OPEN

Outcomes of Endovascular Repair for Abdominal Aortic Aneurysms

A Nationwide Survey in Japan

Katsuyuki Hoshina, MD, PhD, Shin Ishimaru, MD, PhD,† Yusuke Sasabuchi, MD, MPH,‡ Hideo Yasunaga, MD, PhD,§ and Kimihiro Komori, MD, PhD¶, on behalf of the Japan Committee for Stentgraft Management (JACSM)**

Objective: To analyze data on patients treated with a bifurcated stent graft for abdominal aortic aneurysm (AAA).

Background: The Japan Committee for Stentgraft Management (JACSM) was established in 2007 to manage the safety of endovascular aortic aneurysm repair (EVAR) in Japan. The JACSM registry includes detailed anatomical and clinical data of all patients who undergo stent graft insertion in Japan.

Methods: Among 51,380 patients treated with bifurcated stent graft for AAA, we identified 38,008 eligible patients (excluding those with rupture or insufficient data). The analyzed factors included age, sex, comorbidities, AAA pathology and etiology, aneurysm and neck diameters, 7 anti-instructions for use (IFU) factors, and endoleaks at hospital discharge. The endpoints were death, adverse events, sac dilatation ($\geq$5 mm), and reintervention.

Results: The rates of intraoperative and in-hospital mortality were 0.08% and 1.07%, respectively. Infectious aneurysm and pseudo-aneurysm were associated with overall survival and reintervention. Older age, large aneurysm diameter, and all types of persistent endoleaks were strong predictors of adverse events, sac dilatation, and reintervention. Comorbid cerebrovascular disease, renal dysfunction, and respiratory disorders were also risk factors. In total, 47.6% of patients violated the IFU; among the anti-IFU factors assessed, poor access and severe neck calcification were strong risk factors for mortality, reintervention, and adverse events. The sac dilatation rate at 5 years was 23.3%.

Conclusions: Although the analysis included EVAR with poor anatomy, the perioperative mortality rate was acceptable compared with that in previous large population studies.

Keywords: EVAR, JACSM, Japan, registry, stent graft

(*Ann Surg* 2019;269:564–573)

Several large population studies have evaluated the outcomes of endovascular aortic aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA), mainly comparing EVAR to open surgery (OS). Two milestone randomized controlled trials (RCTs) published in 2004 had great impact in revealing the superiority of EVAR to OS with respect to short-term mortality.[1,2] However, the mortality of EVAR cases may have been underestimated, because only patients anatomically suitable for EVAR were selected. A later RCT from the United States (enrollment period 2002–2008) also demonstrated the superiority of EVAR, with lower mortality in both groups.[3] Although the study used newer-generation stent grafts, a patient selection bias still existed because of the anatomical criteria and inclusion of many veterans, who do not represent the general population. Thus, there is an ongoing need for data on EVAR outcomes that are current and reflective of real-world EVAR procedures.

Several reports employing Medicare data have compared EVAR to OS using a propensity score-matched cohort, with an extremely large population and less selection bias.[4,5] However, these studies have critical limitations; they were observational, subject to potential coding error, and lacked anatomical and clinical details. In contrast, the European collaborators on stent graft techniques for abdominal aortic aneurysm repair (EUROSTAR) is a prospective multicenter registry (launched in 1996).[6] Unfortunately, the outcomes in the EUROSTAR study, including operative mortality,[6] are worse compared with those reported in previous studies, possibly because the devices used were of an older generation. Considering recent advances in stent graft devices and EVAR procedures, the effect of new-generation devices on improved outcomes should be investigated.

In July 2006, a commercial stent graft was first approved in Japan (lagging behind other countries). The Japan Committee for Stentgraft Management (JACSM) was established to ensure the safe and appropriate use of commercial stent grafts after their regulatory approval.[7] The JACSM registry is a nationwide EVAR registry in Japan with unique features, including detailed data on preoperative anatomical factors. As data were collected from 2007 to 2015, data from older devices are not included. Another advantage concerns its coverage of almost all EVAR procedures in Japan.

Using JACSM data, we aimed to analyze the factors (including detailed anatomical and clinical characteristics) influencing EVAR outcomes (mortality, adverse events, reintervention, and sac dilatation).

METHODS

Database

Before the approval of stent grafts in Japan, the Japanese Society for Vascular Surgery established a practice standards management committee to serve as the directors' advisory board and develop a regulatory system for stent graft treatments. The JACSM, established in December 2006, was composed of 10 societies related to endovascular treatment, and determined the practical standards for institutions, and practicing and supervising surgeons. Participating institutions were obligated to report data, including preoperative findings and postoperative outcomes, using a web-based

From the *Department of Vascular Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; †Division of Cardiovascular Surgery, Department of Surgery, Toda Chuo General Hospital, Saitama, Japan; ‡Department of Health Services Research, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan; §Department of Clinical Epidemiology and Health Economics, School of Public Health, the University of Tokyo, Tokyo, Japan; and ¶Divison of Vascular Surgery, Department of Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan.

The authors report no conflicts of interest.

Reprints: Kimihiro Komori, MD, PhD, Chairman of the Japanese Committee for Stentgraft Management, Division of Vascular Surgery, Department of Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai, Showa-ku, Nagoya, Aichi 466–8550, Japan. E-mail: komori@med.nagoya-u.ac.jp.

ISSN: 0003-4932/17/26903-0564
DOI: 10.1097/SLA.0000000000002508

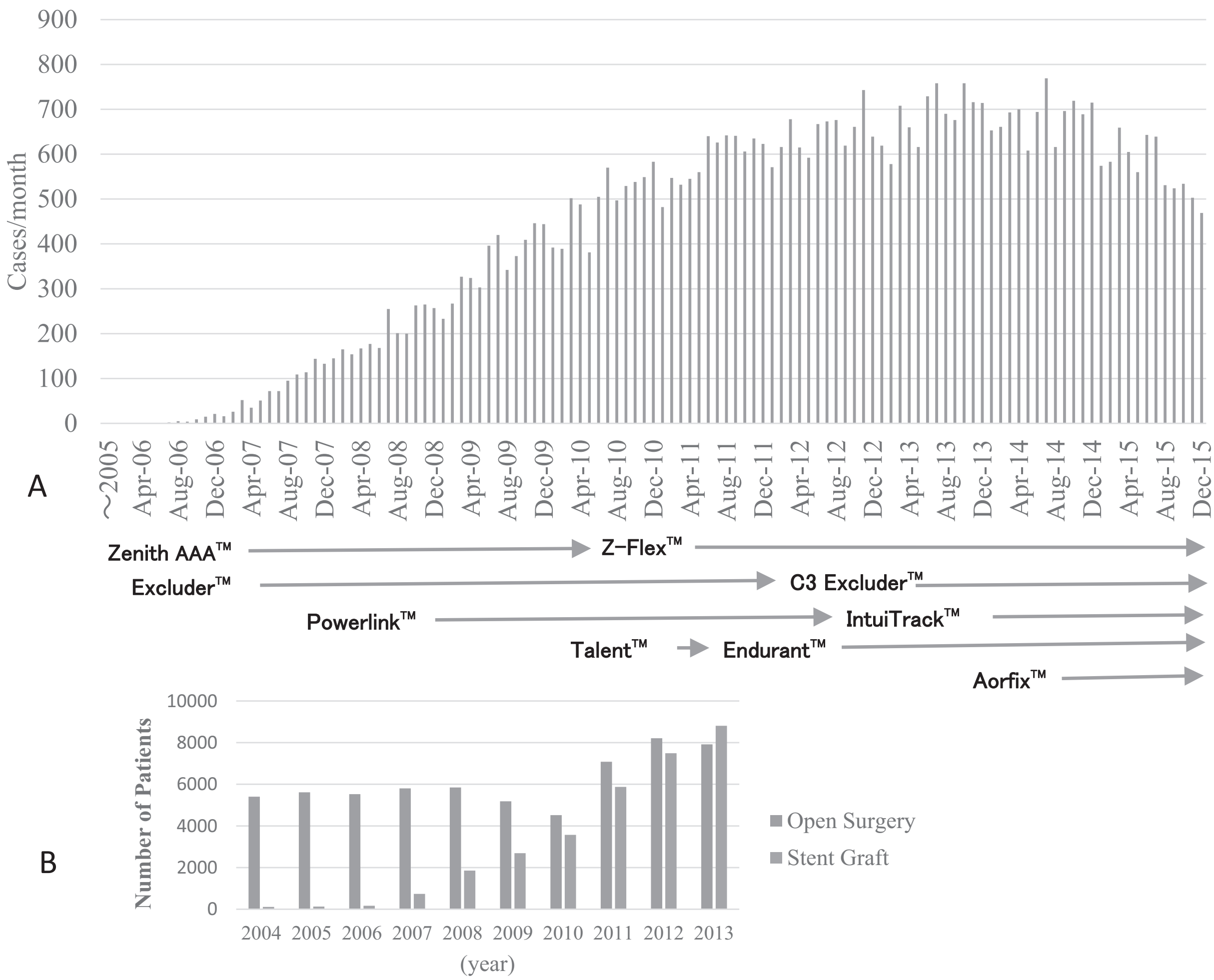

FIGURE 1. (A) Changes in the number of EVAR procedures and devices performed in Japan. (B) Although the data registration system changed to the National Clinical Database in 2011, the total number of surgically treated patients with AAA was roughly determined using the annual report from the Japanese Society for Vascular Surgery (http://www.jsvs.org/ja/).

case-registry form (http://www.stentgraft.jp/). Intraoperative and postoperative data (at discharge, 6 and 12 months postoperative, and every 12 months thereafter) were registered. Participants were obliged to register outcomes for survival, aneurysm diameter, and aneurysm rupture for up to 10 years, and other outcomes for 5 years. For AAA, 494 institutes in Japan were certified, and 51,690 patients were registered as of 2015. Among the 1309 certified operators, there were 1035 surgeons (79%), 171 radiologists (13%), 74 cardiologists (6%), and 19 others (2%).

Devices

Utilized devises included the Zenith AAA endovascular graft (Cook Medical Inc., Bloomington, IN; Japan edition; n = 3681, 9.7%), Gore Excluder aortic stent graft (W.L. Gore & Associates, Inc., Flagstaff, AZ; approved January, 2007; n = 13,315, 35%), the Powerlink system (Endologix, CA; approved February, 2008; n = 2365, 6.2%), and the Talent Stent Graft System (Medtronic, Santa Rosa, CA; approved December, 2010; n = 77, 0.2%). The next-generation devices included the Zenith (Zenith flex; n = 4689, 12.3%), Excluder (C3 Excluder; n = 3502, 9.2%), Talent (Endurant; n = 9815, 25.8%), and Aorfix AAA stent graft system (Lombard Medical, Oxfordshire, UK; approved August 2014; n = 253, 0.7%). The number of stent grafts implanted in Japan has dramatically increased to date (Fig. 1A), and also the number of surgically treated patients with AAA (Fig. 1B).

Inclusion and Exclusion Criteria for Data

Given our interest in "typical" EVAR cases, we selected cases of AAA or AAA with iliac aneurysm that underwent bifurcated stent graft insertion. We excluded cases of solitary iliac aneurysm and ruptured AAA with emergency surgery. Cases were also excluded if all baseline data were not registered or unreasonable data were registered (ie, AAA diameter $<$40 mm, neck diameter $<$10 mm, or $\geq$40 mm, proximal landing zone $\geq$100 mm). Finally, we excluded cases in which stent graft implantation failed.

Collected Data

The database included age, sex, comorbidities, pathology, and etiology of the AAA, and anatomical factors. Comorbidities included hypertension, diabetes mellitus (DM), coronary artery disease (CAD), cerebrovascular disease (CVD), renal dysfunction (serum creatinine level $\geq$1.20 mg/dL), respiratory disorder, and hostile

TABLE 1. Patient Characteristics and Logistic Regression Analysis of In-hospital Mortality

	Univariate Analysis for the Risk Factors of In-hospital Death			Cox Proportional-hazard Regression Analysis for the Risk Factors of In-hospital Mortality		
	Alive At Discharge (n = 36,852)	In-hospital Death (n = 409)	P	Hazard Ratio	95% CI	P
Age, yrs			<0.001			
−60	1234 (3.3)	6 (1.5)		0.57	0.25–1.31	0.186
61–70	6834 (18.5)	27 (6.6)		0.45	0.30–0.68	<0.001
71–80	16,419 (44.6)	151 (36.9)		Reference		
81–90	11,727 (31.8)	202 (49.4)		1.52	1.22–1.90	<0.001
91–	638 (1.7)	23 (5.6)		2.48	1.56–3.95	<0.001
Sex						
Female	6339 (17.2)	79 (19.3)	0.260	1.09	0.84–1.43	0.511
Comorbidities						
Hypertension (n = 26,124, 68.7%)	25,387 (68.9)	291 (71.1)	0.326	0.97	0.78–1.21	0.783
Diabetes mellitus (n = 4611, 12.1%)	4486 (12.2)	52 (12.7)	0.739	1.06	0.78–1.43	0.718
Coronary artery disease (n = 10,713, 28.2%)	10,444 (28.3)	115 (28.1)	0.921	1.01	0.81–1.27	0.911
Cerebrovascular disease (n = 5861, 15.4%)	5661 (15.4)	92 (22.5)	<0.001	1.39	1.09–1.76	0.007
Renal dysfunction (n = 7333, 19.3%)	7000 (19.0)	157 (38.4)	<0.001	1.92	1.56–2.37	<0.001
Respiratory disorder (n = 7565, 19.9%)	7322 (19.9)	119 (29.1)	<0.001	1.4	1.12–1.75	0.003
Hostile abdomen (n = 6674, 17.6%)	6493 (17.6)	66 (16.1)	0.434	0.89	0.68–1.17	0.407
Aneurysm diameter, mm			<0.001			
<50	13,621 (37.0)	61 (14.9)		Reference		
50≤, <55	10,492 (28.5)	75 (18.3)		1.53	1.08–2.15	0.016
55≤, <60	5182 (14.1)	74 (18.1)		2.75	1.95–3.89	<0.001
60≤, <70	4994 (13.6)	96 (23.5)		3.45	2.48–4.80	<0.001
70≤, <80	1709 (4.6)	62 (15.2)		6.18	4.27–8.94	<0.001
80≤	854 (2.3)	41 (10.0)		7.2	4.71–10.99	<0.001
Neck diameter, mm			<0.001			
<22	19,216 (52.1)	172 (42.1)		Reference		
22≤, <25	11,310 (30.7)	124 (30.3)		1.09	0.86–1.39	0.472
25≤, <28	4409 (12.0)	66 (16.1)		1.28	0.95–1.72	0.101
28≤, <31	1480 (4.0)	28 (6.8)		1.42	0.93–2.15	0.103
31≤	437 (1.2)	19 (4.6)		2.73	1.64–4.53	<0.001
Pathology			<0.001			
Atherosclerotic (n = 37,266, 98.1%)	36,146 (98.1)	388 (94.9)		Reference		
Infectious (n = 144, 0.4%)	129 (0.4)	12 (2.9)		5.34	2.57–11.07	<0.001
Inflammatory (n = 281, 0.7%)	278 (0.8)	2 (0.5)		0.6	0.14–2.53	0.489
Others	299 (0.8)	7 (1.7)		0.91	0.37–2.24	0.841
Etiology			<0.001			
True (n = 37,266, 98.1%)	36,162 (98.1)	382 (93.4)		Reference		
Pseudo (n = 367, 1%)	346 (0.9)	16 (3.9)		2.34	1.21–4.51	0.011
Dissection (n = 312, 0.8%)	294 (0.8)	4 (1.0)		1.44	0.51–4.02	0.491
Others	50 (0.1)	7 (1.7)		8.23	3.23–20.93	<0.001
Anatomical factors						
Short proximal neck (n = 2294, 6.0%)	2211 (6.0)	32 (7.8)	0.123	0.96	0.66–1.39	0.837
Severe suprarenal angulation (n = 4673, 12.2%)	4509 (12.2)	76 (18.6)	<0.001	1.04	0.77–1.41	0.784
Severe neck angulation (n = 6623, 17.4%)	6377 (17.3)	105 (25.7)	<0.001	1.11	0.84–1.45	0.464
Poor access (n = 2201, 5.7%)	2096 (5.7)	54 (13.2)	<0.001	1.85	1.33–2.58	<0.001
Short distal landing zone (n = 4381, 11.5%)	4239 (11.5)	73 (17.8)	<0.001	1.15	0.86–1.53	0.348
Severe neck calcification (n = 3330, 8.7%)	3170 (8.6)	78 (19.1)	<0.001	1.81	1.38–2.36	<0.001
Severe neck thrombus (n = 4844, 12.7%)	4632 (12.6)	86 (21.0)	0.001	1.39	1.08–1.80	0.012

abdomen. Anatomical factors included aneurysm diameter, neck diameter, and factors provided by the manufacturer's instructions for use (IFU), subsequently referred to as "anti-IFU" factors: short proximal neck (<15 mm), severe suprarenal angulation (≥45°), severe neck angulation (≥60°), poor access (iliac artery diameter ≤7.5 mm), short distal landing zone (<20 mm), severe neck calcification, and severe neck thrombus. Age, AAA diameter, and neck diameter were each categorized into several groups (see Table 1).

Endoleaks

Endoleaks were evaluated using postoperative enhanced computed tomography (CT) during hospitalization, and were classified into 6 categories: no endoleak; type 1, 2, 3, or 4 endoleak; and 2 or more types of endoleaks (multiple). If the type of endoleak could not be determined, the case was excluded from analyses of long-term outcomes.

Outcomes

The evaluated outcomes included in-hospital mortality, overall survival, event-free survival, dilatation rate, and reintervention-free survival. Event-free survival was defined as survival without stent graft migration, stenosis or occlusion of the stent graft, stent graft infection, acute arterial thrombus or embolus of the lower legs, or rupture of the aortic aneurysm. Reintervention-free survival was survival without reintervention for any reason. Dilatation was an increase ≥5 mm in the aneurysmal diameter from any diameter previously measured and registered. We censored data at the date when the outcome of interest was first recorded, the patient was deregistered, or the end of follow-up was reached. For event-free survival and reintervention-free survival, follow-up ended at 5 years.

Statistical Analyses

Categorical variables are presented as numbers and percentages, and continuous variables are presented as median and interquartile range (IQR). Categorical variables were compared using chi-square tests. Multivariable logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for in-hospital mortality. Multivariable Cox regression analyses were used to estimate hazard ratios (HRs) and 95% CIs for long-term outcomes (overall survival, event-free survival, dilatation, and reintervention-free survival). To analyze specific factors (age, diameters, pathology, etiology, and endoleaks), we set the subcategory with the highest frequency of patients as the reference. The Kaplan–Meier method with the log-rank test was used to analyze the overall survival and sac dilatation-free rates. All statistical analyses were performed using SPSS software version 23 (IBM Corp, Armonk, NY). The threshold for statistical significance was $P < 0.05$.

RESULTS

Between 2006 and 2015, 51,380 cases were registered. After applying the exclusion criteria, a remaining 38,003 cases were analyzed. The mean follow-up period was 2403 ± 15 days.

Preoperative Characteristics

The median age was 77 years (IQR 71–82 years). The mean aneurysm diameter was 51 mm (47–57 mm), and mean proximal neck diameter was 21 mm (19.7–23.8 mm). Females accounted for 17.3% of the cohort (6566 cases). The majority of cases in this population presented with true and atherosclerotic aneurysms (Table 1).

Anatomical Anti-IFU Factors

Information regarding anti-IFU factors is provided in Table 1. A total of 19,907 cases (52.4%) did not violate the IFU. However, 10,512 cases (27.7%) had 1 anti-IFU factor, 5486 cases (14.4%) had 2 anti-IFU factor, 1609 cases (4.2%) had 3 anti-IFU factor, 418 cases (1.1%) had 4 anti-IFU factor, 64 cases (0.2%) had 5 anti-IFU factor, 6 cases (0.02%) had 6 anti-IFU factor, and 1 case had 7 anti-IFU factor.

Short-term (Intraoperative and At Discharge) Outcomes

The rates of intraoperative and in-hospital mortality were 0.08% and 1.07%, respectively. The blood transfusion rate during surgery was 3.84%. Observed complications (with rates intraoperatively and at discharge, respectively) included stent graft migration (0.3% and 0.1%), vascular injury (2.3% and 0.7%), thromboembolism (0.8% and 0.9%), paralysis (0.2% and 0.3%), and rupture (0.2% and 0.1%). Stenosis or occlusion (1.3%), wound complications (1.4%), cerebrovascular events (0.4%), and renal dysfunction (2.6%) were observed during the hospital stay.

Endoleaks

Endoleaks were observed intraoperatively in 12,735 cases (33.5%; no endoleak, n = 25,260, 66.5%; type 1, n = 2032, 5.3%; type 2, n = 6143, 16.2%; type 3, n = 348, 0.9%; type 4, n = 3427, 9.0%; multiple endoleaks, n = 785, 2.1%). In addition, endoleaks were observed in 9471 cases at discharge (24.9%; no endoleak, n = 25,184, 66.3%; type 1, n = 2559, 6.7%; type 2, n = 6301, 16.6%; type 3, n = 235, 0.6%; type 4, n = 229, 0.6%; multiple endoleaks, n = 147, 0.4%).

Factors Affecting In-hospital Mortality

Older age, infectious aneurysms, and pseudo-aneurysms were associated with in-hospital mortality (Table 1). Among comorbidities, CVD, renal dysfunction, and respiratory disorders were significantly associated with mortality. Among the anatomical factors, an aneurysm diameter ≥50 mm, neck >31 mm, poor access, severe neck calcification, and thrombus were risk factors for in-hospital mortality (Table 1).

Background Characteristics and Endoleaks According to Overall Survival

A Cox hazard regression analysis, with endoleak as a background factor, revealed a strong association of mortality with older age, CVD, renal dysfunction, respiratory disorders, hostile abdomen, an aneurysm diameter ≥50 mm, neck diameter 25 to 28 mm, infectious aneurysm, pseudo-aneurysm, short proximal neck, poor access, severe neck calcification, and type 1, type 3, and multiple endoleaks (Table 2). Female sex and hypertension negatively correlated with mortality (Table 2). The overall survival rates were 96.2% at 6 months, 93.5% at 1 year, 88.3% at 2 years, 82.8% at 3 years, 76.2% at 4 years, 69.4% at 5 years, 63.7% at 6 years, 54.4% at 7 years, and 38.8% at 8 years.

Adverse Event-free Survival

Cases with adverse events were compared with cases without adverse events (Table 3). In a Cox hazard regression analysis, older age, female sex, CVD, renal dysfunction, respiratory disorders, and hostile abdomen were significantly associated with adverse events. In addition, an aneurysm diameter ≥55 mm, neck ≥25 mm, short proximal neck, severe neck angulation, poor access, severe neck calcification, and all types of endoleaks were risk factors for adverse events. DM was the only factor that negatively correlated with adverse events (Table 4).

Rupture (a fatal and miserable outcome) was analyzed separately. A subanalysis revealed that female sex, an aneurysm diameter ≥60 mm, infectious and inflammatory aneurysms, and type 1, type 2, and multiple endoleaks were independently associated with rupture (Table 5). No case with a type 3 endoleak resulted in rupture.

Sac Dilatation Rate

Patients with sac dilation >5 mm within 5 years of follow-up were compared with those without dilation (Table 3). Age >60 years, female sex, renal dysfunction, an aneurysm diameter ≥0 mm, neck 22 to 25 mm and ≥28 mm, neck severe angulation, and all types of endoleaks were independently associated with sac dilation. Factors negatively correlating with sac dilatation included DM, respiratory disorders, and severe neck thrombus (Table 4). The dilatation rates were 2.6% at 6 months, 4.4% at 1 year, 8.8% at 2 years, 13.7% at 3 years, 18.5% at 4 years, and 23.3% at 5 years.

Reintervention-free Survival

Patients with reintervention were compared with those without reintervention (Table 3). In a Cox hazard regression analysis, older age, infectious aneurysm, pseudo-aneurysm, CVD, renal dysfunction, respiratory disorder, and hostile abdomen were significantly associated with reintervention. In addition, an aneurysm diameter ≥55 mm, neck 25 to 28 or ≥31 mm, short proximal neck, poor access, severe

TABLE 2. Baseline Characteristics and Endoleaks According to Overall Survival and the Cox Hazard Regression Analysis

	Univariate Analysis for the Risk Factors of Overall Survival			Cox Proportional-hazard Regression Analysis for the Risk Factors of Overall Survival		
	Alive (n = 34,094)	Dead (n = 3500)	P	Hazard Ratio	95% CI	P
Age, yrs						
−60	1198 (3.5)	56 (1.6)	<0.001	0.47	0.36–0.62	<0.001
61–70	6585 (19.3)	380 (10.9)		0.62	0.55–0.70	<0.001
71–80	15,310 (44.9)	1429 (40.8)		reference		
81–90	10,448 (30.6)	1534 (43.8)		1.74	1.61–1.88	<0.001
91–	553 (1.6)	101 (2.9)		2.46	1.98–3.05	<0.001
Sex						
Female	5930 (17.4)	557 (15.9)	0.027	0.88	0.80–0.98	0.015
Comorbidities						
Hypertension	23,451 (68.8)	2382 (68.1)	0.378	0.88	0.81–0.94	0.001
Diabetes mellitus	4147 (12.2)	412 (11.8)	0.499	1.01	0.91–1.13	0.805
Coronary artery disease	9565 (28.1)	1033 (29.5)	0.068	1.04	0.96–1.12	0.360
Cerebrovascular disease	5090 (14.9)	679 (19.4)	<0.001	1.27	1.16–1.38	<0.001
Renal dysfunction	6233 (18.3)	943 (26.9)	<0.001	1.51	1.40–1.64	<0.001
Respiratory disorder	6452 (18.9)	994 (28.4)	<0.001	1.52	1.41–1.64	<0.001
Hostile abdomen	5816 (17.1)	793 (22.7)	<0.001	1.29	1.19–1.40	<0.001
Aneurysm diameter, mm						
<50	12,797 (37.5)	1071 (30.6)	<0.001	Reference		
50≤, <55	9818 (28.8)	875 (25.0)		1.13	1.03–1.24	0.012
55≤, <60	4742 (13.9)	546 (15.6)		1.35	1.21–1.50	<0.001
60≤, <70	4482 (13.1)	636 (18.2)		1.66	1.50–1.85	<0.001
70≤, <80	1508 (4.4)	234 (6.7)		1.91	1.64–2.22	<0.001
80≤	747 (2.2)	138 (3.9)		2.37	1.95–2.86	<0.001
Neck diameter, mm						
<22	17,934 (52.6)	1663 (47.5)	<0.001	Reference		
22≤, <25	10,441 (30.6)	1099 (31.4)		1.07	0.98–1.16	0.119
25≤, <28	3968 (11.6)	519 (14.8)		1.26	1.13–1.39	<0.001
28≤, <31	1351 (4.0)	169 (4.8)		1.13	0.96–1.34	0.140
31≤	400 (1.2)	50 (1.4)		1.30	0.96–1.77	0.094
Pathology						
Atherosclerotic	33,473 (98.2)	3410 (97.4)	<0.001	Reference		
Infectious	105 (0.3)	27 (0.8)		2.37	1.55–3.61	<0.001
Inflammatory	248 (0.7)	31 (0.9)		1.23	0.85–1.77	0.266
Others	268 (0.8)	32 (0.9)		0.74	0.50–1.10	0.138
Etiology						
True	33,498 (98.3)	3386 (96.7)	<0.001	Reference		
Pseudo	272 (0.8)	79 (2.3)		2.65	2.05–3.43	<0.001
Dissection	282 (0.8)	26 (0.7)		1.33	0.89–1.99	0.159
Others	42 (0.1)	9 (0.3)		2.80	1.42–5.51	0.003
Anatomical factors						
Short proximal neck	2007 (5.9)	255 (7.3)	<0.001	1.31	1.15–1.50	<0.001
Severe suprarenal angulation	4095 (12.0)	502 (14.3)	<0.001	1.05	0.94–1.18	0.381
Severe neck angulation	5787 (17.0)	731 (20.9)	<0.001	1.04	0.94–1.15	0.420
Poor access	1876 (5.5)	271 (7.7)	<0.001	1.47	1.29–1.69	<0.001
Short distal landing zone	3857 (11.3)	451 (12.9)	0.005	0.94	0.85–1.05	0.277
Severe neck calcification	2862 (8.4)	390 (11.1)	<0.001	1.37	1.22–1.53	<0.001
Severe neck thrombus	4281 (12.6)	477 (13.6)	0.069	1.06	0.96–1.18	0.259
Perioperative endoleak during hospital stay						
No endoleak	22,750 (73.1)	2287 (69.2)	<0.001	Reference		
Type 1 endoleak	2152 (6.9)	353 (10.7)		1.53	1.36–1.71	<0.001
Type 2 endoleak	5696 (18.3)	591 (17.9)		1.00	0.91–1.10	0.988
Type 3 endoleak	189 (0.6)	40 (1.2)		1.59	1.16–2.18	0.004
Type 4 endoleak	215 (0.7)	13 (0.4)		1.01	0.59–1.75	0.958
Multiple endoleaks	125 (0.4)	22 (0.7)		1.59	1.04–2.44	0.033

neck calcification, and all types of endoleaks were risk factors. Only hypertension was negatively correlated with reintervention (Table 4).

DISCUSSION

In the current healthcare system in Japan, all shipping information regarding EVAR devices is reported to the JACSM. There were some cases (very few) not reported during the EVAR introduction period (2006–2008), mainly involving an emergency EVAR. Thus, this registry includes nearly all stent grafts implanted in Japan. Using this registry, we provided real-world data on the perioperative and long-term outcomes of bifurcated stent graft placement for the treatment of AAA.

The mortality rate in the present study (1.15%) is similar to that in previous large population studies.[1–3] However, the initial study from

TABLE 3. Univariate Analyses of Event-free Survival, Dilatation Rate, and Reintervention-free Survival

	Event-free Survival			Dilatation Rate			Reintervention-free Survival		
	Event (−) (n = 20,250)	Event (+) (n = 16,451)	P	Dilatation (−) (n = 23,793)	Dilatation (+) (n = 4200)	P	Event (−) (n = 23,852)	Event (+) (n = 4767)	P
Age, yrs									
−60	746 (3.7)	487 (3.0)	<0.001	826 (3.5)	131 (3.1)	<0.001	865 (3.6)	94 (2.0)	<0.001
61–70	4091 (20.2)	2734 (16.6)		4640 (19.5)	738 (17.6)		4767 (20.0)	629 (13.2)	
71–80	9352 (46.2)	6995 (42.5)		10,879 (45.7)	1879 (44.7)		10,940 (45.9)	2042 (42.8)	
81–90	5790 (28.6)	5865 (35.7)		7119 (29.9)	1384 (33.0)		6955 (29.2)	1892 (39.7)	
91–	271 (1.3)	370 (2.2)		329 (1.4)	68 (1.6)		325 (1.4)	110 (2.3)	
Sex									
Female	3252 (16.1)	3035 (18.4)	<0.001	3830 (16.1)	891 (21.2)	<0.001	3942 (16.5)	860 (18.0)	<0.001
Comorbidities									
Hypertension	13,910 (68.7)	11,304 (68.7)	0.964	16,341 (68.7)	2942 (70.0)	0.078	16,435 (68.9)	3267 (68.5)	0.614
Diabetes mellitus	2527 (12.5)	1913 (11.6)	0.013	2946 (12.4)	445 (10.6)	0.001	2932 (12.3)	547 (11.5)	0.115
Coronary artery disease	5795 (28.6)	4540 (27.6)	0.031	6853 (28.8)	1184 (28.2)	0.419	6845 (28.7)	1360 (28.5)	0.815
Cerebrovascular disease	2934 (14.5)	2677 (16.3)	<0.001	3550 (14.9)	650 (15.5)	0.352	3498 (14.7)	854 (17.9)	<0.001
Renal dysfunction	3435 (17.0)	3548 (21.6)	<0.001	4235 (17.8)	739 (17.6)	0.750	4054 (17.0)	1135 (23.8)	<0.001
Respiratory disorder	3823 (18.9)	3402 (20.7)	<0.001	4721 (19.8)	701 (16.7)	<0.001	4484 (18.8)	1183 (24.8)	<0.001
Hostile abdomen	3468 (17.1)	2981 (18.1)	0.013	4216 (17.7)	821 (19.5)	0.004	4141 (17.4)	1037 (21.8)	<0.001
Aneurysm diameter, mm									
<50	7964 (39.3)	5584 (33.9)	<0.001	9258 (38.9)	1538 (36.6)	<0.001	9411 (39.5)	1502 (31.5)	<0.001
50≤, <55	5882 (29.0)	4586 (27.9)		6785 (28.5)	1188 (28.3)		6880 (28.8)	1239 (26.0)	
55≤, <60	2761 (13.6)	2381 (14.5)		3253 (13.7)	613 (14.6)		3267 (13.7)	709 (14.9)	
60≤, <70	2445 (12.1)	2539 (15.4)		3016 (12.7)	580 (13.8)		2890 (12.1)	846 (17.7)	
70≤, <80	834 (4.1)	872 (5.3)		1016 (4.3)	183 (4.4)		963 (4.0)	304 (6.4)	
80≤	364 (1.8)	489 (3.0)		465 (2.0)	98 (2.3)		441 (1.8)	167 (3.5)	
Neck diameter, mm									
<22	10,769 (53.2)	8374 (50.9)	<0.001	12,557 (52.8)	2195 (52.3)	0.660	12,719 (53.3)	2317 (48.6)	<0.001
22≤, <25	6187 (30.6)	5082 (30.9)		7276 (30.6)	1309 (31.2)		7274 (30.5)	1484 (31.1)	
25≤, <28	2353 (11.6)	2031 (12.3)		2810 (11.8)	482 (11.5)		2727 (11.4)	678 (14.2)	
28≤, <31	740 (3.7)	734 (4.5)		900 (3.8)	161 (3.8)		886 (3.7)	215 (4.5)	
31≤	201 (1.0)	230 (1.4)		250 (1.1)	53 (1.3)		246 (1.0)	73 (1.5)	
Pathology									
Atherosclerotic	19,865 (98.1)	16,146 (98.1)	0.005	23,338 (98.1)	4140 (98.6)	0.021	23,420 (98.2)	4651 (97.6)	<0.001
Infectious	57 (0.3)	66 (0.4)		71 (0.3)	8 (0.2)		62 (0.3)	31 (0.7)	
Inflammatory	172 (0.8)	98 (0.6)		202 (0.8)	18 (0.4)		195 (0.8)	37 (0.8)	
Others	156 (0.8)	141 (0.9)		182 (0.8)	34 (0.8)		175 (0.7)	48 (1.0)	
Etiology									
True	19,914 (98.3)	16,102 (97.9)	0.001	23,376 (98.2)	4137 (98.5)	0.324	23,463 (98.4)	4638 (97.3)	<0.001
Pseudo	155 (0.8)	179 (1.1)		208 (0.9)	25 (0.6)		178 (0.7)	86 (1.8)	
Dissection	161 (0.8)	139 (0.8)		185 (0.8)	33 (0.8)		190 (0.8)	32 (0.7)	
Others	20 (0.1)	31 (0.2)		24 (0.1)	5 (0.1)		21 (0.1)	11 (0.2)	
Anatomical factors									
Short proximal neck	1100 (5.4)	1084 (6.6)	<0.001	1369 (5.8)	212 (5.0)	0.068	1297 (5.4)	322 (6.8)	<0.001
Severe suprarenal angulation	2257 (11.1)	2210 (13.4)	<0.001	2700 (11.3)	607 (14.5)	<0.001	2734 (11.5)	678 (14.2)	<0.001
Severe neck angulation	3183 (15.7)	3126 (19.0)	<0.001	3844 (16.2)	886 (21.1)	<0.001	3872 (16.2)	1006 (21.1)	<0.001
Poor access	1005 (5.0)	1069 (6.5)	<0.001	1281 (5.4)	160 (3.8)	<0.001	1194 (5.0)	324 (6.8)	<0.001
Short distal landing zone	2252 (11.1)	1925 (11.7)	0.082	2724 (11.4)	498 (11.9)	0.445	2683 (11.2)	621 (13.0)	<0.001
Severe neck calcification	1596 (7.9)	1546 (9.4)	<0.001	1982 (8.3)	300 (7.1)	0.010	1883 (7.9)	479 (10.0)	<0.001
Severe neck thrombus	2454 (12.1)	2145 (13.0)	0.008	2969 (12.5)	387 (9.2)	<0.001	2873 (12.0)	595 (12.5)	0.399
Perioperative endoleak during hospital stay									
No endoleak	14,201 (74.5)	10,178 (70.1)	<0.001	16,716 (74.4)	2521 (62.9)	<0.001	16,804 (74.5)	2935 (64.7)	<0.001
Type 1 endoleak	1132 (5.9)	1289 (8.9)		1395 (6.2)	326 (8.1)		1327 (5.9)	464 (10.2)	
Type 2 endoleak	3429 (18.0)	2741 (18.9)		3996 (17.8)	1066 (26.6)		4113 (18.2)	1019 (22.5)	
Type 3 endoleak	105 (0.6)	118 (0.8)		136 (0.6)	45 (1.1)		119 (0.5)	55 (1.2)	
Type 4 endoleak	112 (0.6)	114 (0.8)		124 (0.6)	28 (0.7)		121 (0.5)	29 (0.6)	
Multiple endoleaks	71 (0.4)	72 (0.5)		91 (0.4)	25 (0.6)		78 (0.3)	31 (0.7)	

the JACSM reported a lower in-hospital mortality rate of 0.4%.[7] The initial data were primarily collected from high-volume centers, which generally achieve better outcomes, as reported for EVAR.[8] The number of participating institutes sharply increased after 2009, which might have worsened overall outcomes. In addition, operators may tend to violate the IFU as indications for EVAR were extended. As EVAR should be a treatment of last resort for high-risk aneurysm patients, violating the IFU for unfavorable anatomy may be inevitable, and indeed approximately half of all patients had at least 1 anti-IFU factor in the present study. Although several reports have discussed the effect of violating the IFU, focusing on the anatomical factors related to EVAR outcome, the factors analyzed and parameter definitions were

TABLE 4. Cox Proportional-hazard Regression Analyses of Event-free Survival, Sac Dilatation Rate, and Reintervention-free Survival

	Event-free Survival			Dilatation			Reintervention-free Survival		
	Hazard Ratio	**95% CI**	***P***	**Hazard Ratio**	**95% CI**	***P***	**Hazard Ratio**	**95% CI**	***P***
Age, yrs									
−60	0.78	0.67–0.90	0.001	0.84	0.70–1.00	0.051	0.64	0.51–0.80	<0.001
61–70	0.85	0.79–0.91	<0.001	0.87	0.80–0.95	0.002	0.76	0.69–0.84	<0.001
71–80	Reference			Reference			Reference		
81–90	1.33	1.25–1.40	<0.001	1.28	1.19–1.38	<0.001	1.37	1.27–1.48	<0.001
91–	1.41	1.16–1.70	<0.001	1.44	1.12–1.85	0.004	1.33	1.03–1.72	0.029
Sex									
Female	1.13	1.06–1.21	<0.001	1.27	1.17–1.38	<0.001	1.10	1.00–1.20	0.048
Comorbidities									
Hypertension	0.97	0.92–1.02	0.293	1.01	0.94–1.08	0.799	0.92	0.86–0.99	0.031
Diabetes mellitus	0.91	0.84–0.98	0.012	0.88	0.79–0.98	0.015	0.96	0.86–1.06	0.421
Coronary artery disease	1.00	0.94–1.05	0.861	0.94	0.88–1.01	0.074	1.01	0.94–1.09	0.738
Cerebrovascular disease	1.11	1.04–1.19	0.001	1.06	0.98–1.16	0.161	1.13	1.04–1.24	0.005
Renal dysfunction	1.23	1.15–1.31	<0.001	1.14	1.04–1.24	0.003	1.27	1.17–1.38	<0.001
Respiratory disorder	1.08	1.02–1.15	0.009	0.88	0.81–0.96	0.003	1.25	1.16–1.36	<0.001
Hostile abdomen	1.13	1.07–1.20	<0.001	1.02	0.94–1.10	0.651	1.26	1.16–1.36	<0.001
Aneurysm diameter, mm									
<50	Reference			Reference			Reference		
50≤, <55	1.02	0.96–1.09	0.447	1.09	1.01–1.18	0.023	1.09	1.00–1.18	0.060
55≤, <60	1.09	1.01–1.17	0.032	1.14	1.04–1.26	0.007	1.16	1.05–1.29	0.005
60≤, <70	1.28	1.19–1.38	<0.001	1.19	1.08–1.32	0.001	1.53	1.39–1.70	<0.001
70≤, <80	1.25	1.11–1.41	<0.001	1.22	1.04–1.43	0.014	1.64	1.41–1.91	<0.001
80≤	1.56	1.34–1.83	<0.001	1.45	1.17–1.80	0.001	1.83	1.49–2.25	<0.001
Neck diameter, mm									
<22	Reference			Reference			Reference		
22≤, <25	1.04	0.99–1.10	0.128	1.08	1.00–1.16	0.046	1.07	0.99–1.15	0.095
25≤, <28	1.09	1.01–1.18	0.026	1.07	0.96–1.18	0.214	1.24	1.12–1.37	<0.001
28≤, <31	1.14	1.01–1.29	0.040	1.18	1.00–1.40	0.045	1.17	0.99–1.38	0.063
31≤	1.37	1.10–1.71	0.006	1.68	1.27–2.24	<0.001	1.45	1.09–1.93	0.012
Pathology									
Atherosclerotic	Reference			Reference			Reference		
Infectious	0.94	0.57–1.56	0.813	0.99	0.49–2.01	0.978	1.74	1.04–2.90	0.034
Inflammatory	0.80	0.58–1.11	0.184	0.65	0.41–1.04	0.071	0.78	0.51–1.20	0.261
Else	0.90	0.68–1.19	0.458	0.94	0.66–1.35	0.744	1.05	0.73–1.51	0.787
Etiology									
True	Reference			Reference			Reference		
Pseudo	1.29	0.99–1.69	0.057	0.94	0.61–1.43	0.758	1.83	1.34–2.49	<0.001
Dissection	1.05	0.78–1.40	0.750	1.16	0.82–1.66	0.402	0.96	0.63–1.47	0.857
Else	1.65	0.85–3.21	0.142	2.11	0.87–5.16	0.100	1.57	0.69–3.56	0.284
Anatomical factors									
Short proximal neck	1.21	1.09–1.34	<0.001	1.01	0.87–1.16	0.938	1.16	1.01–1.33	0.032
Severe suprarenal angulation	1.02	0.94–1.11	0.637	1.06	0.96–1.18	0.232	1.01	0.91–1.13	0.853
Severe neck angulation	1.13	1.05–1.21	0.001	1.21	1.10–1.32	<0.001	1.06	0.97–1.17	0.204
Poor access	1.20	1.08–1.34	0.001	0.85	0.72–1.01	0.058	1.18	1.02–1.37	0.024
Short distal landing zone	1.04	0.97–1.12	0.257	1.06	0.96–1.17	0.267	1.08	0.97–1.19	0.144
Severe neck calcification	1.10	1.00–1.20	0.041	0.96	0.85–1.09	0.512	1.17	1.04–1.31	0.010
Severe neck thrombus	0.95	0.88–1.03	0.235	0.83	0.74–0.93	0.001	0.95	0.86–1.06	0.360
Postoperative endoleak during hospital stay									
No endoleak	Reference			Reference			Reference		
Type 1	1.38	1.26–1.51	<0.001	1.62	1.44–1.82	<0.001	1.62	1.44–1.83	<0.001
Type 2	1.27	1.20–1.35	<0.001	1.59	1.48–1.71	<0.001	1.54	1.42–1.66	<0.001
Type 3	1.69	1.33–2.13	<0.001	2.04	1.52–2.74	<0.001	2.39	1.80–3.18	<0.001
Type 4	1.37	1.00–1.88	0.050	2.26	1.55–3.28	<0.001	1.97	1.34–2.88	0.001
Multiple	1.67	1.23–2.26	0.001	1.95	1.31–2.89	0.001	2.31	1.58–3.36	<0.001

arbitrarily determined. In the present study, we selected seven anti-IFU factors, all of which were previously associated with EVAR outcomes.[9–12] Considering that these factors strongly affected outcomes in the present study, an increase in cases violating the IFU may contribute to worsening outcomes.

A large population study reported that the overall survival rate worsened as age increased, even in the EVAR group.[4] Similarly, we confirmed that older age was a strong risk factor for survival, and also for sac dilatation. Furthermore, aneurysm diameter was a strong predictor of all adverse outcomes. Interestingly, diameters <50 mm were clearly differentiated from other sizes in the hazardous risk analysis. Considering that the average diameter in the present study was relatively smaller compared with that in the previous literatures,[1–3] and that >30% of patients had an aneurysm diameter

TABLE 5. Univariate and Cox Regression Analyses for the Risk Factors of Rupture After EVAR

	Univariate Analysis for the Risk Factors of Rupture After EVAR			Cox Proportional-hazard Regression Analysis for the Risk Factors of Rupture After EVAR		
	Rupture (−)	**Rupture (+)**	***P***	**Hazard ratio**	**95% CI**	***P***
Age, yrs						
−60	1255 (3.32)	3 (3.03)	0.045	0.87	0.26–2.94	0.824
61–70	6969 (18.42)	13 (13.13)		0.84	0.43–1.64	0.613
71–80	16,818 (44.46)	36 (36.36)		Reference		
81–90	12109 (32.01)	46 (46.46)		1.48	0.92–2.40	0.108
91–	673 (1.78)	1 (1.01)		0.55	0.07–4.10	0.562
Sex						
Female	6520 (17.24)	30 (30.30)	0.001	1.98	1.20–3.25	0.007
Comorbidities						
Hypertension	25,996 (68.73)	69 (69.70)	0.836			
Diabetes mellitus	4587 (12.13)	14 (14.14)	0.540			
Coronary artery disease	10669 (28.21)	30 (30.30)	0.644			
Cerebrovascular disease	5829 (15.41)	18 (18.18)	0.446			
Renal dysfunction	7269 (19.22)	27 (27.27)	0.042	1.04	0.62–1.76	0.872
Respiratory disorder	7530 (19.91)	23 (23.23)	0.408			
Hostile abdomen	6647 (17.57)	16 (16.16)	0.712			
Aneurysm diameter, mm						
<50	13,902 (36.75)	19 (19.19)	<0.001	Reference		
50≤, <55	10,742 (28.40)	17 (17.17)		1.64	0.81–3.29	0.166
55≤, <60	5344 (14.13)	10 (10.10)		1.50	0.64–3.56	0.353
60≤, <70	5168 (13.66)	21 (21.21)		3.62	1.82–7.20	<0.001
70≤, <80	1770 (4.68)	23 (23.23)		12.68	6.37–25.22	<0.001
80≤	898 (2.37)	9 (9.09)		8.82	3.53–22.07	<0.001
Neck diameter, mm						
<22	19,679 (52.03)	48 (48.48)	0.090	12,557 (52.8)	2195 (52.3)	0.660
22≤, <25	11,621 (30.72)	27 (27.27)		7276 (30.6)	1309 (31.2)	
25≤, <28	4521 (11.95)	15 (15.15)		2810 (11.8)	482 (11.5)	
28≤, <31	1540 (4.07)	5 (5.05)		900 (3.8)	161 (3.8)	
31≤	463 (1.22)	4 (4.04)		250 (1.1)	53 (1.3)	
Pathology						
Atherosclerotic	37,102 (98.09)	91 (91.92)	<0.001	Reference		
Infectious	139 (0.37)	4 (4.04)		13.14	3.29–52.47	<0.001
Inflammatory	278 (0.73)	3 (3.03)		3.50	1.05–11.65	0.041
Others	305 (0.81)	1 (1.01)		1.00	0.12–8.28	0.998
Etiology						
True	37,098 (98.08)	91 (91.92)	<0.001	Reference		
Pseudo	363 (0.96)	3 (3.03)		2.30	0.56–9.50	0.250
Dissection	308 (0.81)	2 (2.02)		NA	NA	NA
Others	55 (0.15)	3 (3.03)		6.88	1.22–38.69	0.029
Anatomical factors						
Short proximal neck	2273 (6.01)	12 (12.12)	0.011	1.72	0.88–3.37	0.115
Severe suprarenal angulation	4636 (12.26)	20 (20.20)	0.016	1.04	0.55–1.98	0.902
Severe neck angulation	6571 (17.37)	25 (25.25)	0.039	0.80	0.44–1.43	0.447
Poor access	2188 (5.78)	7 (7.07)	0.584			
Short distal landing zone	4362 (11.53)	14 (14.14)	0.417			
Severe neck calcification	3302 (8.73)	10 (10.10)	0.629			
Severe neck thrombus	4820 (12.74)	14 (14.14)	0.677			
Perioperative endoleak during hospital stay						
No endoleak	25,120 (72.76)	39 (44.83)	<0.001	Reference		
Type 1 endoleak	2529 (7.33)	21 (24.14)		5.00	2.87–8.72	<0.001
Type 2 endoleak	6272 (18.17)	23 (26.44)		2.37	1.41–3.99	0.001
Type 3 endoleak	233 (0.67)	0 (0.00)		NA	NA	NA
Type 4 endoleak	227 (0.66)	1 (1.15)		3.17	0.43–23.34	0.257
Multiple endoleaks	144 (0.42)	3 (3.45)		7.81	1.99–30.57	0.003

NA denotes not available, because there were not enough number of events.

<50 mm, a lower threshold might be necessary for a detailed analysis. In addition, this result might affect future indications for EVAR.

There are several possible reasons for the smaller aneurysm diameter in the present study. The aneurysm diameter threshold, 50 mm, is recommended by the Japanese guidelines, reflecting the smaller stature of Japanese patients.[13] Although the indication of EVAR for small AAAs (>40 mm, <50 mm) in the Japanese guidelines has not changed from class IIb, the level of evidence was upgraded from C (in 2006)[13] to B (in 2011),[14] given RCT results for small AAAs.[15,16] We assume that some institutions might have lowered the threshold. In addition, operators in Japan have aggressively extended the operative indication of AAA to regions where

EVAR was belatedly introduced (given its excellent short-term outcomes), and decide to operate immediately after the AAA reaches 50 mm in diameter, as most of the diameters analyzed in the present study were 50 mm.[17]

Several IFU items were analyzed. As severe neck angulation and calcification, and poor access are reflective of systemic atherosclerosis, their significant association with adverse outcomes is plausible. Severe neck angulation is also an important factor for the long-term interaction between the stent graft and native aorta,[18] which might result in adverse events. However, the selection of these seven anti-IFU parameters should be considered a limitation of the present study. For example, we included the neck diameter as a factor in the Cox regression analysis, but not "large neck diameter," because the IFU for diameter differs widely across devices. In addition, stent grafts in patients with a large neck diameter (>34 mm) have rarely been performed in Japan due to the device lag. Therefore, the present results cannot be extrapolated to studies performed in other countries. Furthermore, reliable methods for the quantification and qualification of neck thrombus and calcification have not yet been established. Hoshina et al[19] defined a "shaggy aorta" and concluded that EVAR patients with a massive neck atheroma tend to develop late-phase complications (ischemic colitis, renal dysfunction, and blue toe syndrome), perhaps related to cholesterol crystal embolization. Therefore, we assumed that a massive atheroma would have a greater negative impact on outcomes than severe calcification; however, neck atheroma (thrombus) was not related to survival. Other studies have reported similar conclusions, with neck thrombus showing a protective effect; however, the endpoints differed from those in the present study.[20,21] Furthermore, we did not define severe thrombus in detail, which might be related to the unexpected results.

Based on previous reports,[22–24] we hypothesized that systemic comorbidities would associate with mortality and other adverse outcomes; however, hypertension, DM, and CAD did not correlate with adverse events, sac dilatation, or reintervention. Hypertension was negatively associated with reintervention-free survival; however, an inverse relationship has not been previously reported. As guidelines for antihypertensive medication are established and medication compliance is good in Japan, this factor likely did not significantly affect reintervention. We did not evaluate preoperative drug intake (eg, beta-blockers, statins, and antiplatelet drugs); thus, we could not investigate the effect of these prescriptions on EVAR outcomes.

An inverse association between DM and AAA prevalence has been reported,[25,26] and AAA progresses slowly in patients with DM.[27] This association can be explained by increased arterial wall stiffness,[28] and increased synthesis and formation of advanced glycation end products, leading to smooth muscle proliferation in patients with DM.[29] In addition, increased aortic wall stiffness via increased collagen content has been proposed in patients with chronic obstructive pulmonary disease (COPD).[30] Although COPD is known to associate with AAAs, a previous study found no association between COPD and AAA growth.[31] These explanations may account for the observation that DM and respiratory disorders were negative predictors of sac dilatation. CAD was assumed as a strong predictor of prognosis in patients with AAA[32]; however, CAD did not significantly correlate with outcomes, and the reason remains to be clarified.

Sac dilatation is a recent topic of interest, because it sometimes requires reintervention, including open conversion surgery (a highly invasive technique). In the present study, more than 20% of patients showed sac dilatation up to 5 years postoperatively. Thus, it is imperative to investigate the cause and establish optimal reintervention strategies for sac dilatation. Endoleaks, age ≥80 years, neck diameter ≥28 mm, and severe neck angulation >60° have been reported as independent predictors of sac dilatation,[31] consistent with our data. An interesting finding from the Veterans Affairs Open Versus Endovascular Repair trial was that 16% of isolated type 2 endoleaks appeared >1 year after EVAR.[33] The delayed type 2 endoleak was more associated with sac enlargement than the early endoleak. The present study did not include endoleak time series data. In the future, we plan to perform a subanalysis of endoleak development and reduction, after specific data cleaning has been performed.

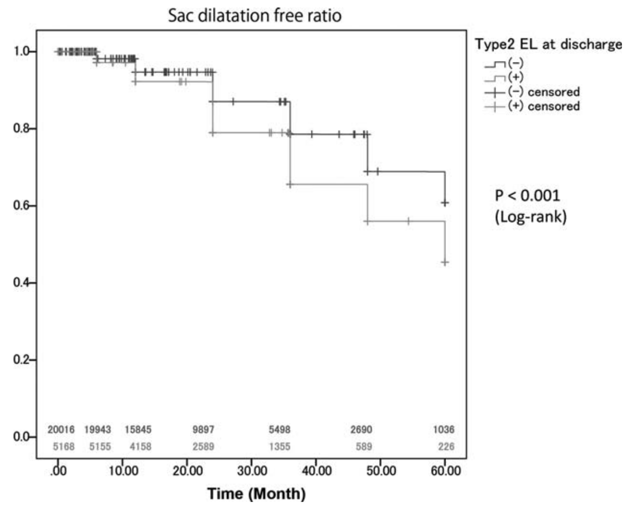

FIGURE 2. Sac enlargement free ratio.

Our data also support the immediate treatment of type 1 and 3 endoleaks, as these were strongly associated with overall survival.[34] In addition, all persistent endoleaks were risk factors for adverse events, sac dilatation, and reintervention. A previous report revealed that any type of endoleak (types were not divided) was associated with sac enlargement.[31] Type 2 endoleaks are believed to be a sign of initial success, reflecting intraoperative aneurysm exclusion and sac pressure decompression, and reintervention for type 2 endoleaks remains controversial. However, the present results might indicate the importance of observing all types of persistent endoleaks closely.

Each surgeon determined the timing of reintervention and the causes for reintervention were not evaluated, as the reintervention details were described in a free-comment item. Although we cannot provide data regarding when to intervene, a sac dilatation ≥5 mm is a strong indicator for intervention. As endoleaks, especially type 2, have been reported to cause sac dilataion,[33] we are interested in the relationship between type 2 endoleaks and the sac dilatation rate. Thus, we performed an exploratory analysis, comparing patients who were positive for type 2 endoleak with those who were negative; the Kaplan–Meier curves of the "sac dilatation ratio" are shown in Fig. 2. Given the observed group differences, surgeons should recognize the potential risk of a type 2 endoleak at discharge, and inform the patients of the possibility of an increased dilatation rate. However, other endoleak types must be analyzed in more detail in future studies to exclude confounding biases.

There are several limitations to this study. First, follow-ups were mainly performed at 6 months or 1 year; consequently, the survival curves had a stepwise shape, which does not reflect reality. Second, the differing methods of device selection and institutional characteristics likely introduced some bias. Third, as the indications for reintervention due to sac dilatation have not been established in any guidelines, and the timing and methods of such reinterventions differ across institutes, the outcome of dilatation is difficult to evaluate. Fourth, as the sac dilatation rate was far greater than that in previous studies, the diagnosis of endoleaks might be inaccurate in this large registry. The methodology for discriminating the type of endoleaks was not detailed; thus, type 1 or 3 endoleaks might be misdiagnosed as type 2. Furthermore, we did not analyze the free-comment items; thus, we cannot easily derive certain hypotheses from this big dataset, especially regarding the association between sac dilatation and endoleaks. Future subanalyses of outcomes associated with different devices and institutional practices are also necessary to resolve these limitations.

CONCLUSIONS

We analyzed data from 38,008 cases of EVAR for AAA in the JACSM registry, covering nearly all aortic stent grafts implanted in Japan. Although the analysis included EVAR with poor anatomy, the perioperative mortality rate was acceptable compared to that in previous large population studies.

ACKNOWLEDGMENTS

We thank the JACSM board members (given below) for providing editorial help and assistance in preparing this manuscript, including editing and checking contents. We specially thank Masaru Kimura M.D. for helping us analyze the data.

Collaborators and affiliated academic societies involved in the Japan Committee for Stentgraft Management (JACSM): Kimihiro Komori, Japan Society for Vascular Surgery (http://www.jsvs.org/); Kunihiro Shigematsu, Japanese College of Angiology (http://j-ca.org/wp/); Atsushi Hirayama, The Japanese Circulation Society (http://www.j-circ.or.jp/); Masanao Toma, Japanese Association of Cardiovascular Intervention and Therapeutics (http://www.cvit.jp/); Kimihiko Kichikawa, Japanese Society of Interventional Radiology (http://www.jsir.or.jp/); Osamu Sato, The Japanese Society for Cardiovascular Surgery (http://square.umin.ac.jp/jscvs/index.html); Hiroyuki Sadogawa, Japanese Society for Phlebology (http://www.js-phlebology.org/); Nobuya Koyama, The Japanese Society of Endovascular Intervention (http://jsei.umin.jp/index.html); Takashi Nishimura, Japanese Society for Artificial Organs (http://www.jsao.org/); Hideyuki Shimizu, The Japanese Association for Thoracic Surgery (http://www.jpats.org/); Shigeru Furui, Auditor of JACSM; Shin Ishimaru, Advisor of JACSM; Masaaki Kato, Secretary-General of JACSM; Katsuyuki Hoshina, Data Manager of JACSM.

REFERENCES

1. Greenhalgh RM, Brown LC, Kwong GP, et al. 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;364:843–848.
2. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351:1607–1618.
3. Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA*. 2009;302:1535–1542.
4. Schermerhorn ML, O'Malley AJ, Jhaveri A, et al. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med*. 2008;358:464–474.
5. Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med*. 2015;373:328–338.
6. Leurs LJ, Buth J, Laheij RJF. Long-term results of endovascular abdominal aortic aneurysm treatment with the first generation of commercially available stent grafts. *Arch Surg*. 2007;142:33–41.
7. Obitsu Y, Ishimaru S, Shigematsu H. The educational system to master endovascular aortic repair in Japan: the Japanese Committee for Stentgraft Management. *Eur J Vasc Endovasc Surg*. 2010;39:55–59.
8. Landon BE, O'Malley AJ, Giles K, et al. Volume-outcome relationship and abdominal aortic aneurysm repair. *Circulation*. 2010;122:1290–1297.
9. AbuRahma AF, Campbell J, Stone PA, et al. The correlation of aortic neck length to early and late outcomes in endovascular aneurysm repair patients. *J Vasc Surg*. 2009;50:738–748.
10. Abbruzzese TA, Kwolek CJ, Brewster D, et al. Outcomes following endovascular abdominal aortic aneurysm repair (EVAR): An anatomic and device-specific analysis. *J Vasc Surg*. 2008;48:19–28.
11. Walker J, Tucker L-Y, Goodney P, et al. Adherence to endovascular aortic aneurysm repair device instructions for use guidelines has no impact on outcomes. *J Vasc Surg*. 2015;61:1151–1159.
12. Antoniou GA, Georgiadis GS, Antoniou SA, et al. A-meta analysis of outcomes of endovascular abdominal aortic aneurysm repair in patients with hostile and friendly neck anatoymy. *J Vasc Surg*. 2013;57:527–538.
13. No author, listed. Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection (JCS 2006) [article in Japanese]. *J Cardiol*. 2007;50:547–577.
14. JCS Joint Working Group. Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection (JCS 2011). *Circ J*. 2013;77:789–828.
15. Ouriel K. The PIVOTAL study: a randomized comparison of endovascular repair versus surveillance in patients with smaller abdominal aortic aneurysms. *J Vasc Surg*. 2009;49:266–269.
16. Cao P, De Rango P, Verzini F, et al. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomized trial. *Eur J Vasc Endovasc Surg*. 2011;41:13–25.
17. Yamamoto K, Komori K, Banno H, et al. Validation of patient selection for endovascular aneurysm repair of open repair of abdominal aortic aneurysm. *Circ J*. 2015;79:1699–1705.
18. Hobo R, Kievit J, Leurs LJ, et al. Influence of severe infrarenal aortic neck angulation on complications at the proximal neck following endovascular AAA repair: a EUROSTAR study. *J Endovasc Ther*. 2007;14:1–11.
19. Hoshina K, Hosaka A, Takayama T, et al. Outcomes after open surgery and endovascular aneurysm repair for abdominal aortic aneurysm in patients with massive neck atheroma. *Eur J Vasc Endovasc Surg*. 2012;43:257–261.
20. Wyss TR, Dick F, Brown LC, et al. The influence of thrombus, calcification, angulation and tortuosity of attachment sites on the time to the first graft-related complication after endovascular aneurysm repair. *J Vasc Surg*. 2011;54:965–971.
21. Bastos Goncalves F, Verhagen HJM, Chinsakchai K, et al. The influence of neck thrombus on clinical outcome and aneurysm morphology after endovascular aneurysm repair. *J Vasc Surg*. 2012;56:36–44.
22. Saratzis A, Sarafidis P, Melas N, et al. Impaired renal function is associated with mortality and morbidity after endovascular abdominal aortic aneurysm repair. *J Vasc Surg*. 2013;58:879–885.
23. Qureshi MA, Greenberg RK, Mastracci TM, et al. Patients with chronic obstructive pulmonary disease have shorter survival but superior endovascular outcomes after endovascular aneurysm repair. *J Vasc Surg*. 2012;56:911–919.
24. Fitridge RA, Boult M, de Loryn T, et al. Predictors of 1-year survival after endovascular aneurysm repair. *Eur J Vasc Endovasc Surg*. 2016;51:528–534.
25. Shantikumar S, Ajjan R, Porter KE, et al. Diabetes and the abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2010;39:200–207.
26. De Rango P, Farchioni L, Fiorucci B, et al. Diabetes and abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2014;47:243–261.
27. Weiss JS, Sumpio BE. Review of prevalence and outcome of vascular disease in patients with diabetes mellitus. *Eur J Vasc Endovasc Surg*. 2006;31:143–150.
28. Baumgartner I, Hirsch AT, Abola MTB, et al. Cardiovascular risk profile and outcome of patients with abdominal aortic aneurysm in out-patients with atherothrombosis data from the Reduction of Atherothrombosis for Continued Health (REACH) Registry. *J Vasc Surg*. 2008;48:808–814.
29. Forsell C, Swedenborg J, Roy J, et al. The quasi-static failure properties of the abdominal aortic aneurysm wall estimated by a mixed experimental-numerical approach. *Ann Biomed Eng*. 2013;41:1554–1566.
30. Takagi H, Umemoto T. No association of chronic obstructive pulmonary disease with abdominal aortic aneurysm growth. *Heart Vessels*. 2016;31:1806–1816.
31. Schanzer A, Greenberg RK, Hevelone N, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation*. 2011;123:2848–2855.
32. Brown LC, Thompson SG, Greenhalgh RM, et al. Incidence of cardiovascular events and death after open or endovascular repair of abdominal aortic aneurysm in the randomized EVAR trial 1. *Br J Surg*. 2011;98:935–942.
33. Lal BK, Zhou W, Li Z, et al. Predictors and outcomes of endoleaks in the Veterans Affairs Open Versus Endovascular Repair (OVER) trial of abdominal aortic aneurysms. *J Vasc Surg*. 2015;62:1394–1404.
34. Hoshina K, Kato M, Hosaka A, et al. Middle-term results of endovascular aneurysm repair in Japan: does intraoperative endovascular management against the hostile aneurysmal neck prevent the proximal type I endoleak? *Int Angiol*. 2011;30:467–473

