	0.60
Sex (male:female)	27:1	19:3	0.19
Aneurysmal diameter			
(antero-posterior)(mm)	51.5 ± 9.8	54.2 ± 10.8	0.36
Massive thoracic atheroma	8/28	2/22	0.11
Aspirin use	8/28	7/22	0.80
Statin use	10/28	4/22	0.17
Co-morbidities			
Elder age (>80)	8/28	7/22	0.80
Hypertension	17/28	16/22	0.37
Diabetes Mellitus	4/26	6/22	0.25
Ischemic heart disease	5/28	11/22	0.01
Cerebrovascular disease	4/28	3/22	0.94
Chronic kidney disease	5/28	3/22	0.68
Glasgow aneurysm score	80.9 ± 9.6	81.4 ± 10.4	0.42

Patient co-morbidities including advanced age (≥80 years), hypertension, diabetes mellitus, ischaemic heart disease, cerebrovascular disease and chronic kidney disease as well as the Glasgow Aneurysm Score (GAS) are shown in Table 2. The GAS is one of the most useful methods for predicting the prognosis of patients who undergo OS; it is defined by the following equation: GAS = age + (17 for shock) + (7 for myocardial disease) + (10 for cerebrovascular disease) + (14 for renal disease).[6,7] Our definitions of cardiac, cerebrovascular and renal diseases are the same as those described by Samy.[6]

Two commercially available devices were used in this study: a Gore Excluder® AAA endoprosthesis (W.L. Gore and Associates, Newark, DE, USA) and a Zenith® endovascular graft (COOK Medical Inc., Bloomington, IN, USA). The Excluder and Zenith were used in 17 and 11 patients, respectively. Regarding the neck anatomy, nine patients did not meet the instructions for use of the devices (length ≥15 mm, neck angulation <60° and no severe calcification). None of the 28 patients exhibited intra- or post-operative type I endoleaks. Touch-up using balloons for the proximal neck was performed in all cases to prevent initial type I endoleaks. In the OS procedures, straight and bifurcated graft replacements were performed in six and 14 patients, respectively. Suprarenal clamping was performed in four patients; the clamping times were 12, 24, 49 and 59 min in these patients.

The eosinophil blood count and urine protein, which indicate one of the clinical aspects of cholesterol crystal embolism (CCE), were examined at three time points: preoperatively, during the hospital stay and within 6 months after discharge. The extent of proteinuria was graded as −, ±, 1+, 2+ or 3+.

Differences between the two groups were analysed using unpaired Student's t-tests. All-cause mortality was calculated using the Kaplan–Meier method. We used the log-rank test to detect differences between the two groups. Values are reported as mean (standard deviation (SD)). The level of significance was set at $P < 0.05$.

Results

The EVAR and OS groups were comparable with respect to age, sex, and almost all co-morbidities (Table 2). There were significant baseline differences with respect to ischaemic heart disease and short neck ($P = 0.01$). GAS was not significantly different between these high-risk patient groups.

Patients in the EVAR group had significantly less intra-operative blood loss (EVAR vs. OS: 167 ml [124] vs. 1643 ml [1181]; $P < 0.001$), shorter operation times (173 min [61] vs. 272 min [79]; $P < 0.001$), and a shorter postoperative hospital stay (10.8 d [5.5] vs. 20.6 d [9.6]; $P < 0.001$). No perioperative death (30-day mortality) or secondary intervention occurred in either group during the follow-up period.

Table 3
outcomes of the EVAR and OS groups.

	EVAR		OS		P-value
Perioperative mortality	None		None		–
Early complication (in-hospital)	3 cases		5 cases		0.68
	Case 1	Renal (gr.2) Peripheral (gr.2)	Case 1	Renal (gr.2) Cardiac (gr.2) Bowel (gr.2)	–
	Case 2	Renal (gr.2) Bowel (gr.2)	Case 2	Spinal (gr.2)	
	Case 3	Renal (gr.2) Cardiac (gr.3)	Case 3	Cardiac (gr.2)	
			Case 4	Renal (gr.2)	
			Case 5	Bowel (gr.2)	
Late complication (outpatient within 6 mo)	7 cases		None		0.01
	Case 1	Renal (gr.3) Peripheral (gr.2)	–		–
	Case 2	Renal (gr.3) Bowel (gr.2)			
	Case 4	Bowel (gr.2)			
	Case 5	Bowel (gr.2)			
	Case 6	Renal (gr.2)			
	Case 7	Renal (gr.2)			
	Case 8	Renal (gr.2)			

gr: grades; Renal: Renal insufficiency; Peripheral: Peripheral embolization; Bowel: Bowel ischaemia; Spinal: Spinal cord ischaemia.

Major complications (grades 2 and 3) were included in this study and categorised as early (in-hospital) or late (outpatient, within 6 months). In the OS and EVAR groups, five and three patients exhibited early complications, respectively; however, the difference was not significant ($P = 0.68$). By contrast, the EVAR group had seven patients who developed late complications, compared to 0 patients in the OS group ($P = 0.011$; Table 3). Among the seven patients with late complications, two had both initial and continually worsening complications and were counted twice (Table 4). Both cases with normal renal functions exhibited renal deterioration leading to permanent dialysis. All five patients with 'late' renal complications had normal preoperative creatinine levels (<1.0 mg dl^{-1}).

Among the five patients with early complications in the OS group, suprarenal clamping was performed in two; the clamping times were 24 and 59 min.

The patency of the inferior mesenteric artery (IMA) and bilateral hypogastric arteries (HAs) was examined with postoperative contrast CT scan and ultrasonography. IMA was excluded in all

Table 4
Details of complications in the EVAR group. Two cases (case 1 and 2) had initial and continuous worsening of complications and were counted twice.

	Early complication	Late complication
Case 1	Cr level got worse to 2.5 Blue toe syndrome	Permanent dialysis Blue toe syndrome got worse
Case 2	Cr level got worse to 2.5 Ischaemic colitis (severe diarrhoea)	Permanent dialysis Ischaemic colitis (remission and progression)
Case 3	Temporary dialysis Acute myocardial infarction	
Case 4		Ischaemic colitis (severe diarrhoea and fever)
Case 5		Ischaemic colitis (severe diarrhoea and fever)
Case 6		Cr level got worse to 2.2
Case 7		Cr level got worse to 3.0
Case 8		Cr level got worse to 2.7

patients in the EVAR group. Four patients exhibited lateral HA occlusion; intra-operative coil embolisation was performed in three patients, and the ipsilateral HA was originally occluded in one patient. These four patients exhibited neither early nor late bowel complications. In the OS group, one patient underwent IMA reconstruction with bilateral HA ligature, and another patient exhibited IMA and HAs occlusion; neither of these two patients had any complications.

The overall survival rates of the EVAR and OS groups were calculated using Kaplan–Meier analysis. The EVAR group had significantly higher mortality than the OS group ($P = 0.011$) (Fig. 1). The causes of death varied widely: one due to thoracic–aortic dissection; two sudden deaths; one gastric perforation; one gastrointestinal bleeding; one remnant gastric cancer; two lung cancers and one of unknown cause in the EVAR group. No direct relationships between late-phase complications and the cause of death were found. Meanwhile, one case of pneumonia and renal failure each were detected in the OS group.

In the OS group, preoperative percutaneous coronary intervention (PCI) was performed in six patients; no patients received PCI in the EVAR group. Coronary artery bypass grafting was not performed in either of the groups.

Mild blood eosinophilia (absolute eosinophil count, 600–1500 cells/μl)[8] was not observed in the OS group but was observed in 10 patients in the EVAR group; Three, six, and one patients exhibited eosinophilia in hospital, after discharge, and throughout the postoperative follow-up period. Neither moderate nor severe eosinophilia (absolute eosinophil count >1500 cells/μl) was detected in either group. Among the three EVAR patients with early complications, only one exhibited eosinophilia after discharge (Table 3). Among the seven EVAR patients with late complications, the patients in cases 4 and 7 showed eosinophilia in-hospital; those in cases 1 and 8 showed eosinophilia after discharge. Increases in the urine protein levels were examined in patients for whom data were available: one of 14 OS patients (± to 1+) and five of 16 EVAR patients (1+ to 3+, ± to 3+, − to 3+, ± to 1+, ± to 3+).

Discussion

Aortic surgery for shaggy aorta sometimes results in catastrophic shower embolisation. Endovascular procedures are considered a contraindication for atheromatous aorta because the catheter and other endovascular devices can extensively 'rake off' atheromatous debris.[1,2,9] However, very little reliable evidence supporting the use of EVAR for shaggy aorta has been obtained in large-scale studies. Furthermore, shaggy aorta has not been defined clearly. In the present study, we defined a shaggy aorta as a "massive aortic atheromatous thrombus" (infrarenal neck and thoracic aorta) and validated this definition. At present, the specific

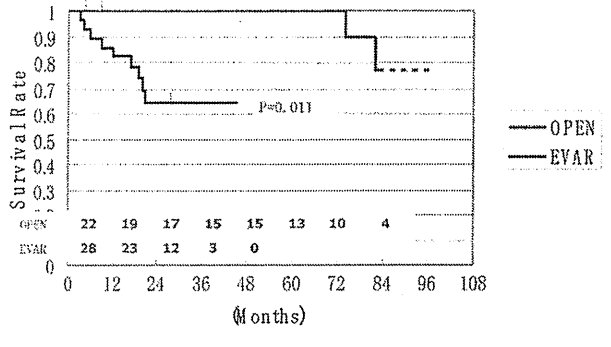

Figure 1. The Kaplan–Meier curve shows superior overall survival in the OS group. The log-rank test revealed a significant difference between groups ($P = 0.011$).

roles of endovascular procedures are attracting increasing attention; thus, it is necessary to understand the risks of manipulation-related embolisation. We limited the follow-up period to within 6 months after procedures to evaluate complications because causal relationships between manipulations and complications become less clear beyond this time.

Gitlitz et al. first reported the use of EVAR in patients with massive neck atheroma; they also conclude that the presence of a neck atheroma may not necessarily be a contraindication to EVAR because of the lack of primary endoleaks, migration and significant distal embolisation.[10] However, two patients (10.5%; 2/19) exhibited embolisation; one asymptomatic renal infarction and one asymptomatic embolisation of the tibial artery. Available records do not detail the time courses of complications including renal function and ischaemic colitis which might be due to CCE; therefore, the conclusion regarding the suitability of EVAR for shaggy aorta may require further investigation.

Interestingly, late outcomes in our study were clearly different between the two groups despite the fact that early outcomes were similar. We intuitively recognised that late complications (which are usually included in short-term results) might be affected by inflammation due to CCE. Clinical features resulting from shower embolisation varied including abnormal kidney function, cutaneous findings (e.g. livedo reticularis), blue toe syndrome and gastrointestinal ischaemia. CCE is a facet of such showers[11] and might result in delayed clinical symptoms. Weeks or months may pass before scattering and migration of cholesterol crystals induce an endothelial inflammatory reaction leading to complete obstruction.[9,11]

Nine of the 10 late complications in the present study occurred in two organs; the kidneys and the bowel. Renal dysfunction is thought to be caused by two main factors: nephrotoxicity in response to contrast agents and nephropathy due to CCE. Contrast agents induce renal vasoconstriction and interfere with water and sodium absorption by the renal tubules; this leads to increased vascular resistance and decreased glomerular filtration rates.[12] In cases of chronic renal insufficiency, contrast agents are excreted at a slow rate, which increases the risk of nephrotoxicity.[13] By contrast, massive crystals in the renal arterial tree exhibit a sub-acute time course via an inflammatory reaction. They are difficult to distinguish, which may be the reason why most studies finding adverse events after AAA repair do not distinguish renal dysfunction types.

We hypothesise that the bowel ischaemia found in the present series was derived from a CCE scenario rather than from simple blood-flow shortage. No HA-occluded cases (four, and two in the EVAR and OS groups each) in this study exhibited bowel ischaemic complications, which potentially supports our hypothesis. However, ischaemic colitis itself results from the use of perioperative antibiotics or haemodynamic realignment of colonic marginal arteries. As in renal CCE, a definite diagnosis of colonic complications is difficult to make because it requires invasive organ biopsy.[14] Since the onset of CCE is sometimes late and fatal, monitoring clinical features even after hospital discharge and over-diagnosing of CCE in EVAR patients with shaggy aorta should be performed.

For diagnostic methods less invasive than tissue biopsy, we examined the laboratory data of eosinophil and urine protein.[8,15] Among 29 patients in the EVAR group whose data were available, 10 patients (34%) exhibited mild eosinophilia, which might indicate some inflammatory reaction after the catheter manoeuvre. However, the time course of complications possibly related to CCE did not coincide with eosinophilia. Therefore, eosinophil data is only one of the non-specific prognostic factors for CCE complication. Similarly, proteinuria was more common in the EVAR group. Although it is certain that proteinuria indicates deteriorating renal function, it cannot be used as a very specific indicator of CCE.[11]

The main limitation of the present study is that we did not categorise the shapes and properties of the atheromas. Normally, a protruding atheroma is easily exfoliated by wire manipulations. In addition, a fragile atheroma, similar to a 'soft' carotid plaque, might be present.[16] A larger study is required to categorise the types of atheromas; magnetic resonance imaging or intravenous ultrasonography may be useful for evaluating atheroma vulnerability.

In addition, massive atheroma in the thoracic aorta, which was not significantly different between groups ($P = 0.11$) but probably affected the co-morbidities in both groups, might affect shower embolisation. In this study, it was difficult to evaluate the effects of thoracic massive atheroma with the small number of patients. Five of the eight patients in the EVAR group and none in the OS group had postoperative complications. We cannot ignore the effects of the stiff wire delivered up to the descending thoracic aorta or arch in a typical EVAR manoeuvre. However, we think that complete obstruction and touch-up on the atheroma-rich aneurysmal neck is far more hazardous than the effect of the wire movement in the thoracic aorta.

In conclusion, compared to OS patients, EVAR patients with a massive neck atheroma tend to develop very late-phase complications perhaps related to CCE. OS should be the first-line treatment for massive atheroma because of its better outcomes than EVAR.

Conflict of Interest

None.

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References

1 Hollier LH, Kazmier FJ, Ochsner J, Bowen JC, Procter CD. "Shaggy" aorta syndrome with atheromatous embolization to visceral vessels. *Ann Vasc Surg* 1991;5:439–44.
2 Zempo N, Sakano H, Ikenaga S, Harada M, Yamashita A, Morikage N, et al. Fatal diffuse atheromatous embolization following endovascular grafting for an abdominal aortic aneurysm: report of a case. *Surg Today* 2001;**31**:269–73.
3 Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG, EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;**364**:843–8.
4 Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;**351**:1607–18.
5 Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002;**35**:1048–60.
6 Samy AK, Murray G, MacBain G. Glasgow aneurysm score. *Cardiovasc Surg* 1994;**2**:41–4.
7 Patterson BO, Holt PJE, Hinchliffe R, Loftus IM, Thompson MM. Predicting risk in elective abdominal aortic aneurysm repair: a systematic review of current evidence. *Eur J Vasc Endovasc Surg* 2008;**36**:637–45.
8 Tefferi A. Blood eosinophilia: a new paradigm in disease classification, diagnosis, and treatment. *Mayo Clin Proc* 2005;**80**:75–83.
9 Meyrier A. Cholesterol crystal embolism: diagnosis and treatment. *Kidney Int* 2006;**69**:1308–12.
10 Gitlitz DB, Ramaswami G, Kaplan D, Hollier LH, Marin ML. Endovascular stent grafting in the presence of aortic neck filling defects: early clinical experience. *J Vasc Surg* 2001;**33**:340–4.
11 Paraskevas KI, Koutsias S, Mikhailidis DP, Giannoukas AD. Cholesterol crystal embolization: a possible complication of peripheral endovascular interventions. *J Endovasc Ther* 2008;**15**:614–25.
12 El Sayed AA, Haylor JL, El Nahas AM, Salzano S, Morcos SK. Haemodynamic effects of water-soluble contrast media on the isolated perfused rat kidney. *Br J Radiol* 1991;**64**:435–9.
13 Mehta M, Veith FJ, Lipsitz EC, Ohki T, Russwurm G, Cayne NS, et al. Is elevated creatinine level a contraindication to endovascular aneurysm repair? *J Vasc Surg* 2004;**39**:118–23.
14 Miller A, Marotta M, Scordi-Bello I, Tammaro Y, Marin M, Divino C. Ischaemic colitis after endovascular aortoiliac aneurysm repair. *Arch Surg* 2009;**14**:900–3.
15 Kato A, Ohtsuji A, Terada T, Goto T, Fukasawa H, Yasuda H, et al. Recovery from hemodialysis therapy in a patient with renal cholesterol crystal embolism. *Nephron* 2002;**92**:240–3.
16 Oikawa M, Ota H, Takaya N, Miller Z, Hatsukami TS, Yuan C. Carotid magnetic resonance imaging. A window to study atherosclerosis and identify high-risk plaques. *Circ J* 2009;**73**:1765–73.

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Surgical Treatment of Patients with Congenital Vascular Malformation-associated Aneurysms

J. Suzuki, T. Miyata*, K. Hoshina, H. Okamoto, H. Kimura, K. Shigematsu

Division of Vascular Surgery, Department of Surgery, Graduate school of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

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Surgical treatment

Abstract *Objectives:* Aneurysms associated with congenital vascular malformation (CVM) comprise critical complication. We review our experience with extracranial CVM-associated aneurysms and attempt to clarify their clinical features.
Patients and methods: The prevalence, site, size and morphology of the accompanying aneurysms of 48 consecutive CVM patients, who were managed at our hospital from 1999 to 2008, were evaluated. After diagnosis or treatment, the patients were followed up, and the recurrence of aneurysms and patient survival were assessed.
Results: CVM-associated aneurysms were found in 14 patients (29%). CVMs were classified according to the Hamburg classification. The patients were classified into groups as follows: four (31%), in the 'predominantly arteriovenous (AV) shunting defect type'; eight (47%), 'combined vascular defects + predominantly AV shunting defects type'; and two (11%), 'combined vascular defects type'. All aneurysms except one situated at the CVM were saccular, whereas nine were fusiform aneurysms; all the ruptured aneurysms and seven out of the nine enlarging aneurysms were saccular. Surgical treatment was performed 8 times in six patients. During the postoperative follow-up period, recurrence and an aneurysm rupture were encountered in one patient each.
Conclusion: Aneurysm is not a rare complication of CVM. It is important to treat CVM before the emergency presents. In addition to the treatment for malformation, regular screening for and proper management of the aneurysms in CVM patients are indispensable.

Congenital vascular malformation (CVM) is a relatively rare disease. It can occur anywhere in the body, including the cranium, face, abdomen or extremities, and can be potentially limb- or life threatening. Congestive heart failure (CHF) could be induced in the presence of arteriovenous (AV) shunts because of increased cardiac output. Major bleeding is also one of the severe complications. Patients also complain of brush or mass lesions, leg-length differences, venous stasis symptoms and cutaneous ulcers.

* Corresponding author. Tel.: +81 3 5800 8653; fax: +81 3 3811 6822.
E-mail address: tmiyata-tky@umin.ac.jp (T. Miyata).

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The treatment strategy for CVM should focus on both the malformation and the secondary disorders. The goal of CVM treatment, especially for the extra-truncular type originating at the early stage of embryogenesis, should be complete destruction of the nidus that retains the mesenchymal cell characteristics. This includes occlusion of the nidas and fistura or surgery followed by sclerotherapy using ethanol to destroy the nidus and its mesenchymal cells to eliminate the risk of recurrence. Ligation of feeding vessels alone results in the enlargement of numerous smaller feeding and draining vessels.[1] However, aggressive treatment of CVM in the limb always carries a risk of limb loss.

Although a critical complication, CVM-associated aneurysms have infrequently been described.[2] After experiencing a few cases of aneurysm rupture associated with extracranial aneurysm rupture, we reviewed our experience and attempt to clarify its clinical features.

Patients and Methods

We reviewed 48 consecutive patients with extracranial CVM, who were managed at the University of Tokyo Hospital from 1999 to 2008. We diagnosed CVM in the patients on the basis of clinical presentations and/or computed tomography (CT), magnetic resonance imaging (MRI) and/or conventional angiography. CVMs were classified according to the Hamburg classification (Table 1)[3] of vascular anomalies and malformations. Aneurysmal lesions were defined as follows: (1) saccular-form proptosis and (2) dilatation more than twice the normal size. We evaluated the prevalence, site, size and morphology of the aneurysm accompanying the CVM. We then assessed the growth or recurrence of the aneurysm as well as patient survival during the follow-up period; the follow-up visits were conducted in an outpatient clinic once or twice a year.

Results

During the study, 48 patients (24 men and 24 women) with a mean age (SD) of 37.1 (17.9) years at the initial visit were diagnosed with extracranial CVM, that were located in the body trunk in nine patients, in the upper extremity in 14 (right, seven; left, seven) and in the lower extremity in 31 (right, 16; left, 15). Multiple lesions were detected in five patients: in the body trunk and left-lower extremity in two, in the body trunk and right-lower extremity in one patient, in the bilateral lower extremities in one and in the body trunk and both right upper and lower extremities in one. Fourteen patients (29%) had CVM-associated aneurysms. Of these 14 patients, two (14%) exhibited New York Heart Association (NYHA) grade III CHF. On the contrary, 34 patients without aneurysms did not show any signs of CHF. Each CVM was classified according to the Hamburg classification (Table 2). The patients with aneurysms were classified into the following groups: four (31%) patients in the 'predominantly AV shunting defects type'; eight (47%), 'combined vascular defects + predominantly AV shunting defects type'; and two (11%), 'combined vascular defects type'. As per this classification, Parkes–Weber syndrome (PWS) can be included in the 'combined vascular defects + predominantly AV shunting defects type',

Table 1 (A) Hamburg Classification[a,6]-of congenital vascular malformations (CVM) – types; (B) Hamburg Classification of CVM[b]: forms – embryological subtypes.

(A)
Predominantly arterial defects
Predominantly venous defects
Predominantly arteriovenous (AV) shunting defects
Predominantly lymphatic defects
Combined vascular defects
(B)
Extratruncular forms
Infiltrating, diffuse
Limited, localized
Truncular forms
Aplasia or obstruction
Hypoplasia, aplasia, hyperplasia
Stenosis, membrane, congenital spur
Dilation
Localized (aneurysm)
Diffuse (ectasia)

[a] Based on the consensus on CVM through the International Workshop in Hamburg, Germany, 1988, and subsequently modified -Capillary malformation was not included Developmental arrest at the different stages of embryonic life: earlier stage – extratruncular form; later stage – truncular form.
[b] Both forms may exist together; may be combined with other various malformations (e.g. capillary, arterial, AV shunting, venous, haemolymphatic, and/or lymphatic); and/or may exist with haemangioma.

Table 2 Patient characteristics.

Gender (male:female)	24:24
Age (years)	37.1 (range, 2–82)
Mean follow-up period (months)	35.5 (range, 1–146)
Lesion of CVM	
Upper extremity (right:left)	7:7[d]
Lower extremity (right:left)	16:15[d]
Body trunk	9[d]
CVM type (Hamburg classification)	
AV shunting[a]	13 (4 aneurysms, 31% and 1 heart failure)
Combined + AV shunting[b]	17 (8 aneurysms, 47% and 1 heart failure)
Combined type[c]	18 (2 aneurysms, 11% and no heart failure)

[a] Predominantly arteriovenous (AV) shunting defects type in Humburg Classification.
[b] Combined vascular defects + predominantly AV shunting defects type in Humburg Classification.
[c] Combined vascular defects type in Humburg Classification.
[d] Duplicative lesions of the body trunk and left-lower extremity in 2 patients; body trunk and right-lower extremity in 1; bilateral lower extremity in 1; and body trunk, and right-upper and right-lower extremities in 1.

whereas the Klippel–Trenaunay syndrome (KTS) can be included in the 'combined vascular defects type'. In each of the 'predominantly AV shunting defects type' and the 'combined vascular defects + predominantly AV shunting defects type', one patient was found to have CHF.

The demographic data of the patients with aneurysms are shown in Table 3. Fourteen patients had a total of 24 aneurysms, of which all but one was situated at the CVM. There were 15 saccular and nine fusiform aneurysms; all the ruptured aneurysms and seven out of the nine enlarging aneurysms were saccular in shape.

Our indications for surgery for CVM complicated by aneurysm were as follows: (1) a ruptured or an impending ruptured aneurysm, (2) an aneurysm enlarging during the follow-up, (3) an aneurysm with the risk of distal embolism with endovascular treatment and (4) CHF or uncontrollable bleeding expected to improve upon closure of the AV shunt. Surgical treatment was performed 8 times in six patients (patients #1–#6). During the postoperative follow-up period, recurrence and an aneurysm rupture was encountered in one patient each.

Of the eight patients (patients #7–#14) who were followed up without surgery, recent aneurysm enlargement was observed in two patients (patients #10 and #13); they were under consideration for surgical treatment. All patients survived, and none underwent limb amputation.

Model cases of CVM-associated aneurysm are presented below.

A case of ruptured aneurysm (Patient 1)

A 73-year-old woman with a CVM that was classified as a 'combined vascular defect + predominantly AV shunting defects type', had been conscious of the CVM in her left-upper extremity since childhood. After her condition was diagnosed 9 years previously, she discontinued her hospital visits until the rupture of the aneurysm at her left radial artery (Fig. 1(a)). She underwent emergency aneurysmectomy with ligation of both inflow and outflow vessels. An aneurysm that had also been discovered in her left brachial artery was also discovered at that time, but she had stopped visiting the hospital on her own. She

Table 3 The patients with the aneurysm associated with CVM.

Patient No. (admission number)	Age, Gender	CVM type	CVM location	Aneurysm				Heart failure	Treatment strategy	Follow-up (month)	Indication for surgery
				Specified artery	Size (mm),		form				
1(1)	73,F	C + AV	Lt.arm	Lt.radial A	50	s		no	surgery	108	
(2)				Lt.brachial A	10	s		no	surgery	82[a]	Rupture
2(1)	50,F	C + AV	Rt.arm-chest	Rt.ulnal A	18	s		no	surgery	24	Rupture
(2)				Rt.radial A	8	s		no	surgery	15[a]	rapid enlargement
				Rt.ulnal A	10	s					
				Rt.AIOA	10	s					
3	37,F	CV	Lt.leg	Lt.popliteal A	36	f		no	surgery	117	Enlargement, for limb salvage
4	68,F	C + AV	Lt.groin-thigh	Lt.CFA-DFA	25	f		yes	surgery	21	Severe heart failure
				Aorta	46	f			w/w		
				Lt.CIA	45	f					
5	64,M	AV	pelvis	Rt.IIA	50	s		yes	surgery	37	deteriorating Heart failure
6	55,F	C + AV	Rt.arm	Rt.brachial A	30	s		no	surgery	23	rupture
7	73,M	AV	pelvis	Lt.IIA	25	s		no	w/w	1	
8	28,M	AV	Rt.pararenal	Rt.renal A	15	s		no	w/w	2	
9	53,M	AV	Rt.calf-foot	Rt.PTA	30	f		no	w/w	7	
10	10,M	C + AV	Rt.leg	Rt.ATA	12	s		no	w/w	123	
				Rt.peroneal A	20	s					
				Rt.PTA	12	f					
11	70,F	C + AV	Rt.leg	Rt.obturator A	15	s		no	w/w	35	
				Rt.SFA	11	s					
12	33,F	C + AV	Rt.forearm	Rt.radial A	10	f		no	w/w	19	
				Rt.ulnal A	10	f					
13	47,M	C + AV	Rt.calf	branches	100	s		no	w/w	18	
14	28,M	CV	Lt.upper arm	Lt.brachial A	18	f		no	w/w	16	

C + AV, Combined vascular defects + Predominantly arteriovenous (AV) shunting defects type; CV, Combined vascular defects type; AVS, Predominantly AV shunting defects type; AIOA, anterior interosseous artery; CFA, common femoral artery; DFA, deep femoral artery; CIA, common iliac artery; IIA, internal iliac artery; PTA, posterior tibial artery; ATA, anterior tibial artery; SFA, superficial femoral artery; f, fusiform; s, saccular; w/w, taking a wait and watch approach.

[a] The follow-up terms from the last operation.

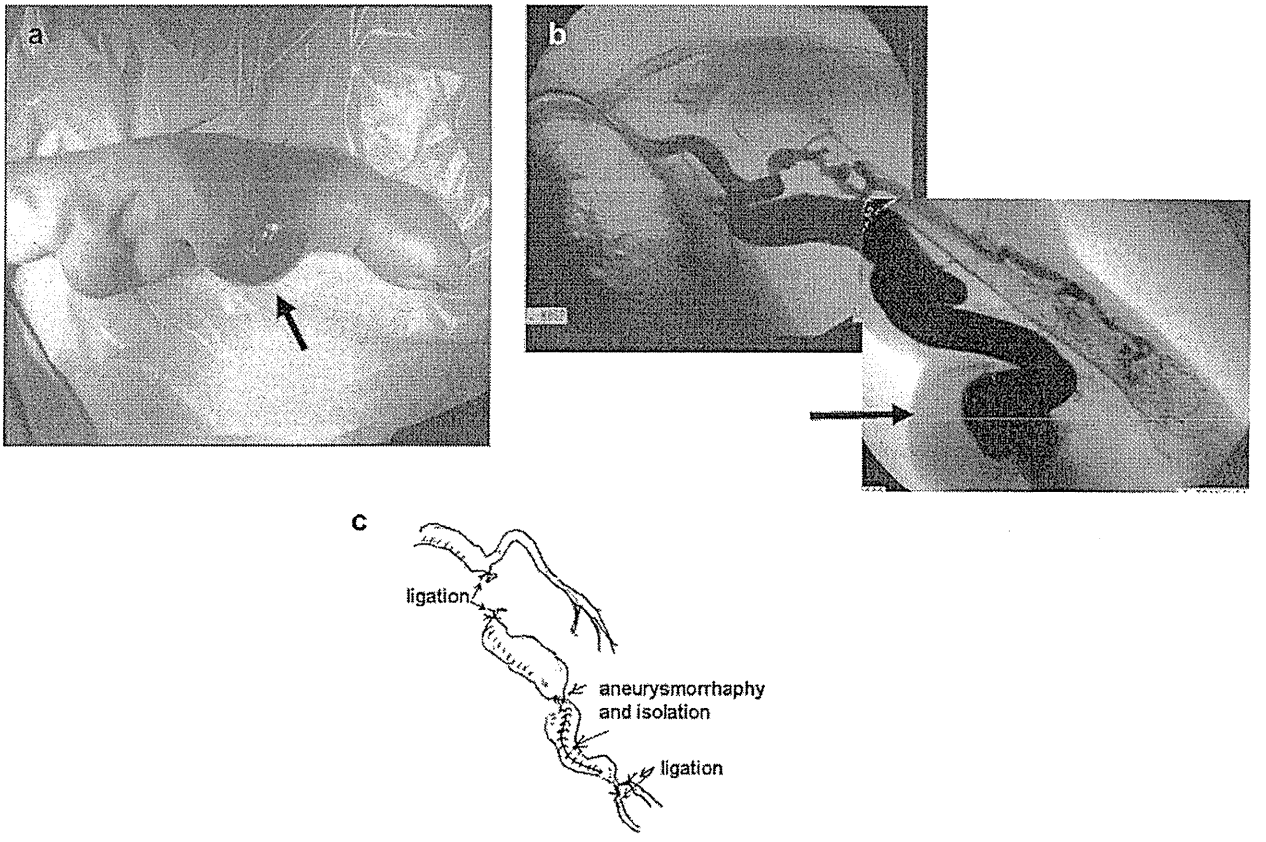

Figure 1 Patient 1. a, Physical findings of the left forearm. Marked swelling and purpura were observed at the forearm (arrow). b, Angiography of the left forearm at the time of first rupture. The aneurysm of the left brachial artery was recognized at this time (arrow). c, Illustration of the surgery performed to treat the rupture of the brachial artery aneurysm. The aneurysm was isolated by the ligation of inflow and outflow arteries.

presented again after 15 months with ruptured aneurysm (Fig. 1(b) and (c)). Aneurysmorrhaphy and aneurysm isolation were performed. No aneurysm recurrence occurred thereafter.

A case of ruptured aneurysm (Patient 2)

A 50-year-old woman had a CVM in the rightupper extremity since childhood. She had undergone surgical shunt closure 17 times at other hospitals. She experienced sudden swelling of her right forearm immediately prior to the admission to our hospital. After being diagnosed with ruptured aneurysm in the right ulnar artery, she underwent aneurysmectomy and AV shunt closure at our hospital. Six months later, three new aneurysms developed in her right forearm, and she subsequently received additional aneurysmectomies.

A case of CVM-associated heart failure (Patient 4)

A 68-year-old woman with CVM that was classified as a 'combined vascular defects + predominantly AV shunting-defects type', was diagnosed with CHF. The CVM was located in her left thigh, and the increased shunt flow complicated the CHF. She had aneurysms at the abdominal aorta, left common iliac artery, left common femoral artery (CFA) and left deep femoral artery (DFA). Dilated left iliac and femoral veins were also observed (Fig. 2(a) and (b)). Surgical disconnection of the DFA from the CFA was simultaneously performed together with CFA banding under blood pressure monitoring at the ankle (Fig. 2(c)). After the surgery, the patient's CHF improved from 3rd to 2nd degree according to the NYHA classification of cardiac performance, and her brain natriuretic peptide (BNP) level decreased from 552 to 246 pg ml^{-1}. One year later, she underwent additional endovascular treatments in her left leg by using a sclerosing agent for the nidus and the feeding vessels.

A case of uncontrollable bleeding (Patient 6)

A 55-year-old woman with CVM that was classified as a 'combined vascular defects + predominantly AV shunting defects type', was admitted to our hospital because of bleeding from the AVM at the top of her right finger. She had an aneurysm at the right brachial artery (RBA). Because the bleeding was difficult to control and the aneurysm was large, she had undergone emergency surgical aneurysmectomy with ligation of the RBA (Fig. 3).

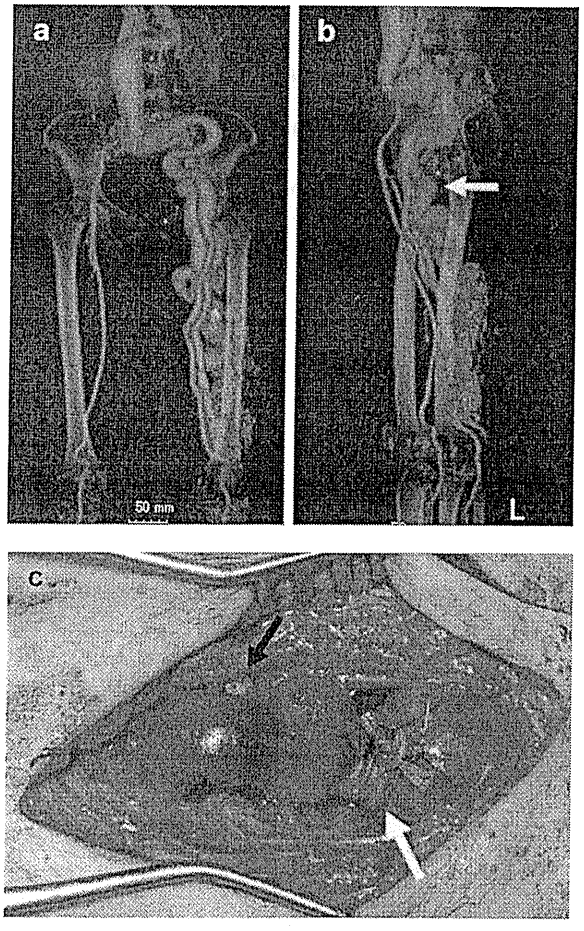

Figure 2 Patient 4. a,b, Preoperative computed tomography angiogram (a, frontal; b, from the left side). The congenital vascular malformation located at the left thigh was mainly fed through the aneurysm at the left deep femoral artery (DFA) (arrow). Aneurysmal dilatation was recognized at the abdominal aorta, left common iliac artery, left common femoral (CFA), and left DFA. c, Photograph after DFA cutoff (stump; black arrow)and CFA banding (white arrow). CFA banding was performed to monitor ankle pressure. After the banding, pulmonary arterial pressure and cardiac output decreased from 36 to 34 mmHg and 8 to 6 L/min, respectively.

After the surgery, the bleeding could be controlled, and the swelling of the CVM in her forearm and hand considerably improved.

Discussion

Only a few reports of extracranial CVM-associated aneurysms are available, including the report of Akagi et al. on six cases of Klippel–Trenaunay syndrome.[2] Aneurysms associated with CVM are not involved in either its clinical classification[4] or its treatment indications, as propounded by Schobinger staging.[5] Although the system of referrals from other hospitals and clinics to our hospital

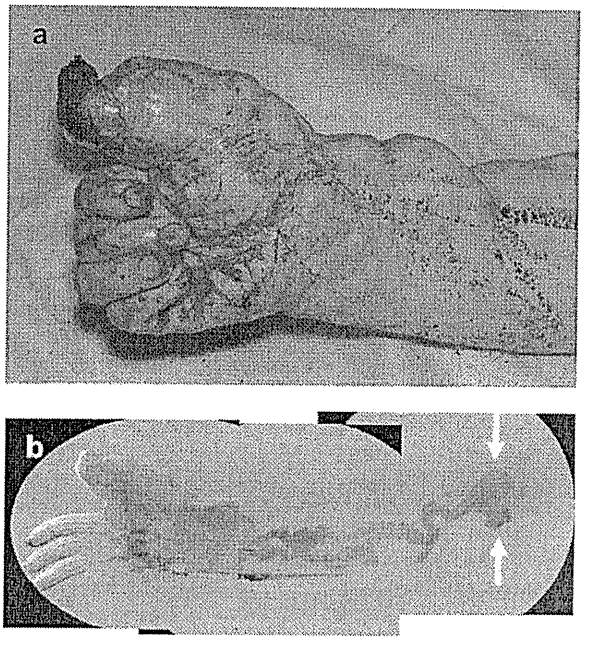

Figure 3 Patient 6. a, Physical finding of the right hand upon admission because of bleeding from an ulcerative lesion at the top of the first digit. b, Angiography; 2 aneurysms were recognized at the right brachial artery (arrow).

mightpredispose our results to some bias, the present study suggests that aneurysm prevalence was 29% in patients with extracranial CVM, indicating that aneurysm formation is not a rare complication of CVM.

The pathogenesis of aneurysm formation can partly be explained by the congenital weakness of the vessel walls[6] in CVM patients. In addition, the secondary reaction to the abnormal haemodynamic stress caused by continuous high pressure and high-flow turbulence might partly contribute to aneurysm formation in CVM, especially in the presence of AV shunts. The prevalence of aneurysm formation was higher in patients with CVM and AV shunts than in those without shunts. The reappearance of aneurysms shortly after the resection in some patients with AV shunts may support our suspicion.

We considered aneurysm rupture or enlargement as indicator for the surgical treatment of CVM-complicated aneurysms. The risk factors of aneurysm rupture in the presence of CVM have not been clarified, and the aneurysm size, shape and growth rate should be taken into account while considering surgery. In this study, we reconfirmed that saccular-form aneurysms tend to enlarge or rupture. Surgery is not the basis for treatment, but is part of a multidisciplinary approach for treating patients with AVM. In general, a myriad number of AV shunts, ranging from microscopic to macroscopic in size, may occur in patients with CVM. Major surgery for CVM contains significant risks of bleeding and associated complications.[7] We restrict surgery to CVM mainly for the treatment of accompanying lesions, including aneurysms, bleeding and/or large AV fistula causing CHF. Considering the possible need for repeated treatment, minimally invasive techniques, such as

catheter embolisation and sclerotherapy, should be the basis of treatment, and surgery should be minimally used. Irrespective of the treatment procedure, use of repeated condition-specific therapies is indispensable for CVM patients. Rockman et al. reported that >70% of CVM patients had already undergone initial therapies.[8] In our series, one patient underwent 17 surgical shunt ligations. Mendel at al. have reported 12 recurrences in 17 cases of surgically treated CVMs of the upper extremity.[9] In another report, 12 CVM patients were mainly treated with endovascular embolisation, and eight experienced recurrence.[10] Some patients in our series have not undergone any additional treatments, such as endovascular procedures, after surgery. Although we never opine that endovascular treatment is not necessary and that 'wait and watch' is the best choice for CVM patients, we selected a 'wait and watch approach' in most cases, taking into account the results of previous reports.

Aggressive treatment for CVM in the limb may result in critical limb ischaemia. In an emergency case (such as patient #1) involving ligation of the brachial artery connecting to the ruptured aneurysm, a lateral branch of the brachial artery might serve as an abnormal vessel feeding the nidus. We preserved the vessel fearing limb loss and eventually obtained a good long-term result. Ankle-pressure measurement was an effective monitoring tool for preventing ischaemic complications after major artery ligation. In addition, skin-perfusion-pressure measurement at distal sites with arterial compression may also be useful for predicting limb prognosis after arterial ligation.

There are some reports of CVM-associated CHF located in the extremities or body trunk.[3,8,11,12] In such cases, endovascular embolisation procedures were mainly performed for shunt closure with acceptable outcomes. However, in patient #4 of the present study, large inflow arteries and broad areas of AV shunt lesions led us to select femoral-artery ligation and banding as the surgical procedures to decrease the shunt flow, while avoiding necrosis, which might occur with catheter embolisation or sclerotherapy in high-flow conditions. In this case, after surgical closure of the large AV fistula, additional endovascular therapy was also performed for the other feeding vessels and the nidus.

We consider it necessary to search for the presence of aneurysms upon initial consultation or to examine for aneurysm formation during follow-up visits, especially in patients with CVM classified as 'predominantly AV shunting defect type' or 'combined vascular defects + predominantly AV shunting defects type'. Once an aneurysm is detected, regular follow-up to check its growth is mandatory. As our study possibly indicates that saccular aneurysms are likely to enlarge or rupture, such aneurysms should be observed more carefully. In some cases, planned preventive surgery is indicated before an aneurysm emerges.

Conclusion

Aneurysm is not a rare complication of extracranial CVM. In CVM patients, it is important to treat CVM before an aneurysm emerges. In addition to treatment for CVM, regular screening for and appropriate management of aneurysms in CVM patients are indispensable.

Conflict of Interest

None declared.

Funding

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References

1 Jacobowitz GR, Rosen RJ, Rockman CB, Nalbandian M, Hofstee DJ, Fioole B, et al. Transcatheter embolization of complex pelvic vascular malformations: results and long-term follow-up. *J Vasc Surg* 2001;**33**:51–5.
2 Akagi D, Ishii S, Kitagawa T, Nagawa H, Miyata T. Popliteal arterial aneurysm associated with Klippel–Trenaunay syndrome: case report and literature review. *J Vasc Surg* 2006;**43**:1287–9.
3 Lee BB, Laredo J, Lee TS, Huh S, Neville R. Terminology and classification of congenital vascular malformations. *Phlebology* 2007;**6**:249–52.
4 Lee BB, Do YS, Yakes W, Kim DI, Mattassi R, Hyon WS. Management of arteriovenous malformations: a multidisciplinary approach. *J Vasc Surg* 2004;**39**:590–600.
5 Kohout MP, Hansen M, Pribaz JJ, Mulliken JB. Arteriovenous malformations of the head and neck: natural history and management. *Plast Reconstr Surg* 1998;**102**:643.
6 Paes EH, Vollmar JF. Aneurysmal transformation in congenital venous angiodysplasia in lower extremities. *Int Angiol* 1990;**9**:90–6.
7 Maftei N, Howard A, Brown LC, Gunning MP, Standfield NJ. The surgical management of 73 vascular malformations and preoperative predictive factors of major haemorrhage—a single centre experience. *Eur J Vasc Endovasc Surg* 2009;**38**:488–97.
8 Rockman CB, Rosen RJ, Jacobowitz GR, Weiswasser J, Hofstee DJ, Fioole B, et al. Transcatheter embolization of extremity vascular malformations: the long-term success of multiple interventions. *Ann Vasc Surg* 2003;**17**:417–23.
9 Mendel T, Louis DS, Arbor A. Major vascular malformations of the upper extremity: long-term observation. *J Hand Surg* 1997; **22A**:302–6.
10 Carr MM, Mahoney JL, Bowen CV. Extremity arteriovenous malformations: review of a series. *Can J Surg* 1994;**37**:293–9.
11 White Jr RI, Pollak J, Persing J, Henderson KJ, Thomson JG, Burdge CM. Long-term outcome of embolotherapy and surgery for high-flow extremity arteriovenous malformations. *J Vasc Interv Radiol* 2000;**11**:1285–95.
12 Anoop TM, Sreejith P, Thomas JK, Gailin B, Jabber PK, Ittycheria CC, et al. Congenital subclavian arteriovenous malformation causing cardiac failure in an adult. *J Am Soc Echocardiogr* 2009;**22**:864. e5–6.

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Middle-term results of endovascular aneurysm repair in Japan: does intraoperative endovascular management against the hostile aneurysmal neck prevent the proximal type I endoleak?

K. HOSHINA [1], M. KATO [2], A. HOSAKA [2], T. MIYAHARA [1], A. MIKURIYA [2], N. OHKUBO [2], T. MIYATA [1]

[1]*Department of Vascular Surgery, the University of Tokyo Hospital, Tokyo, Japan*
[2]*Department of Cardiovascular Surgery, Morinomiya Hospital, Osaka, Japan*

Aim. Endovascular aneurysm repair (EVAR) was first approved in Japan in 2007. In order to avoid the learning curve generally seen in the initial stages of implementation, we have aimed for procedural perfection. As the proximal type I endoleak (EL) is associated with a higher risk of late conversion and rupture, so we have treated the intraoperative type I EL scrupulously. The hostile neck, which is known to be a risk for perigraft leakage, is the focus of this study. We showed both the middle-term results of EVAR in our country and the possible necessity of intraoperative management for the hostile neck.

Methods. From a consecutive series of 134 patients who underwent EVAR of abdominal aortic aneurysms, 129 cases in which contrast agent was used intraoperatively were selected. All cases had at least 12-month follow-up postoperatively (12-40 months). Of the 129 selected cases, 49 cases (37%) that did not fulfill the commercially recommended criteria of the aneurysmal neck (length <15 mm and angle >60° of the aneurysm or >45° of the suprarenal aorta) were assigned to the off-label group. The other 80 cases were assigned to the on-label group. We carefully observed the completion angiography and when we found or suspected a type I EL, we performed a re-touch up, changed to a non-compliant balloon, and used a supportive device, such as a Palmaz™ stent or aortic cuffs, in sequence.

Results. No postoperative type I ELs were detected within the follow-up period. Intraoperative type I ELs were detected more frequently in the off-label group (51%) than the on-label group (20%) ($P<0.01$). The rate of type I EL in the off-label group in terms of the neck length criteria (11/14 cases) was higher than that in the on-label group (30/115 cases) ($P<0.01$). In terms of the neck angle, patients in the off-label group had a greater tendency to develop the type I EL than those in the on-label group (18/42 *vs.* 23/87 cases) ($P=0.06$).

Conclusion. Off-label usage regarding aneurysmal neck length and angle tends to be incomplete without additional procedures. Conversely, various techniques, including non-compliant balloon usage and aortic stenting or cuffs, produce good results for the intraoperative type I EL. We found a relationship between the neck condition and the intraoperative type I EL, and showed the importance of strictly obeying our simple algorithm against the proximal type I EL.

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Key words: Endoleak - Endovascular aneurysm repair - Neck.

The stent-graft was first approved in Japan in 2007. Although we do not reach the level of other countries in the use of this procedure, we have learnt about the pros and cons of endovascular aneurysm repair (EVAR) techniques from a number of previous studies.[1-3] One of the drawbacks of this stressless treatment is the high reintervention rate, which is mainly caused by endoleaks (ELs). We have performed EVAR with scrupulous care in order to prevent the development of proximal perigraft leakage.

The type I EL, which is defined as the persistence of a perigraft aperture of blood flow caused by an inadequate and ineffective seal at the proximal and distal attachment zones,[4] has been correlated with a higher risk of late conversion [1] and rupture.[2] An inexperienced operator sometimes overlooks the proximal type I EL, as it is more difficult to detect than the distal type. Some skilled operators often leave a slight proximal type I EL because they have experienced that such leakage is often stopped by a thrombus within several days. However, we have attributed the high reintervention rate due to the type I EL to such incomplete procedures. We also believe that our intraoperative (intra-op) management

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