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.1) In patients with ruptured VADAs, a high incidence of rebleeding and a high mortality rate at the time of rebleeding was reported.2,3) 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.4–10)

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 (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, intra procedural 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.

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

|          | JR-NET1 (n = 213) | JR-NET2 (n = 381) | p value |
|----------|-------------------|-------------------|---------|
| Age (SD) | 52.5 (± 10.4)     | 54.6 (± 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)           |         |

**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, WFNS: World Federation of Neurosurgical Societies.
which had a significant difference (p < 0.0001) 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).

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% (n = 381). JR-NET: Japanese Registry of Neuroendovascular Therapy, mRS: modified Rankin scale.

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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   |
| Timing               |                |                |         |
| After introduction   | n = 188        | n = 300        |         |
| of sheath            | 97 (51.6%)     | 194 (64.7%)    | 0.004   |
| After navigation     | 22 (11.7%)     | 29 (9.7%)      | 0.47    |
| of a microcatheter   |                |                |         |
| After placement      | 64 (34.0%)     | 68 (22.7%)     | 0.005   |
| of first coil        |                |                |         |
| Others               | 5 (2.7%)       | 9 (3.0%)       |         |
| Postprocedural       | 135 (63.4%)    | 242 (63.5%)    | 0.97    |
| antithrombotic       |                |                |         |
| therapy, yes         |                |                |         |
| Mode                 | 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    | 45 (33.3%)     | 84 (34.7%)     | 0.79    |
| antiplatelet         |                |                |         |
| Unknown              | 2 (1.5%)       | 35 (14.5%)     |         |

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

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         | Unfavorable outcome | Univariate p value | OR (95% CI) p value |
|---------------------------------|----------------|--------------------|--------------------|--------------------|
| **Variable**                    | **Number**     | **Favorable outcome** |                 |                    |
| **Age**                         | 54.2 (± 10.5)  | 50.6 (± 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              |
| 24 h 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         | Unfavorable outcome | Univariate p value | Multivariate p value |
|---------------------------------|----------------|--------------------|--------------------|----------------------|
| **Variable**                    | **Number**     | **Favorable outcome (n = 187)** |                 |                     |
| **Age**                         | 54.6 (± 11.7)  | 50.8 (± 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) | p value | OR (95% CI) | p value |
|---------------------------------|-------------------|-------------------|---------|-------------|---------|
|                                | Univariate | Multivariate |       | Univariate | Multivariate |       |
| 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 (0.56–2.97) | 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) | 0.01    |
| Favorable outcome   | 30/47 (63.8)     | 56/83 (67.5)   | 22 (44.0)*    | 20 (69.0) | 2 (50.0) |         |
| 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

*Statistically significant. AD: aneurysmal dilatation, GC: guiding catheter, PICA: posterior inferior cerebellar artery.
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.\(^2,^3\) 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.\(^11\)

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.

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

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

Approximately 50% of all the cases in both studies were categorized as poor WFNS grade, which was compatible with previous reports.\(^4,^12\) 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,\(^13,^14\) and also with a single-center study regarding ruptured VADA\(^13\) (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%.\(^14\) 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
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. 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. 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 (Table 6).

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 rerupture. A recent report from Japan, however, demonstrated that the postoperative medullary infarction was associated with unfavorable outcomes after internal coil trapping for ruptured VADAs. Furthermore, the fact that the hemorrhagic complication occurred only in one case (4.3%) in which PICAs were preserved in this group may imply that the proximal occlusion may be enough for the prevention of rerupture in ruptured VADA.

### 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 (%) |
|-----------------|--------|------------|-----------------------|---------------------|------------------------|-------------------------|-------------|
| Kurata et al.   | 18     | 52         | 9 (50.0)              | IT (18)             | GOS                    | 14 (77.7)               | 3 (33.3)    | 3 (16.7) |
| Ravinov et al.  | 21     | 52         | 6 (28.6)              | IT (11), PO (7)     | mRS                    | 11 (52.4)               | 1 (16.7)    | 0 (0.0)  |
| Yuki et al.     | 27     | 45         | 8 (29.6)              | IT (26), PO (1)     | mRS                    | 14 (51.8)               | 1 (12.5)    | 5 (9.3)  |
| Sugiu et al.    | 20     | 56         | 8 (40.0)              | IT (19), SAC (1)    | GOS                    | 15 (75.0)               | 3 (37.5)    | 4 (20.0) |
| Endo et al.     | 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),  | mRS                    | 130 (61.0)              | 33 (25.4)   | 33 (15.5) |
|                 |        |            |                       | SAC (3), SM (4)     |                        |                         |             |           |
| 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.
across phase as proposed by authors.\textsuperscript{5)}

Regarding use of a balloon-guiding catheter, its necessity remains an enigma\textsuperscript{17)} although the merits of this method were considered as prevention of distal embolism and reduction of subarachnoid bleeding at the time of intraprocedural rupture.\textsuperscript{19)} In group Pi, however, the territory of PICa was forced to be fed by retrograde blood flow via contralateral VA, which should run through coil mass when proximal flow control was performed.\textsuperscript{19)} The anxiety for thromboembolism in PICa territory might be the major reason for the smallest number of cases with this method in group Pi.

Stent-assisted coiling and stent monotherapy including the use of flow diverters are becoming an alternative method of NET for this disease and the initial results seem feasible.\textsuperscript{20–22)} Stent was used only in seven cases in Jr-NET1, and unfortunately the use of stent was not in the collected datasets in Jr-NET2. The number of stents use in ruptured VADA was considered to be small as stents designed for intracranial use were not available in Japan during the study period. A prospective, multi-centered study on the efficacy and safety of stenting along with antithrombotic therapy is strongly awaited.

This study has several limitations. This study was retrospective, and data were missing in some patients. The clinical evaluation during the study period and angiographic examinations were not evaluated by physicians who were blinded to the therapy. Furthermore, lack in unity in the datasets among two studies may have dimmed the influence of procedural/medical factors for favorable outcome. If all the datasets in Jr-NET1 were collected in Jr-NET2, influence of age, PICa-involved lesion, postprocedural antithrombotic therapy upon favorable outcome could be clarified for the better guidelines for NET and periprocedural management in ruptured VADA. Also, the determinants of favorable outcome after NET in poor grade patients might be presented.

Nevertheless, this study provides important information as to the current status of NET in Japan, especially the correlation among patients’ status at onset, procedural results, and clinical outcomes.

**Conclusion**

Ruptured VADA treated by NET, mainly by proximal occlusion and internal trapping, resulted in high technical success rate up to 98.7%, and approximately 50% to 60% of the patients had a favorable outcome at 30 days after onset. Poor WFNS grade and intraprocedural complication were detected as negative factors for favorable outcomes. The results of this study may be used as baseline data for validation of future NET including the novel devices in Japan.

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**Conflicts of Interest Disclosure**

The authors declare that there are no conflicts of interest.

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