

# Endovascular Therapy for Ruptured Vertebral Artery Dissecting Aneurysms: Results from Nationwide, Retrospective, Multi-Center Registries in Japan (JR-NET3)

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## Abstract

Ruptured vertebral artery dissecting aneurysm (VADA) causes subarachnoid hemorrhage (SAH), and parent artery occlusion (PAO) with endovascular technique (EVT) has been the first-line treatment for ruptured VADA. In this study, we have extracted 530 ruptured VADA, treated through PAO with EVT, from a nationwide, retrospective, multi-center registration in Japan (JR-NET3), and analyzed factors associated with outcome at 30 days and procedure-related complications. Complete occlusion was achieved in 497 cases (93.8%) and favorable outcome was obtained in 303 cases (59.1%). Older age ( $\geq 60$  years), male sex, use of general anesthesia, non-specialist as the responsible doctor, and time delay from onset to treatment ( $\geq 24$  h) were negative factors for favorable outcome in multivariate analysis, although these factors were not associated with procedure-related complications. Compared with previous studies (JR-NET1 and 2), the number of endovascular treatments for patients with VADA and severe SAH increased in this decade; however, the percentage of patients with favorable outcome did not decrease. This might be due to not only the improvement of endovascular treatment itself, but also increased access to endovascular specialists or standardization of management.

Key words: dissecting aneurysm, vertebral artery, endovascular therapy

## Introduction

Ruptured vertebral artery dissecting aneurysm (VADA) causes subarachnoid hemorrhage (SAH), and its re-bleeding rate in the acute phase is higher than that of saccular aneurysms.<sup>1,2)</sup> Parent artery occlusion (PAO) with endovascular technique (EVT) has been the first-line treatment for ruptured VADA, because it is feasible even for severe SAH with cerebellar swelling or increased intracranial pressure.

In this study, we have evaluated a clinical data of ruptured VADA extracted from nationwide, retrospective, multi-center registries in Japan (JR-NET3), to investigate factors that influenced outcome and procedure-related complications. Additionally, we

have compared the results with data from previous studies (JR-NET1 and 2)<sup>3)</sup> to identify changes in treatment trends during this decade in Japan.

## Materials and Methods

The Japanese Registry of Neuroendovascular Therapy (JR-NET) is a nationwide, retrospective, multi-center registration of therapeutic procedures and outcomes from the certified board members of the Japanese Society for Neuroendovascular Therapy (JSNET). This registration began in January 2005, and data were collected in three different periods (2005–2006, 2007–2009, and 2010–2013). In this study, we have extracted information concerning ruptured VADA from JR-NET3, which is the latest data from 775 EVT specialists between January 2010 and December 2013. We then analyzed factors associated with outcome at 30 days and procedure-related complications.

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The total number of intracranial aneurysms treated with EVT was 15,851 (unruptured: 9546, ruptured: 6305) in JR-NET3. Among 6305 ruptured aneurysms, the incidence of VADA was 610 (9.7%), and 530 patients underwent PAO (Fig. 1). Data on the following factors were collected from these 530 patients, and factors associated with outcome or complications were analyzed: age, sex, and World Federation of Neurosurgical Societies (WFNS) grade on admission (WFNS grades 4–5 was considered severe SAH) as patient-derived factors; time from onset to treatment, mode of anesthesia, treatment procedure, features of coils, results of treatment, intra-procedural use of heparin, timing of heparin administration, post-procedural antithrombotic therapy, and type of procedural complications as periprocedural factors; modified Rankin scale (mRS) score at 30 days after treatment as patient outcome (mRS 0–2 was considered a favorable outcome).

Mean and frequency data were compared using the Student *t*-test and the  $\chi^2$  test, respectively. Clinical variables were examined using univariate and multivariate logistic analysis to identify predictors of favorable outcome and complications. All statistical analyses were performed with JMP version 13.2.0 software (SAS Institute, Cary, NC, USA). The significance threshold was established at  $P < 0.05$ .

## Results

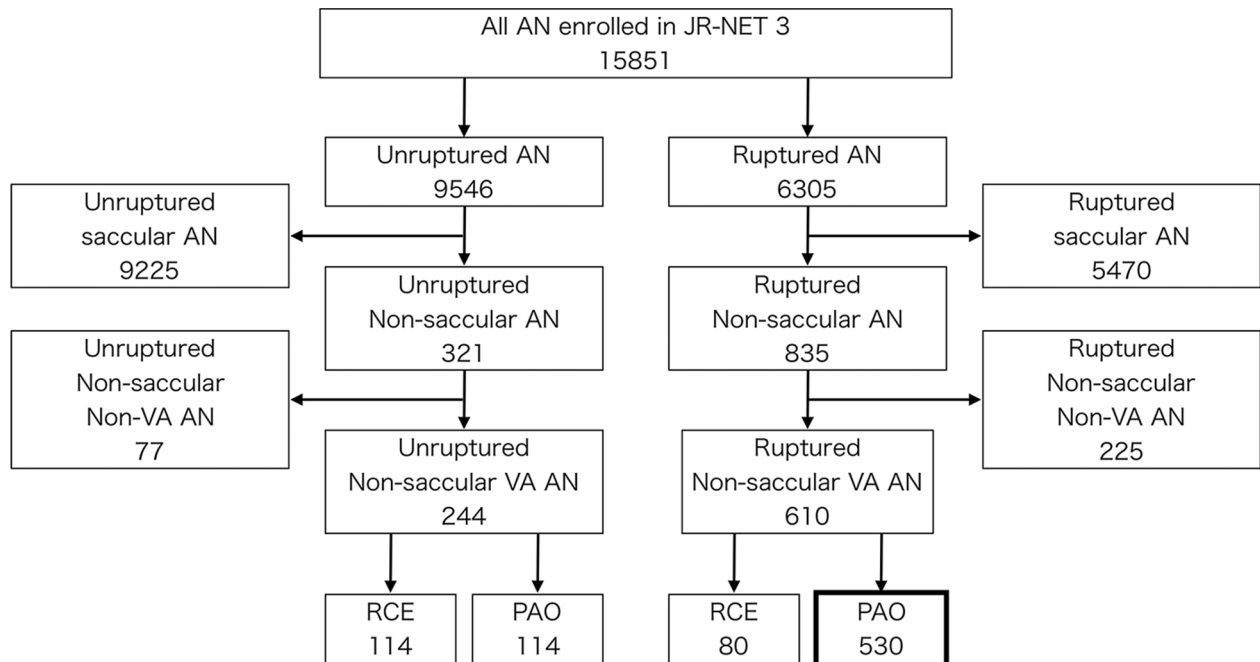
### Patient characteristics

We analyzed periprocedural data of 530 ruptured VADAs extracted from JR-NET3. Table 1 reports patients' baseline characteristics. Mean age  $\pm$  standard deviation was  $54.5 \pm 13.0$ , and no statistical difference was seen between JR-NET3 and previous data (JR-NET1 and 2). In total, 295 (55.7%) patients were male and 304 (57.4%) patients had severe SAH. The proportion of males was lower ( $P = 0.0004$ ), and the percentage of severe SAH was higher ( $P = 0.03$ ) compared to JR-NET1. Regarding the time from onset to treatment, 424 (80.0%) patients were within 24 h, which was higher than JR-NET1 and 2 ( $P < 0.0001$ ,  $P = 0.02$ ).

### Treatment procedures and complications

The details of treatment procedure and complications are summarized in Table 2. Internal trapping and proximal occlusion were performed in 480 (90.6%) and 43 (7.9%) patients, respectively. Complete occlusion was achieved in 497 (93.8%) patients. Embolization was performed in 430 (76.0%) patients with bare platinum coil only. Bioactive and hydrogel coil were used in 56 (11.1%) and 63 (11.9%) patients, respectively.

Heparin was used in 463 (87.4%) patients intra-operatively, and the timing of administration was



**Fig. 1** Summary of aneurysm data in JR-NET3. We evaluated clinical data of 530 ruptured vertebral artery dissecting aneurysms to investigate factors that influence the outcome and procedure-related complications. AN: aneurysm, PAO: parent artery occlusion, RCE: reconstructive coil embolization, VA: vertebral artery.

**Table 1** Patients' baseline characteristics of ruptured VADA treated with PAO

	JR-NET1 (2005–2006) n = 213	JR-NET2 (2007–2009) n = 381	JR-NET3 (2010–2013) n = 530	P-value
Age, mean ± SD	52.5 ± 10.4	54.6 ± 11.7	54.5 ± 13.0	
Male (%)	143 (67.1)	232 (60.9)	295 (55.7)	0.0004*
WFNS grade				
1	20 (9.4)	33 (8.7)	50 (9.4)	
2	52 (24.4)	72 (18.9)	92 (17.4)	
3	37 (17.4)	71 (18.6)	81 (12.3)	
4	47 (22.1)	89 (23.4)	127 (24.0)	
5	57 (26.8)	109 (28.6)	177 (33.4)	
N/A	0 (0.0)	7 (1.8)	3 (0.6)	
Severe SAH (WFNS grade: 4–5)	104 (48.9)	198 (52.0)	304 (57.4)	0.03*
Time from onset to treatment				
<24 h	105 (49.2)	283 (74.3)	424 (80.0)	
24–72 h	68 (32.0)	57 (15.0)	49 (9.2)	
4–7 days	14 (6.6)	13 (3.4)	17 (3.2)	
8–14 days	8 (3.8)	8 (2.1)	14 (2.6)	
15–30 days	16(7.6)	20 (5.2)	11 (2.1)	
>30 days			10 (1.9)	
N/A	2 (0.9)	0 (0)	5 (1.0)	
<24 h	105 (49.2)	283 (74.3)	424 (80.0)	*<0.0001 †0.02

N/A: not available, WFNS: World Federation of Neurosurgical Societies, \*JR-NET1 versus JR-NET3, †JR-NET2 versus JR-NET3.

after sheath introduction in 364 (68.7%) patients, after microcatheter navigation in 25 (4.7%) patients, and after placement of the first coil in 62 (11.7%) patients.

Regarding post-procedural antithrombotic therapy, no drug was used in 224 (42.3%) patients, antiplatelet agent was used in 132 (24.9%) patients, anticoagulant agent was used in 52 (9.8%) patients, and both antiplatelet and anticoagulant agents were used in 101 (19.1%) patients.

Procedural complications occurred in 107 (20.2%) patients. Ischemic and hemorrhagic complications occurred in 84 (15.8%) and 14 (2.6%) patients, respectively.

### Clinical outcome at 30 days

Table 3 and Fig. 2 show clinical outcome at 30 days, in which the data of JR-NET1 and 2 are also referred. Favorable outcome (mRS 0–2) was obtained in 303 (59.1%) patients in JR-NET3; no statistical difference was seen between JR-NET3 and previous studies in terms of the percentage of favorable outcome.

### Factors associated with favorable outcome

In 513 patients whose clinical outcome at 30 days was confirmed, factors associated with favorable outcome were analyzed (Table 4). Older age ( $\geq 60$  years), male sex, use of general anesthesia, and non-specialist as the responsible doctor were negative factors for favorable outcome in univariate analysis. In multivariate analysis, the odds ratios (95% confidence intervals) for age ( $\geq 60$  years), male sex, and use of general anesthesia were 0.49 (0.32–0.74), 0.43 (0.29–0.65), and 0.50 (0.31–0.81) patients, respectively. Regarding the time from onset to treatment (OTT) and responsible doctor, the odds ratios (95% confidence intervals) for time from OTT (<24 hours) and responsible doctors (supervisory doctor certified by JSNET) were 1.62 (1.00–2.62) and 5.03 (2.17–11.71) patients, respectively.

### Factors related to complications

Several factors (time from OTT, use of general anesthesia, treatment procedure, result of treatment, responsible doctor, intraoperative use of heparin, and timing of heparin administration) were analyzed

**Table 2 Treatment procedures and complications**

	JR-NET3 (2010–2013) <i>n</i> = 530
Treatment procedure	
Internal trapping	480 (90.6)
Proximal occlusion	42 (7.9)
Other	4 (0.8)
N/A	4 (0.8)
Result of treatment	
Complete occlusion	497 (93.8)
Partial occlusion	23 (4.3)
Attempt	0 (0.0)
N/A	10 (1.9)
Coil	
Only bare platinum coil	403 (76.0%)
With bioactive coil	59 (11.1%)
With hydrogel coil	63 (11.9%)
Intraprocedural use of heparin	463 (87.4)
Timing of heparin administration	
After sheath introduction	364 (68.7)
After micro-catheter navigation	25 (4.7)
After placement of first coil	62 (11.7)
Other	12 (2.3)
N/A	67 (12.6)
Postprocedural antithrombotic therapy	
Both	101 (19.1)
Only antiplatelet	132 (24.9)
Only anticoagulant	52 (9.8)
None	224 (42.3)
N/A	21 (4.0)
Procedural complication	
Total	107 (20.2)
Ischemic	84 (15.8)
Hemorrhagic	14 (2.6)
Puncture site	2 (0.4)
Others	7 (1.3)

N/A: not available.

as risk factors of procedure-related complications. However, no association was identified between these factors and complications, even after dividing complications into ischemic and hemorrhagic categories (Table 5).

### Comparison of profiles and outcome between JR-NET3 and previous studies (JR-NET1 and 2)

To understand the changes in treatment trends during this decade, we compared data from JR-NET3 with that from previous studies (JR-NET1 and 2) (Table 6). In patients who underwent PAO with EVT, the percentage of severe SAH increased gradually from JR-NET1 to 3 (48.8%, 52.9%, and 57.7%, respectively). The percentage of patients with favorable outcome, however, did not decrease statistically.

The rate of favorable outcome in severe SAH increased from 31.7%, 31.3%, and 56.2% in JR-NET1, 2, and 3, respectively. However, in mild SAH (WFNS grade 1-3), no improvement in favorable outcome was identified (30.3%, 17.8%, and 37.0% in JR-NET1, 2, and 3, respectively).

### Discussion

Vertebral artery dissecting aneurysm has a different pathologic mechanism from that of saccular aneurysm, and is common in patients in their forties and fifties.<sup>4–6</sup> In cases of ruptured VADA, the rebleeding rate in the acute phase is higher than that of saccular aneurysms; thus, it must be treated promptly with precise techniques.<sup>2,5,7</sup>

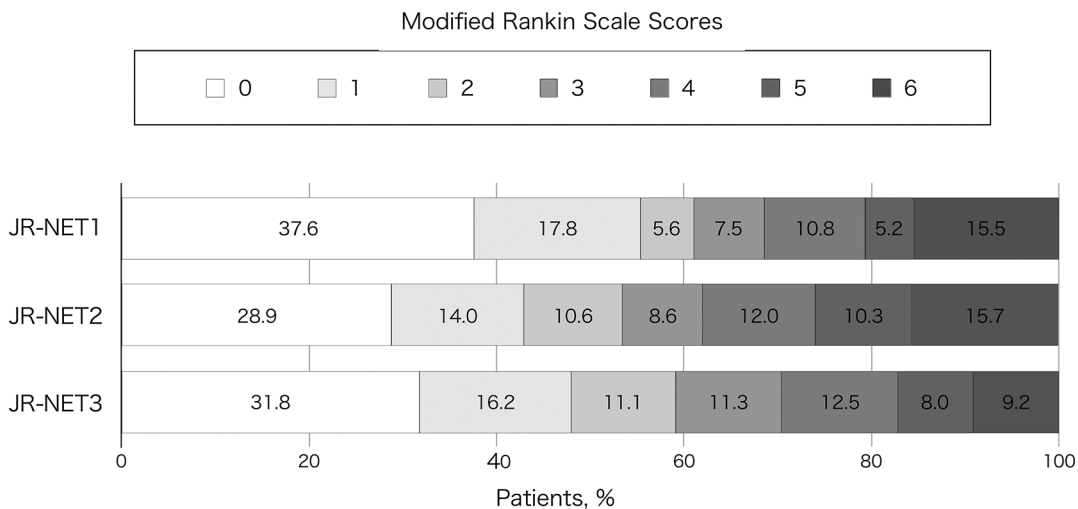
In 610 ruptured VADA, 530 (86.9%) patients underwent PAO and 80 (13.1%) patients underwent reconstructive coil embolization. In 530 patients treated with PAO, internal trapping and proximal occlusion were performed in 480 (90.6%) and 43 (7.9%) patients, respectively (Table 2). Although we could not identify the reason why the operators decided the treatment strategies due to the characteristics of this registry study design, reconstructive coil embolization might be chosen instead of PAO if the contralateral vertebral artery (VA) was hypoplastic. Proximal occlusion might be selected instead of internal trapping if aneurysmal segment involved ipsilateral branching arteries [posterior inferior cerebellar artery (PICA) or anterior spinal artery].

In JR-NET3, the proportion of males with VADA was less than that of JR-NET1 (55.7% vs. 67.1%), and patients with severe SAH were more common than in JR-NET1 (57.4% vs. 48.9%). Though we cannot determine the exact reason why the proportion of males decreased, improved recognition of blood pressure control in Japan may have contributed, as hypertension is one of the risk factors for intracranial VA dissection.<sup>8,9</sup> The increase in the number of patients with severe SAH treated with EVT might be derived from the increased availability

**Table 3 Clinical outcome at 30 days**

	JR-NET1 (2005–2006) n = 213	JR-NET2 (2007–2009) n = 350	JR-NET3 (2010–2013) n = 513	P-value
mRS at 30 days				
0	80 (37.6)	101 (28.9)	163 (31.8)	
1	38 (17.8)	49 (14.0)	83 (16.2)	
2	12 (5.6)	37 (10.6)	57 (11.1)	
3	16 (7.5)	30 (8.6)	58 (11.3)	
4	23 (10.8)	42 (12.0)	64 (12.5)	
5	11 (5.2)	36 (10.3)	41 (8.0)	
6	33 (15.5)	55 (15.7)	47 (9.2)	
Favorable outcome (mRS: 0–2)	130/213 (61.0)	187/350 (53.4)	303/513 (59.1)	0.62* 0.10†

mRS: modified Rankin scale, \*JR-NET1 vs. JR-NET3, †JR-NET2 vs. JR-NET3.



**Fig. 2 Modified Rankin scale scores at 30 days. Outcomes are compared between JR-NET1, 2, and 3.**

of endovascular specialists who recognize the effect of EVT even in patients with severe SAH, as more than 30% patients can achieve favorable outcome.<sup>10–12)</sup> The gradual increase in the proportion of patients receiving early treatment within 24 h (49.2%, 74.3%, and 80.0% in JR-NET1, 2, and 3, respectively) might be also due to more widespread availability of trained neuroendovascular specialists in Japan.<sup>12)</sup>

Regarding clinical outcome, favorable outcome (mRS  $\leq 2$ ) was obtained in 59.1%, compatible with recent reports.<sup>7,13–15)</sup> We also analyzed factors associated with favorable outcome, and older age ( $\geq 60$  years), male sex, use of general anesthesia, non-specialist as the responsible doctor, and time delay from onset to treatment ( $\geq 24$  h) were negative factors for favorable outcome on multivariate analysis (Table 4). Although it is difficult to determine why male sex and use of general anesthesia were negative factors for favorable outcome, one

possible explanation is that males in their 40s or 50s tend to have several risk factors for treatment, such as hypertension, diabetes mellitus, smoking, and ethanol use, as compared to females,<sup>16)</sup> and these risk factors could have increased the rate of poor outcome. Concerning general anesthesia, one possible explanation for its association with negative outcome is that it is in some cases necessary to wait on an anesthesiologist for treatment, and unexpected deterioration can occur during the waiting time. Unfortunately, we could not obtain detailed information about the time from OTT, or the occurrence of rebleeding before treatment; thus, we cannot prove this hypothesis. There was no correlation between the use of general anesthesia and procedure-related complications; therefore, general anesthesia itself might not be harmful in terms of treatment and we should not recommend local anesthesia from the point of view of safety.

**Table 4** Factors associated with favorable outcome.

	Total	Favorable outcome (mRS: 0–2)	Poor outcome (mRS: 3–6)	Univariate analysis	Multivariate analysis	
				<i>P</i> -value	OR (95% CI)	<i>P</i> -value
	<i>n</i> = 513	303 (59.1%)	210 (40.9%)			
Olderly age (≥60)	161 (31.4)	83 (27.4)	78 (37.1)	0.02	0.49 (0.32–0.74)	0.0008
Male	286 (56%)	148 (49%)	138 (65%)	0.0002	0.43 (0.29–0.65)	<0.001
Severe SAH (WFNS grade: 4–5)	297 (57.9)	167 (55.1)	130 (61.9)	0.13	0.76 (0.51–1.12)	0.16
General anesthesia	396 (77.2)	219 (72.3)	177 (84.3)	0.0014	0.50 (0.31–0.81)	0.0047
Early treatment (OTT <24 h)	410 (80.0)	249 (82.2)	161 (76.7)	0.17	1.62 (1.00–2.62)	0.048
Responsible doctor						
Supervisory doctor	202 (39.4)	133 (43.9)	69 (32.9)			
Specialist	278 (54.2)	160 (52.8)	118 (56.2)	0.0005	5.03 (2.17–11.71)* 3.41 (1.50–7.79) <sup>†</sup>	0.0002* 0.0035 <sup>†</sup>
Non-specialist	33 (6.4)	10 (3.3)	23 (11.0)			
Intraoperative use of Heparin	447 (87.1)	267 (88.1)	180 (85.7)	0.41	1.32 (0.71–2.46)	0.38
Postprocedural antithrombotic therapy						
Both	97 (18.9)	60 (19.8)	37 (17.6)			
Only anticoagulant	51 (9.9)	28 (9.2)	23 (11.0)		1.28 (0.45–1.35) <sup>#</sup>	0.37 <sup>#</sup>
Only antiplatelet	131 (25.5)	79 (26.1)	52 (24.8)	0.78	0.84 (0.43–1.64) <sup>§</sup> 1.12 (0.69–1.83) <sup>**</sup>	0.61 <sup>§</sup> 0.63 <sup>**</sup>
None	215 (41.9)	123 (40.6)	92 (43.8)			
Procedural complication						
All	107 (20.9)	57 (18.8)	50 (23.8)	0.17	0.69 (0.16–2.96)	0.62
Ischemic	84 (16.4)	45 (14.9)	39 (18.6)	0.26	0.79 (0.18–3.56)	0.76
Hemorrhagic	14 (2.7)	7 (2.3)	7 (3.3)	0.48	0.60 (0.10–3.70)	0.58

CI: confidence interval, OTT: onset to treatment, WFNS: World Federation of Neurosurgical Societies, \*supervisory doctor vs. non-specialist, <sup>†</sup>specialist vs. non-specialist, <sup>#</sup>both vs. none, <sup>§</sup>only anticoagulant vs. none, <sup>\*\*</sup>only antiplatelet vs. none.

In JR-NET 1 and 2, severe SAH and procedural complications were reported as negative factors for favorable outcome;<sup>3)</sup> however, a significant correlation between these two factors and poor outcome was not found in JR-NET3 (*P*-values calculated by multivariate analysis, 0.16 and 0.62, respectively). We suggest that early and aggressive treatment for severe SAH may lead to a decreased rebleeding rate and improved outcome, therefore severe SAH may not be a negative factor for favorable outcome statistically. In contrast, the complication rate in JR-NET3 (20.9%) was higher than that in JR-NET1 and 2 (10.0% and 6.2%). This trend is more obvious regarding ischemic complications (6.2%, 3.1%, and 16.4% in JR-NET1, 2, and 3).<sup>3)</sup> Though the detailed information about complications was not acquired from the data set (e.g. perforation

of aneurysmal wall in treatment, rebleeding after treatment, embolic complication, cerebellar infarction in PICA territory, or brain stem infarction due to perforators occlusion, with or without clinical symptoms), this data implies that asymptomatic ischemic change, detected as small hyper-intensity spots on diffusion weighted imaging, might be counted in the most recent study as ischemic complications. We, therefore, may not be able to identify a correlation between complications and poor outcome.

Surprisingly, the most influencing factor for favorable outcome was the responsible doctor for treatment. From this data, we recognize that education and training in EVT is the most important factor to improve the outcome of patients with ruptured VADA.

**Table 5 Factors related to complications**

	Total <i>n</i> = 530	All complications <i>n</i> = 107 (20.2%)	<i>P</i> -value	Ischemic complication <i>n</i> = 84 (15.8%)	<i>P</i> -value	Hemorrhagic complication <i>n</i> = 14 (2.6%)	<i>P</i> -value
	Number (%)	Number (%)		Number (%)		Number (%)	
Time from onset to treatment							
<24 h	424 (80.0)	85 (79.4)	0.88	64 (76.2)	0.35	13 (92.9)	0.24
≥24 h	101 (19.1)	21 (19.6)		19 (22.6)		1 (7.1)	
General anesthesia							
Yes	406 (76.6)	86 (80.4)	0.12	71 (84.5)	0.06	9 (64.3)	0.27
No	124 (23.4)	21 (19.6)		13 (15.5)		5 (35.7)	
Treatment procedure							
Internal trapping	480 (90.6)	98 (91.6)	0.6	75 (89.3)	0.81	14 (100)	0.26
Proximal occlusion	42 (8.0)	6 (5.6)		6 (7.1)		0 (0.0)	
Result of treatment							
Complete occlusion	497 (93.8)	99 (95.2)	0.96	77 (93.9)	0.42	13 (100)	0.43
Partial occlusion	23 (4.3)	5 (4.8)		5 (6.1)		0 (0.0)	
Responsible doctor							
Supervisory doctor	213 (40.2)	37 (34.6)	0.6	28 (33.3)	0.21	6 (42.9)	0.62
Specialist	284 (53.6)	62 (57.9)		48 (57.1)		8 (57.1)	
Non-specialist	33 (6.2)	8 (7.5)		8 (9.5)		0 (0.0)	
Intraoperative use of Heparin							
Yes	463 (87.4)	91 (85.1)	0.32	70 (83.3)	0.08	12 (85.7)	0.69
No	57 (10.8)	16 (15.0)		14 (16.7)		2 (14.3)	
Timing of heparin administration							
After sheath introduction	364 (68.7)	77 (72.0)	0.25	60 (71.4)	0.12	10 (71.4)	0.69
Others (later than above)	99 (18.7)	14 (13.1)		10 (11.9)		2 (14.3)	

**Table 6 Comparison of profiles and outcome between JR-NET1, 2 and 3**

	JR-NET1 (2005–2006) <i>n</i> = 213	JR-NET2 (2007–2009) <i>n</i> = 381	JR-NET3 (2010–2013) <i>n</i> = 530	<i>P</i> -value
Severe SAH (WFNS grade: 4–5)	104/213 (48.8)	198/374 (52.9)	297/527 (57.7)	0.03*
Favorable outcome (mRS: 0–2)	130/213 (61.0)	187/350 (53.4)	303/513 (59.1)	
Favorable outcome in severe SAH patients	33/104 (31.7)	62/198 (31.3)	167/297 (56.2)	<0.0001* <0.0001†
Poor outcome (mRS: 3–6) in mild SAH patients	33/109 (30.3)	27/152 (17.8)	80/216 (37.0)	<0.0001†
Negative factors for favorable outcome	Severe SAH Procedural complication PICA-involved lesion	Severe SAH Procedural complication Olderly age Postprocedural ATT (-)	Olderly age Male Late treatment (≥24 h) General anesthesia Non-specialist	

ATT: antithrombotic therapy, \*JR-NET1 vs. JR-NET3, †JR-NET2 vs. JR-NET3.

There was no correlation between the following factors and complications: time from OTT, use of general anesthesia, treatment procedure, result of treatment, responsible doctor, intraoperative use of heparin, and timing of heparin administration (Table 5). We, however, did identify a trend toward a higher rate of ischemic complications in patients treated with general anesthesia ( $P = 0.06$ ) and without intraoperative heparin use ( $P = 0.08$ ). Although heparin was injected after sheath introduction in approximately 70% of patients, timing of heparin administration had no effect on ischemic and hemorrhagic complications.

Regarding the responsible doctor, no relation to complication was identified, even though it was the most influencing factor for favorable outcome. We speculate that the major difference between specialist and non-specialist was not the incidence but the severity of complications, because there was statistical difference between specialist and non-specialist on the outcome of complication cases. As shown in Table 5, complication occurred in 99 patients by specialist (supervisory doctor and specialist) and 8 patients by non-specialist. Fifty-six (56.6%) out of 99 had favorable outcome in specialist group, whereas 1 (12.5%) out of 8 had favorable outcome in non-specialist group ( $P = 0.02$ ). This data implies that specialist can avoid severe complications or manage the patients appropriately, and get favorable outcome even in cases of complications.

Table 6 reports data from JR-NET1, 2, and 3, to identify changes in treatment trends during this decade. The percentage of patients with severe SAH who underwent PAO with EVT increased gradually (48.8%, 52.9%, and 57.7%, respectively); however, the percentage of patients with favorable outcome did not decrease (61.0%, 53.4%, and 59.1%, respectively). This data encourages us to perform PAO with EVT even in case of severe SAH. In patients with severe SAH, the percentage with favorable outcome at 30 days has certainly increased during the past decade (31.7%, 31.3%, and 56.2%, respectively), and the recent data is more robust than that of another recent report.<sup>14)</sup> This might be due to not only earlier treatment, as shown in Table 1 (80.0% of patients were treated within 24 h in JR-NET3), but also the increase in trained neuroendovascular specialists.

This study has several limitations. We extracted information regarding VADAs treated through PAO with EVT from a nationwide registry data, but this does not represent all data in Japan. Our results could be inherently biased because the treating physicians themselves assessed clinical outcomes and procedure-related complications. Decisions on

treatment indications might also have introduced inclusion bias.

In conclusion, we analyzed data from 530 cases of ruptured VADA treated using PAO with EVT between January 2010 and December 2013 in Japan. Complete occlusion was achieved in 497 (93.8%) patients and favorable outcome was obtained in 303 (59.1%) patients. Older age ( $\geq 60$  years), male sex, use of general anesthesia, non-specialist as the responsible doctor, and time delay from OTT ( $\geq 24$  h) were negative factors for favorable outcome in multivariate analysis, though these factors were not associated with procedure-related complications.

Even as treatment has been increasingly performed for severe SAH in this decade, the percentage of patients with favorable outcome did not decrease. This might be due to not only the improvement in endovascular treatment itself, but also the increased availability of endovascular specialists or standardization of management with the use of recognized guidelines.

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### Conflicts of Interest Disclosure

All authors who are members of the Japanese Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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