

5 bare platinum coils (Figure 1E). Her symptoms disappeared immediately, and she remained asymptomatic for 5 years without recurrence of the shunts.

### Patient 19

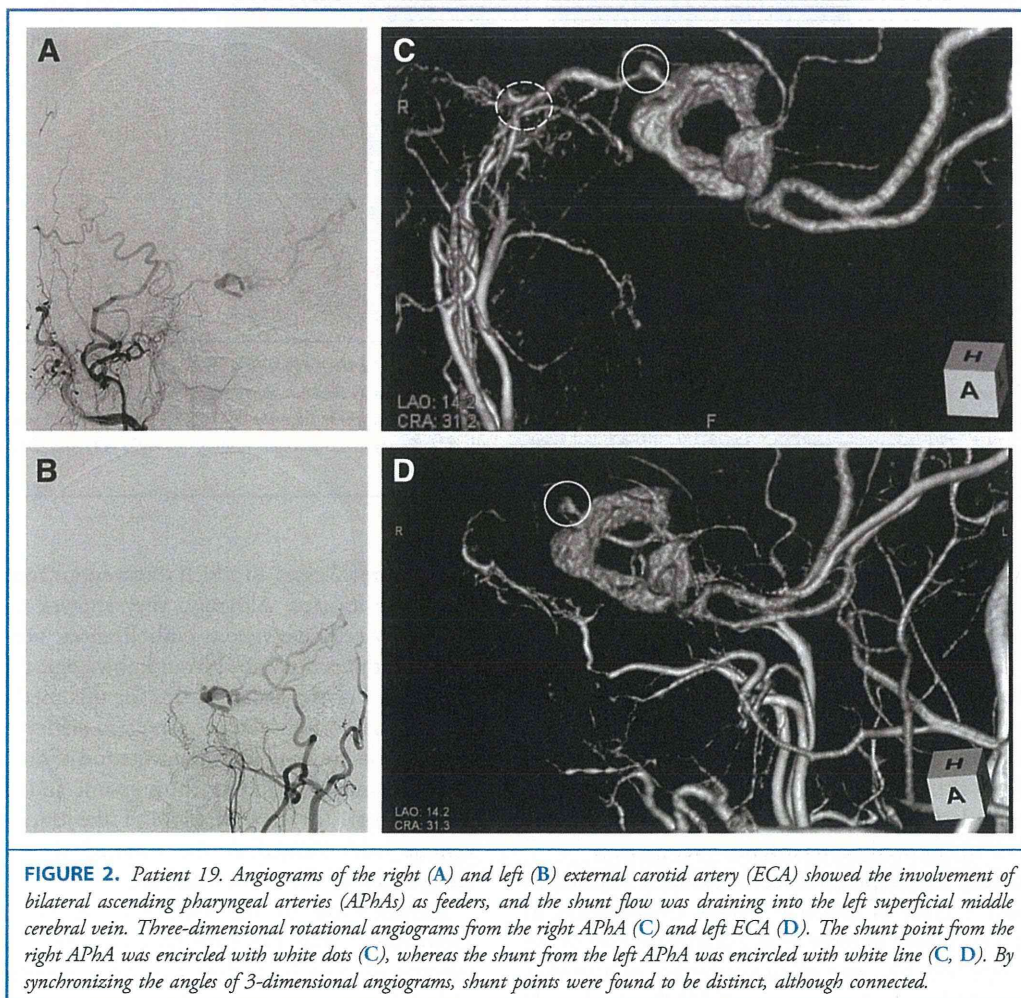
This 71-year-old man had left abducens palsy and tinnitus. Cerebral digital subtraction angiography revealed a CSdAVF, the feeders of which were bilateral ascending pharyngeal arteries (Figures 2A and 2B). 3-D RA revealed 2 distinct shunt segments located just outside the medial compartment of the left CS (Figures 2C and 2D). At the time of the procedure, a microcatheter was advanced to the shunt segment, with proper working angles obtained by 3-D RA. Shunt segments were obliterated with 8 bare platinum coils after the confirmation step, resulting in the disappearance of the shunt and prompt resolution of his symptoms (Figure 3).

## DISCUSSION

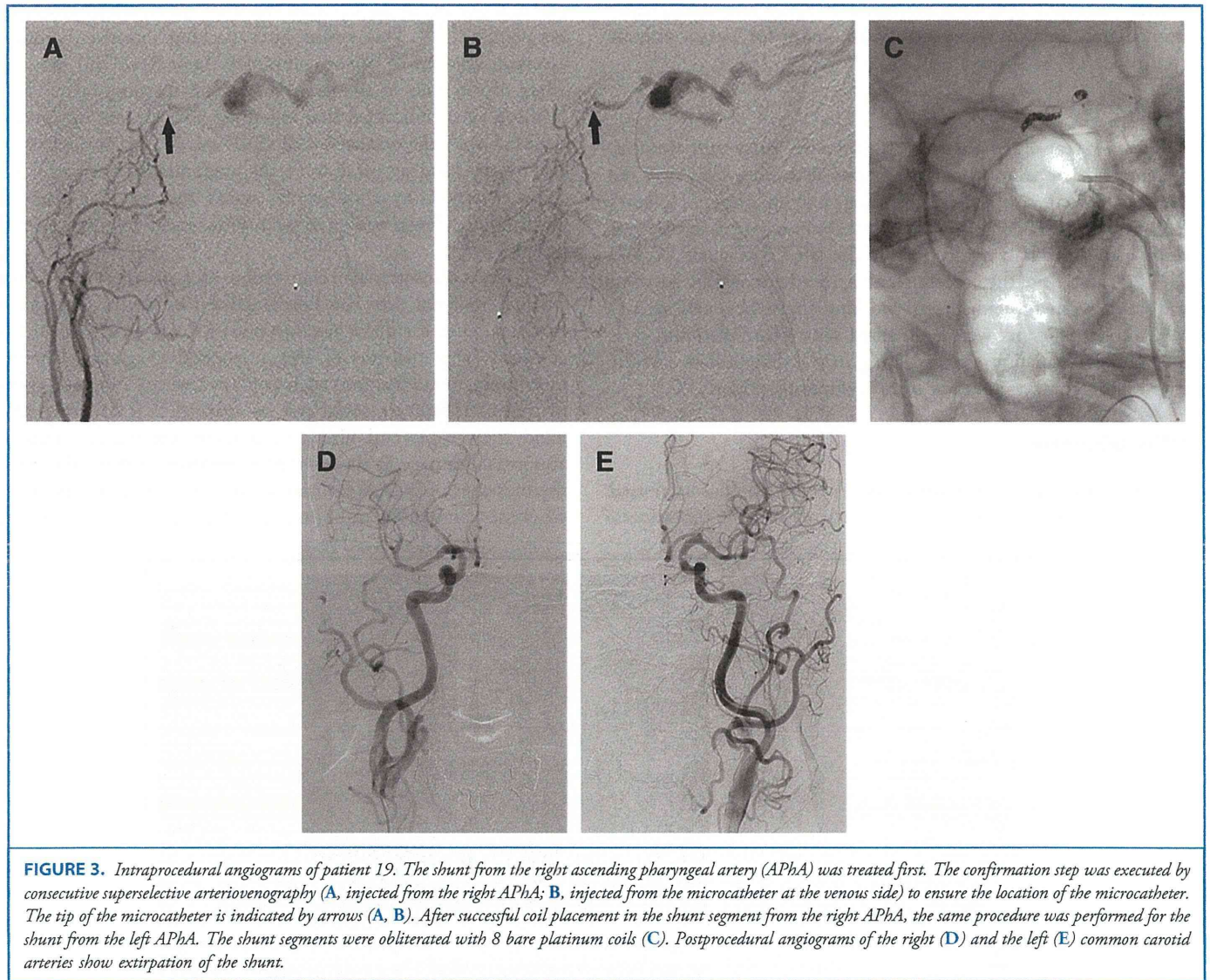
In treating CSdAVFs, transvenous embolization has been used for decades since the prevalence of neuroendovascular procedures,

and obliteration of the CS itself has been the standard procedure for years.<sup>1,2,10,12</sup> This entire sinus packing, however, requires a certain amount of coils to eliminate shunt flow, and the mass effect of the coils in the sinus may result in subsequent CNP. Nishino et al<sup>3</sup> described that when the coil volume was greater than 0.2 cm<sup>3</sup>, the occurrence of CNP was 77.8% in their series, and overpacking appeared to be the predominant cause of CNP. Another report by Bink et al<sup>4</sup> stated that the incidence of persistent CNP was as high as 44% with a mean follow-up period of 4.4 years.

Recently, transarterial or transvenous embolization using Onyx, a liquid material, has also been reported by several authors. A complete cure for dural arteriovenous fistulae (AVFs) could be achieved with the use of this nonadhesive agent. However, unfavorable complications such as bradycardia, CNP, and gluing of the microcatheter could not be ignored.<sup>13-15</sup> On the other hand, transvenous embolization enables the direct interruption of abnormal drainage to the orbit and cerebrum without damaging the branches of ECAs that may supply the cranial nerves. Thus, we chose transvenous embolization as the first-line therapy in this



**FIGURE 2.** Patient 19. Angiograms of the right (A) and left (B) external carotid artery (ECA) showed the involvement of bilateral ascending pharyngeal arteries (APhAs) as feeders, and the shunt flow was draining into the left superficial middle cerebral vein. Three-dimensional rotational angiograms from the right APhA (C) and left ECA (D). The shunt point from the right APhA was encircled with white dots (C), whereas the shunt from the left APhA was encircled with white line (C, D). By synchronizing the angles of 3-dimensional angiograms, shunt points were found to be distinct, although connected.



**FIGURE 3.** Intraprocedural angiograms of patient 19. The shunt from the right ascending pharyngeal artery (APhA) was treated first. The confirmation step was executed by consecutive superselective arteriovenography (A, injected from the right APhA; B, injected from the microcatheter at the venous side) to ensure the location of the microcatheter. The tip of the microcatheter is indicated by arrows (A, B). After successful coil placement in the shunt segment from the right APhA, the same procedure was performed for the shunt from the left APhA. The shunt segments were obliterated with 8 bare platinum coils (C). Postprocedural angiograms of the right (D) and the left (E) common carotid arteries show extirpation of the shunt.

study. The unavailability of Onyx for treating dural AVFs in Japan was another reason.

Our data demonstrated the excellent results of SSSO in CSdAVFs. In all 12 patients with SSSO, initial symptoms resolved within 1 month; only 3 patients (25%) had postprocedural transient abducens palsy, and there were no permanent deficits. The possible cause of transient symptoms may be due to the inflammatory effect of the rather small coil mass to the abducens nerve, which only lasted for a short period. Clinical and radiographic follow-up showed no recurrence over 3 years.

This idea has already been reported in several articles. Nakamura et al<sup>6</sup> first reported 3 cases of selective venous embolization in which many coils were placed in more than 2 compartments of the CS. Piske et al<sup>7</sup> reported 12 cases of superselective transvenous sinus occlusion, in which only 2 cases were CSdAVFs. Agid et al<sup>8</sup>

also reported 2 cases, in which transvenous approaches via the facial vein were focused. Although they showed cases with CSdAVFs treated by selective venous embolization, none of them reported details of this procedure. To our knowledge, this is the first detailed description of the technical tips for this method.

There are 4 indispensable steps to achieve SSSO: (1) identification of the shunt point, (2) navigation of the microcatheter to the shunt segment (including shunt point and the adjacent venous component), (3) confirmation of the microcatheter (from the venous side) located at the targeted shunt segment, and (4) obliteration of the shunt segment.

Identification of the shunt is mainly done by diagnostic angiography with fast sequences of 4 to 6 frames/s. Instead of selective venography in the CS, superposing the early arterial phase with full venous phases and using oblique views as reported in

previously,<sup>6,7</sup> we preferentially used 3-D RA to clarify the location of shunts. 3-D RA usually showed the arterial segment as denser than the venous component in fistulous lesions, thus allowing comprehensive visualization of the fistulae. Furthermore, the working angles at the time of the procedure could be easily obtained. If available, a 3-D C-arm mounted flat panel detector cone-beam CT system may also be useful in this identifying step, as reported by Hiu et al.<sup>16</sup>

Navigation of the microcatheter to the shunt segment was easy when the angioarchitecture of the affected CS was clearly demonstrated by angiograms with appropriate working angles obtained by 3-D RA.

Exploring the CS with the microcatheter before reaching the shunt segment is important to understand the structure of the CS. Access to the major venous outlets such as the superior orbital vein or sphenoparietal sinus should be assessed and assured in case SSSO failed to eliminate the shunt. SSSO failed in 2 patients in this series, in which sinus packing was performed subsequently with ease due to this exploration before starting SSSO.

Confirmation of the position of the microcatheter is usually achieved by consecutive superselective arteriovenography. This method is superior to superselective venography, as it clearly visualizes shunt flow exclusively to ensure proper positioning of the microcatheter located in the venous side.

Obliteration of the shunt segment was performed with soft coils because the shunt segment in each case was a small space and also to prevent dislocation of the microcatheter from the segment.

As to the location of the shunt, we report an interesting finding in the current study. In 7 of 12 cases with SSSO, the shunt segment was found outside the CS. This paracavernous venous plexus is reported to exist frequently.<sup>17</sup> The reason why shunts were located in these paracavernous structures still remains unknown, as paracavernous structures are constructed in the fetal stage, whereas dural AVFs are known to be an acquired disease.<sup>18,19</sup> A possible explanation for this question is that inflammation, which is considered to be the cause of the occurrence of dural arteriovenous shunts, may be more prone to take place in these restricted small structures than the vast sinus wall itself.<sup>20</sup>

There are several limitations to this study. This was a retrospective study of the experience at a single center. The total number of patients is rather small; thus the success rate of SSSO may vary with the accumulation of cases. Furthermore, longer follow-up may be required to ensure that there is no clinical or radiological recurrence.

Nevertheless, the technical details described here are very comprehensive and should be considered useful to physicians who deal with neuroendovascular therapy.

## CONCLUSION

In treating CSdAVFs, SSSO could be achieved in considerable cases with excellent long-term results. The appropriate use of 3-D RA and consecutive superselective arteriovenography provides enough information to use this method, which should be considered before sinus packing or mere obliteration of dangerous venous outlets.

## Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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## Special Theme Topic: Japanese Surveillance of Neuroendovascular Therapy in JR-NET/JR-NET2—Part II

# Endovascular Treatment for Ruptured Vertebral Artery Dissecting Aneurysms: Results from Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2

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### Abstract

In treating ruptured vertebral artery dissecting aneurysms (VADAs), neuroendovascular therapy (NET) represented by coil obliteration is considered to be a reliable intervention. However, there has been no multi-center based study in this setting so far. In this article, results of NET for ruptured VADA obtained from Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2 were assessed to elucidate the factors associated with favorable outcome. A total of 213 in JR-NET1 and 381 patients in JR-NET2 with ruptured VADA were included, and they were separately analyzed because several important datasets such as vasospasm and site of dissecting aneurysms in relation to the posterior inferior cerebellar artery (PICA) were collected only in JR-NET1. The ratio of poor World Federation of Neurosurgical Societies (WFNS) grade (4 and 5) was 48.8% and 53.9%, and the ratio of favorable outcome (modified Rankin scale, mRS 0 to 2) at 30 days after onset was 61.1 % and 49.1% in JR-NET1 and 2, respectively. In both studies, poor WFNS grade and procedural complication were independently correlated as negative factors for favorable outcome. In JR-NET1, PICA-involved lesion was also designated as a negative factor while elderly age and absence of postprocedural antithrombotic therapy was detected as other negative factors in JR-NET2. The ratios of favorable outcome in poor grade patients were 25.4% in JR-NET1 and 31.3% in JR-NET2, which seemed compatible with the previous studies. These results may provide a baseline data for the NET in this disease and could be useful for validating the benefits of novel devices.

Key words: vertebral artery, dissecting aneurysm, subarachnoid hemorrhage, neuroendovascular therapy, nationwide survey

### Introduction

Vertebral artery dissecting aneurysm (VADA) is nowadays increasingly recognized as a cause of subarachnoid hemorrhage and ischemic stroke.<sup>1)</sup> In patients with ruptured VADAs, a high incidence of rebleeding and a high mortality rate at the time of rebleeding was reported.<sup>2,3)</sup> Recently, catheter-based

neuroendovascular approach has emerged as first-line therapy for ruptured VADA along with the development of new techniques and devices and their results are favorable so far.<sup>4-10)</sup>

There was no report, however, as to the detailed data of the relationship between NET and patient's outcome in a large multi-center based study.

This study was aimed to clarify the current status and results of NET for ruptured VADA in Japan from the data of Japanese Registry of Neuroendovascular Therapy

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(JR-NET) 1 and 2, thereby extracting a clue for elucidating the appropriate therapy for this harmful disease.

## Materials and Methods

The data in this study were collected from JR-NET1 and 2. Briefly, JR-NET1 was the registration of therapeutic procedures and outcomes from the certified board members of Japanese Society for Neuroendovascular Therapy (JSNET) between 2005 and 2006 while JR-NET2 was that of JSNET board members between 2007 and 2009. The Institutional Review Board at each center approved the use of retrospective data from the patients.

The total numbers of registration were 11,213 cases in JR-NET1 and 20,751 cases in JR-NET2. Among all the datasets, the incidence of ruptured VADA was 213 (1.9%) and 381 (1.8%) in JR-NET1 and JR-NET2, respectively.

The following factors were collected in both studies: age, sex, and World Federation of Neurosurgical Societies (WFNS) grade on admission as patient-derived factors while the timing of neuroendovascular therapy (NET), mode of anesthesia, technical success which was defined as the absence of blood flow to the ruptured lesion, participation of board members as in charge of the procedure, intraprocedural use of heparin, postprocedural antithrombotic therapy, and ischemic/hemorrhagic complications as periprocedural factors. No detailed information about used devices for the lesion such as coils (bare platinum or surface modified), stents, and balloons were collected in both studies. A modified Rankin scale (mRS) score at 30 days after the onset was used for evaluation of patients' outcome and defined as the primary endpoint. The point of 0 to 2 in mRS, which means independence of the patients, was considered as a favorable outcome.

The relationship between factors listed above and mRS scores at 30 days were analyzed to clarify the influencing factors for favorable outcome.

As the datasets collected only in JR-NET1 noted above were expected to influence on the outcome, we analyzed the data of each study separately.

### Statistical analysis

Analyses were performed using JMP version 9.0 (SAS Institute, Cary, North Carolina, USA). Statistical significance for intergroup differences was assessed using the z test for categorical variables and the Mann-Whitney U test for continuous variables. A logistic regression analysis was carried out using the factors with statistically significant differences by univariate analyses to determine any factors that

were significantly related to the favorable outcome. P values < 0.05 were considered to indicate a significant difference.

## Results

### I. Patient characteristics

The patients' demographics are shown in Table 1. The mean age was 52.5 and 54.6 years in JR-NET1 and JR-NET2, respectively. Male preponderance was noted in both studies. As to WFNS grade on admission, the incidence of poor grade (Grades 4 and 5) was 48.9% and 52.0% in JR-NET1 and JR-NET2, respectively.

Table 2 summarized the timing of intervention. 49.2% of the cases in JR-NET1 while 74.3% in JR-NET2 were treated within 24 hours after onset, which had a significant difference ( $p < 0.0001$ )

**Table 1** Patients' baseline characteristics in JR-NET1 and 2

	JR-NET1 (n = 213)	JR-NET2 (n = 381)	p value
Age (SD)	52.5 ( $\pm$ 10.4)	54.6 ( $\pm$ 11.7)	0.17
Male (%)	143 (67.1)	232 (60.9)	0.13
WFNS grade (%)			
1	20 (9.4)	33 (8.7)	
2	52 (24.4)	72 (18.9)	
3	37 (17.4)	71 (18.6)	
4	47 (22.1)	89 (23.4)	
5	57 (26.8)	109 (28.6)	
Poor (4 and 5, %)	104 (48.9)	198 (52.0)	0.46
Unknown (%)	0 (0.0)	7 (1.8)	

JR-NET: Japanese Registry of Neuroendovascular Therapy, WFNS: World Federation of Neurosurgical Societies.

**Table 2** Interval from admission to treatment in JR-NET1 and 2

	JR-NET1 n = 213	JR-NET2 n = 381	p value
< 24 h	105 (49.2)	283 (74.3)	< 0.0001
24 h to 72 h	68 (32.0)	57 (15.0)	
< 72 h	173 (81.2)	340 (89.3)	0.006
Days 3 to 7	14 (6.6)	13 (3.4)	
Days 8 to 14	8 (3.8)	8 (2.1)	
After day 14	16 (7.6)	20 (5.2)	

Figures in the parentheses indicate column percentages. h: hours, JR-NET: Japanese Registry of Neuroendovascular Therapy.

between the two studies.

Approximately three-fourth of the cases were under general anesthesia (74.6% and 80.1% in JR-NET1 and JR-NET2, respectively).

## II. Therapeutic demographics

Technical success was noted in 98.6% and 98.7% in JR-NET1 and JR-NET2, respectively.

As shown in Table 3, intraprocedural use of heparin was noted in 88.3% and 78.8% of the cases in JR-NET1 and JR-NET2, respectively. In more than half of the cases with heparin use, the administration of heparin was performed after the placement of sheath introducers. Postprocedural antithrombotic therapy was performed in approximately two-third of the cases (63.4% in JR-NET1 and 63.5% in JR-NET2). The ratios of anticoagulant use were 53.3% and 43.4% in JR-NET1 and JR-NET2, respectively. Antiplatelet agents were used approximately in 80% of all the cases in both studies, and concomitant use were observed approximately in one-third of the cases throughout two studies.

Procedural complication was observed in 9.9% and 10.8% in JR-NET1 and JR-NET2, respectively. The clinical outcome at 30 days after the onset was favorable in 61.0% and 49.1% whereas fatal in 15.5% and 14.4% in JR-NET1 and JR-NET2, respectively (Table 4).

**Table 3** Periprocedural antithrombotic therapy in JR-NET1 and 2

	JR-NET1 n = 213	JR-NET2 n = 381	p value
Intraprocedural use of heparin, yes	188 (88.3)	300 (78.8)	0.004
<i>Timing</i>	n = 188	n = 300	
After introduction of sheath	97 (51.6)	194 (64.7)	0.004
After navigation of a microcatheter	22 (11.7)	29 (9.7)	0.47
After placement of first coil	64 (34.0)	68 (22.7)	0.005
Others	5 (2.7)	9 (3.0)	
Postprocedural antithrombotic therapy, yes	135 (63.4)	242 (63.5)	0.97
<i>Mode</i>	n = 135	n = 242	
Anticoagulant only	27 (20.0)	21 (8.7)	0.001
Antiplatelet only	61 (45.2)	102 (42.1)	0.57
Anticoagulant and antiplatelet	45 (33.3)	84 (34.7)	0.79
Unknown	2 (1.5)	35 (14.5)	

Figures in the parentheses indicate column percentages. JR-NET: Japanese Registry of Neuroendovascular Therapy.

## III. Relationship between patient characteristics, procedural factors and clinical outcome

In JR-NET1, univariate analysis showed that age, poor WFNS grade, posterior inferior cerebellar artery (PICA)-involved lesion, use of heparin, and procedural complication were significantly related to the favorable outcome. Among them, poor WFNS grade, PICA-involved lesion, and procedural complication were identified as independent factors by multivariate analysis (Table 5).

Similarly, univariate analysis showed that age, poor WFNS grade, postprocedural antithrombotic therapy, and absence of procedural complication were significantly related to the favorable outcome in JR-NET2. Multivariate analysis in this registry revealed that age, poor WFNS grade, postprocedural antithrombotic therapy, and procedural complication were independently correlated with the favorable outcome (Table 6).

In addition, factors associated with favorable outcome in poor grade patients were also analyzed. However, there were no significant factors detected as positive or negative factors for favorable outcome, except for the ischemic complication in JR-NET1 (Table 7).

## IV. Relationship between location of the lesion and NET in JR-NET1

Information as to the locations of VADA and site of intervention in relation to the dissecting aneurysms which were only available in JR-NET1 study is shown in Table 8. Locations of VADA were classified into four groups: proximal to PICA (pP), distal to PICA (dP), PICA involved (Pi), and no PICA (nP). Coil placement in the aneurysmal dilatation (AD) were performed in 78.7% (37/47) of group pP, 95.2% (79/83) of group dP, 80% (40/50) of group Pi, and 100% (29/29) of group nP. Balloon guiding catheter

**Table 4** Clinical outcome at 30 days in JR-NET1 and 2

	JR-NET1 n = 213	JR-NET2 n = 381	p value
mRS 0	80 (37.6)	101 (26.5)	
1	38 (17.8)	49 (12.9)	
2	12 (5.6)	37 (9.7)	
0-2	130 (61.0)	187 (49.1)	0.005
3	16 (7.5)	30 (7.9)	
4	23 (10.8)	42 (11.0)	
5	11 (5.2)	36 (9.4)	
6	33 (15.5)	55 (14.4)	
Unknown	0 (0)	31 (8.1)	

JR-NET: Japanese Registry of Neuroendovascular Therapy, mRS: modified Rankin scale.

**Table 5 Results of univariate and multivariate analyses for favorable outcome in JR-NET1**

Variable	Number	Favorable outcome	Univariate	Multivariate	
			p value	OR (95% CI)	p value
Age	54.2 ( $\pm$ 10.5)	50.6 ( $\pm$ 10.1)	0.034	0.99 (0.95–1.02)	0.46
Male	143/213 (67.1)	85/130 (65.4)	0.49		
Poor WFNS grade (4 and 5)	104/213 (48.8)	33/130 (25.4)	< 0.0001	0.066 (0.026–0.16)	< 0.0001
OTT					
> 24 h	103/192 (53.6)	62/124 (50.0)	0.23	1.61 (0.66–4.04)	0.29
24h to 72 h	67/192 (34.9)	45/124 (36.3)	0.098	0.62 (0.24–2.98)	0.81
> 72 h	22/192 (11.5)	17/124 (13.7)	0.23	1.16 (0.38–4.98)	0.62
Board members in charge of procedure	180/210 (85.7)	110/129 (85.2)	1.00		
PICA involved lesion	50/213 (23.5)	22/130 (16.9)	0.02	0.41 (0.15–1.05)	0.05
Use of heparin	188/210 (89.5)	121/129 (93.8)	0.01	2.41 (0.17–9.31)	0.17
Postprocedural antithrombotic therapy	135/207 (65.2)	89/128 (69.5)	0.09	1.26 (0.33–1.98)	0.67
Procedural complications	21/210 (10.0)	8/130 (6.2)	0.0007		
Ischemic	13/210 (6.2)	4/130 (3.1)	0.001	0.11 (1.59–59.9)	0.012
Hemorrhagic	5/210 (2.4)	0/130 (0.0)	< 0.0001	< 0.0001 (0–0.04)	0.039
Vasospasm	24/195 (12.3)	11/130 (9.5)	0.06	0.24 (0.04–1.08)	0.08

Standard deviation or percentages are in parentheses otherwise indicated. CI: confidence interval, h: hours, OR: odds ratio, OTT: Onset-to-treat time, PICA: posterior inferior cerebellar artery, WFNS: World Federation of Neurosurgical Societies.

**Table 6 Results of univariate and multivariate analyses for favorable outcome in JR-NET2**

Variable	Number	Favorable outcome (n = 187)	Univariate	Multivariate	
			p value	OR (95% CI)	p value
Age	54.6 ( $\pm$ 11.7)	50.8 ( $\pm$ 10.1)	< 0.0001	1.06 (1.04–1.09)	< 0.0001
Male	232 (60.9)	108 (57.5)	0.21		
Poor WFNS grade (4 and 5)	198 (52.0)	62 (31.3)	< 0.0001	0.13 (0.08–0.21)	< 0.0001
OTT					
> 24 h	283 (74.3)	141 (75.4)	0.21	0.74 (0.36–1.50)	0.4
24 h to 72 h	57 (15.0)	27 (14.4)	0.17	0.87 (0.33–2.33)	0.78
> 72 h	41 (10.7)	19 (10.2)	0.20	1.55 (0.71–3.46)	0.28
Board members in charge of procedure	341 (89.5)	167 (89.3)	1.00		
Use of heparin	300 (78.3)	150 (80.2)	0.13	0.97 (0.53–1.77)	0.91
Postprocedural antithrombotic therapy	211 (55.4)	122 (65.2)	0.0002	2.15 (1.32–3.54)	0.002
Procedural complications	41 (10.8)	15 (8.0)	0.09		
Ischemic	33 (8.7)	15 (8.0)	0.71	0.39 (0.16–0.92)	0.03
Hemorrhagic	8 (2.1)	0 (0.0)	0.007	< 0.0001 (0–0.19)	0.0005

Standard deviation or percentages are in parentheses otherwise indicated. CI: confidence interval, h: hours, OR: odds ratio, OTT: onset-to-treat time, WFNS: World Federation of Neurosurgical Societies.

**Table 7 Results of univariate and multivariate analyses for favorable outcome in patients with poor WFNS grade on admission**

Variable	JR-NET1 (n = 104)			JR-NET2 (n = 198)		
	Univariate	Multivariate		Univariate	Multivariate	
	p value	OR (95% CI)	p value	p value	OR (95% CI)	p value
Age	0.59	0.96 (0.92–1.02)	0.25	0.02	1.05 (0.98–1.09)	0.06
Male	0.82			0.53		
OTT						
> 24 h	0.49	0.55 (0.18–1.63)	0.28	0.29	0.85 (0.32–2.44)	0.75
24 h to 72 h	0.64	0.84 (0.15–5.18)	0.84	0.61	1.87 (0.60–7.15)	0.28
> 72 h	0.48	1.52 (0.29–9.19)	0.62	0.45	2.20 (0.51–10.7)	0.29
BM in charge of procedure	0.77	1.46 (0.35–6.06)	0.59	0.81	1.16 (0.42–3.53)	0.78
PICA involved lesion	0.64	0.68 (0.19–2.22)	0.54	n/a		
Use of heparin	0.78	2.11 (0.56–9.37)	0.28	0.35	1.28 (0.58–3.03)	0.55
Postprocedural AT	0.78	1.12 (0.39–3.29)	0.82	0.36	1.46 (0.78–2.79)	0.23
Procedural complications	0.01			0.23		
Ischemic	0.05	0.13 (0–0.008)	0.008	0.51	0.41 (0.05–1.93)	0.28
Hemorrhagic	< 0.0001	0.01 (0–11.7)	0.41	0.56	0.19 (0.02–2.35)	0.16
Vasospasm	0.08	0.25 (0.03–1.56)	0.14	n/a		

AT: antithrombotic therapy, BM: board members, CI: confidence interval, h: hours, JR-NET: Japanese Registry of Neuroendovascular Therapy, n/a: not applicable, OR: odds ratio, OTT: onset-to-treat time, WFNS: World Federation of Neurosurgical Societies.

**Table 8 Obliterated sites and location of aneurysmal dilatation in JR-NET1**

	Proximal to PICA	Distal to PICA	PICA involved	No PICA	Unknown	p value
Number (%)	47 (22.1)	83 (39.0)	50 (23.5)	29 (13.6)	4 (1.9)	
Favorable outcome	30/47 (63.8)	56/83 (67.5)	22 (44.0)*	20 (69.0)	2 (50.0)	0.01
Obliterated site (%)	n = 47	n = 83	n = 50	n = 29	n = 4	
Proximal only	8 (16.8)	1 (1.2)	10 (20.0)	0 (0.0)	3 (75.0)	
AD only	14 (29.8)	54 (65.1)	24 (24.0)	13 (44.8)	1 (25.0)	
Distal only	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Proximal and AD	19 (40.4)	16 (19.3)	11 (22.0)	10 (34.5)	0 (0.0)	
Distal and AD	1 (2.1)	2 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Proximal, distal, and AD	2 (4.2)	6 (7.2)	4 (8.0)	6 (20.7)	0 (0.0)	
AD and stenting	1 (2.1)	1 (1.2)	1 (2.0)	0 (0.0)	0 (0.0)	
Stenting only	1 (2.1)	3 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	
Use of balloon GC (%)	13 (27.7)	13 (15.7)	16 (34.0)	12 (41.4)	1 (25.0)	
Postprocedural status of PICA						
Preserved	46	83	23	10	1	
Occluded	1	0	23	0	0	
With bypass surgery	0	0	4	0	0	
Unknown	0	0	0	19	3	

AD: aneurysmal dilatation, GC: guiding catheter, PICA: posterior inferior cerebellar artery. \*Statistically significant.



was used in 27.7%, 15.7%, 34.0%, and 41.4% in cases of group pP, dP, Pi, and nP, respectively.

In group Pi, the ratio of favorable outcome was smaller than other groups (44%,  $p = 0.01$ ). The proportion of using a balloon guiding catheter was rather small, and PICA was sacrificed in approximately half of the cases. Ischemic complication was noted in 21.7% cases with sacrifice of PICA, resulting in smaller proportion of favorable outcome comparing with cases in which PICA was preserved (34.8% versus 52.2%) although there was no statistic difference in favorable outcome ( $p = 0.11$ , Table 9).

### Discussion

It is well known that the prognosis of ruptured VADA is very poor. Two major reasons are poor grade on admission and high incidence of rerupture at ultra-early stage.<sup>2,3)</sup> With the invent of NET, the first-line therapy for ruptured VADA has been shifted to NET in this decade because of its less invasiveness and time consciousness: direct access to the lesion without damaging the cerebellum and cranial nerves is possible and the therapeutic procedures can be performed in conjunction with the diagnostic angiography.<sup>11)</sup>

This is the first nationwide survey of NET for ruptured VADA and provides important information about current status of NET and its relationship with clinical outcomes. Although the protocols were almost the same in JR-NET1 and 2, several datasets including the location of the lesion and vasospasm which were collected only in JR-NET1 seemed to be associated with favorable outcomes (Table 5). Thus, JR-NET1 and 2 were analyzed separately instead of analyzing these two studies as a composite to provide the accurate information.

Approximately 50% of all the cases in both studies were categorized as poor WFNS grade, which was

compatible with previous reports.<sup>4,12)</sup> There was a significant difference in terms of onset-to-treatment time (OTT) between two studies and approximately three-fourth of the patients were treated within 24 hours after onset in JR-NET2 (Table 2). This result may be due to widespread recognition as to the importance of preventing ultra-early rebleeding and nationwide prevalence of NET itself.

In both studies, poor WFNS grade and procedural complication were independently detected as negative factors for favorable outcome. This finding was compatible with previous studies on the outcome of subarachnoid hemorrhage including a recent study from our country,<sup>13,14)</sup> and also with a single-center study regarding ruptured VADA<sup>12)</sup> (Tables 5 and 6). The ratios of favorable outcome of patients with poor WFNS grade at onset were 25.4% and 31.3% in JR-NET1 and JR-NET2, respectively. These results were compatible with the previous studies as shown in Table 10, and were better than the result of PRESAT study, which dealt only with saccular aneurysms, whose ratio of favorable outcome in the patients with poor grade was 20.0%.<sup>14)</sup> The clinical course of poor grade SAH caused by ruptured VADA might be more promising than SAH with ruptured, saccular aneurysms.

We also analyzed the relationship between collected datasets and favorable outcome in poor grade patients, only to find that the ischemic complication in JR-NET1 was negatively associated with favorable outcome. A possible explanation is that the determinants other than poor grade itself as detected in Tables 5 and 6 were less correlated with favorable outcome in this subgroup mainly due to sample size.

In JR-NET2, age and postprocedural antithrombotic therapy were demonstrated as independent factors for favorable outcome. As to age, the odds ratio was only 1.06 although elderly age is considered as an indicator for poor outcome in previous

**Table 9** Procedural complication, favorable outcome, and postprocedural status of PICA in JR-NET1

	Procedural complication n = 9	Hemorrhagic complication n = 3	Ischemic complication n = 5	Favorable outcome	p value
PICA preserved	1/23 (4.3)	1/23 (4.3)	0/23 (0.0)	12/23 (52.2)	0.11
PICA occluded	8/23 (34.8)	2/23 (8.6)	5/23 (21.7)	8/23 (34.8)	
OA-PICA bypass	0/4 (0.0)	0/4 (0.0)	0/4 (0.0)	2/4 (50.0)	

Percentages are in parentheses, OA: occipital artery, PICA: posterior inferior cerebellar artery.

**Table 10 Comparison of profiles and outcomes between previous studies on ruptured VADA and JR-NET studies**

Series	Number	Age (mean)	Poor WFNS grade n (%)	Techniques used (n)	Used scale for outcome	Favorable outcome n (%)		Death n (%)
						All	Poor WFNS grade	
Kurata et al. <sup>6)</sup>	18	52	9 (50.0)	IT (18)	GOS	14 (77.7)	3 (33.3)	3 (16.7)
Ravinov et al. <sup>8)</sup>	21	52	6 (28.6)	IT (11), PO (7)	mRS	11 (52.4)	1 (16.7)	0 (0.0)
Yuki et al. <sup>10)</sup>	27	45	8 (29.6)	IT (26), PO (1)	mRS	14 (51.8)	1 (12.5)	5 (9.3)
Sugiu et al. <sup>9)</sup>	20	56	8 (40.0)	IT (19), SAC (1)	GOS	15 (75.0)	3 (37.5)	4 (20.0)
Endo et al. <sup>11)</sup>	38	53	19 (50.0)	IT (38)	mRS	23 (60.5)	9 (47.4)	6 (15.8)
JR-NET1	213	54	104 (48.8)	IT (183), PO (23), SAC (3), SM (4)	mRS	130 (61.0)	33 (25.4)	33 (15.5)
JR-NET2	381	55	198 (52.0)	n/a	mRS	187 (49.1)	62 (31.3)	55 (14.4)

A favorable outcome is considered for patients with an mRS score of 0–2, or with GR or MD by GOS. GOS: Glasgow outcome scale, GR: good recovery, IT: internal trapping, JR-NET: Japanese Registry of Neuroendovascular Therapy, MD: moderate disability, mRS: modified Rankin scale, n/a: not available, PO: proximal occlusion, SAC: stent-assisted coiling, SM: stent monotherapy, VADA: vertebral artery dissecting aneurysm, WFNS: World Federation of Neurosurgical Societies.

studies listed above.<sup>13,14)</sup> This might be explained by the fact that the age at onset in this disease was relatively young as compared with studies dealing with saccular aneurysms<sup>6,7,12)</sup> (Table 6).

The efficacy and safety of antithrombotic therapy during and after the NET for ruptured aneurysms remains an unsolved issue. One systematic review suggested that the antiplatelet drugs reduced the risk of delayed cerebral ischemia in patients with subarachnoid hemorrhage.<sup>15)</sup> On the contrary, a subanalysis of International Subarachnoid Aneurysm Trial (ISAT) revealed that antiplatelet therapy during or after endovascular coiling improved outcome in patients with SAH.<sup>16)</sup> The majority of the procedures in our studies were parent artery occlusion, thus use of antiplatelets or anticoagulants might favor in avoiding thromboembolic complications especially with small branches originating from affected VA, and unfavorable outcomes such as re-rupture due to recanalization in acute stage might have occurred less frequently than coiling of saccular aneurysms.

However, this factor was not independently correlated with favorable outcome in JR-NET1 which had more variables; it seems to be premature to recommend postprocedural antithrombotic therapy. The detailed information of antithrombotic therapy especially such as dose, mode, and duration of the used drugs is needed to validate the efficacy of periprocedural antithrombotic therapy for NET in ruptured VADA.

Comparing two studies, the proportion of patients with favorable outcome at 30 days decreased from 61.0% in JR-NET1 to 49.1% in JR-NET2 (Table 4). The reason for this decline is difficult to describe as there were no differences between two studies

in the proportion of poor grade patients, technical success, and incidence of procedural complication. Although the OTT was shorter in JR-NET2, no correlation between OTT and favorable outcome was observed by either univariate or multivariate analysis. The participation of board members as in charge of the procedure also did not correlate with the outcome in each study. No major change was found in the used devices or techniques between two periods. According to the results shown in Table 10, it may be more reasonable to understand that the ratio of favorable outcome in patients with ruptured VADA who underwent NET lies between these numbers noted above.

Regarding the location of the lesion and the mode of the procedure in JR-NET1, the result in group Pi demonstrated that the occlusion of PICA did not affect the ratio of favorable outcome despite the increased incidence of ischemic complication (Table 9). This result should be dealt with special care as there was no information about the perfusion territory of the affected PICA in this series. Complete obliteration of the lesion might be preferred in group Pi in this study as the most important role of NET for ruptured VADAs was the prevention of re-rupture. A recent report from Japan, however, demonstrated that the postoperative medullary infarction was associated with unfavorable outcomes after internal coil trapping for ruptured VADAs.<sup>11)</sup> Furthermore, the fact that the hemorrhagic complication occurred only in one case (4.3%) in which PICA were preserved in this group may imply that the proximal occlusion may be enough for the prevention of re-rupture in acute phase as proposed by authors.<sup>5)</sup>

Regarding use of a balloon-guiding catheter, its