

# Outcome after Endovascular Treatment of Patients with Acute Ischemic Stroke with Large Vessel Occlusion over 90 Years of Age

Fuminori SHIMIZU,<sup>1</sup> Kazutaka UCHIDA,<sup>2</sup> Hiroto KAKITA,<sup>1</sup> Sou SAWAMURA,<sup>1</sup>  
Akihiro KANBARA,<sup>1</sup> Yuji KITADA,<sup>1</sup> Yoshinori AKIYAMA,<sup>1</sup> Takashi YOSHIDA,<sup>1</sup>  
Satoru FUJIWARA,<sup>3</sup> Hirotoshi IMAMURA,<sup>4</sup> Chiaki SAKAI,<sup>5</sup> Manabu SHIRAKAWA,<sup>2</sup>  
Shinichi YOSHIMURA,<sup>2</sup> Nobuyuki SAKAI,<sup>1</sup> and the JR-NET4 Study Group

<sup>1</sup>Department of Neurosurgery, Shimizu Hospital, Kyoto, Kyoto, Japan

<sup>2</sup>Department of Neurosurgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan

<sup>3</sup>Department of Neurology, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan

<sup>4</sup>Department of Neurosurgery, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan

<sup>5</sup>Department of Neurosurgery, Kyoto University Graduate School of Medicine, Kyoto, Kyoto, Japan

## Abstract

The effectiveness of endovascular therapy for patients aged 90 years and over ( $\geq 90$  years) is still not well understood. We compared the patients aged  $\geq 90$  years with those aged 85-89 years, 80-84 years, and  $< 80$  years using data from the Japanese Registry of NeuroEndovascular Therapy that enrolled acute large vessel occlusion patients from January 2015 to December 2019. The primary outcome was the rate of return of the modified Rankin Scale to at least the premorbid modified Rankin Scale after 30 days. Secondary outcomes were the incidences of intracranial hemorrhage and mortality. Among 13,540 patients, patients aged  $\geq 90$  years, 85-89 years, 80-84 years, and  $< 80$  years were 1,104, 1,925, 2,477, and 8,034. The prevalence of female gender, the premorbid Rankin Scale, and the National Institutes of Health Stroke Scale score before endovascular therapy were highest in the patients aged  $\geq 90$  years ( $n$  [%], 819 [74.2]; median [interquartile range]; 2 [0-3], and 21 [15-26]). The primary outcome of the adjusted odds ratio (95% confidence intervals) for the patients aged 85-89 years, 80-84 years, and  $< 80$  years for  $\geq 90$  years was 0.89 (0.72-1.10), 0.95 (0.77-1.16) and 1.07 (0.89-1.28). However, the incidence of symptomatic intracranial hemorrhage was lower in patients aged  $\geq 90$  years compared with patients aged 85-89 years and  $< 80$  years (adjusted odds ratio [95% confidence intervals]; 1.86 [1.16-2.98] and 1.71 [1.11-2.64]). The return of the modified Rankin Scale to at least the premorbid modified Rankin Scale after 30 days in patients aged  $\geq 90$  years with large vessel occlusion was not significantly different in other groups but symptomatic intracranial hemorrhage was less observed than in younger patients.

Keywords: very elderly patient, acute ischemic stroke, premorbid modified Rankin Scale, intracranial hemorrhage

## Introduction

Given the natural history, acute ischemic stroke (AIS) due to large vessel occlusion (LVO) was a common condition in the elderly,<sup>1)</sup> but there were a few reports on treatment outcomes for patients over 90 years of age.<sup>2,3)</sup> In actual clinical practice, the indication for endovascular treatment (EVT) in patients over 90 years of age with AIS due

to LVO is based on the patient's level of independence in daily living and health status, with the family's wishes being an important factor. Recanalization through EVT is one of the promising treatments, however, very elderly patients aged over 90 years often have tortuous vessels and atherosclerotic lesions resulting in additional technical difficulties and may be responsible for higher rates of thromboembolic complications or difficulty in achieving techni-

Received September 17, 2024; Accepted December 10, 2024

Copyright © 2025 The Japan Neurosurgical Society

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives International License.

cal success.<sup>4)</sup>

Therefore, we investigated the outcomes and results of EVT for acute stroke with LVO in very elderly patients aged over 90 years.

## Materials and Methods

Data from the Japanese Registry of NeuroEndovascular Therapy 4, which was a retrospective, nationwide, multicenter, observational study on neuroendovascular treatments in Japan were analyzed.<sup>5)</sup> The study included patients who received EVT for AIS with LVO from January 1, 2015, to December 31, 2019. The Institutional Review Boards of Kobe City Medical Center General Hospital (approval number zn200107) and all 166 participating hospitals approved this study. Written informed consent from each patient was waived because we used clinical information obtained in routine clinical practice. The institutional review boards approved the exemption in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan.

The indications for treatment, as well as treatment approach and perioperative management, were determined at the discretion of the treating physician.

### Data collection and definitions

Clinical information was collected through a review of hospital charts. Demographic data included age, sex, the premorbid modified Rankin Scale (pre-mRS),<sup>6)</sup> the National Institutes of Health Stroke Scale (NIHSS) score,<sup>7)</sup> occlusion sites, Alberta Stroke Program Early computed tomography (CT) Score (ASPECTS).<sup>8)</sup> Neurologists selected the imaging modalities. Computed tomography angiography was performed to determine the occlusion site when AIS due to LVO was suspected on non-contrast CT. If magnetic resonance imaging was performed, the ASPECTS was evaluated using diffusion-weighted imaging (DWI).<sup>9)</sup> For patients with posterior circulation stroke, we evaluated the posterior circulation ASPECTS on DWI.<sup>10)</sup> DWI-ASPECTS was scored using the 11-point method including deep white matter lesions. LVO was defined as occlusion of the intracranial internal carotid artery, middle cerebral artery (MCA; M1, M2, or M3 segments),<sup>11)</sup> anterior cerebral artery (ACA; A1, A2, or A3 segments), and posterior circulation including posterior cerebral artery (PCA; P1, P2, or P3 segments), intracranial vertebral artery (V4 segment), posterior inferior cerebellar artery, or basilar artery. Medium vessel occlusion (MeVO) was defined as LVO with occlusion of the M2 or M3 segment of the MCA, A2 or A3 segment of the ACA, or PCA.<sup>12)</sup> Additionally, we collected information on the administration of recombinant tissue plasminogen activator (rt-PA), onset to puncture time, general anesthesia, technical characteristics, and type of device used. The combined technique was defined as the concurrent use of a stent retriever and aspiration catheter. The degree of reperfusion

was classified using the modified thrombolysis in cerebral infarction (mTICI) grading system based on the digital subtraction angiography findings obtained immediately after the EVT procedures.<sup>13)</sup> We also collected data on antiplatelet therapy after the procedure and stroke etiology.<sup>14)</sup>

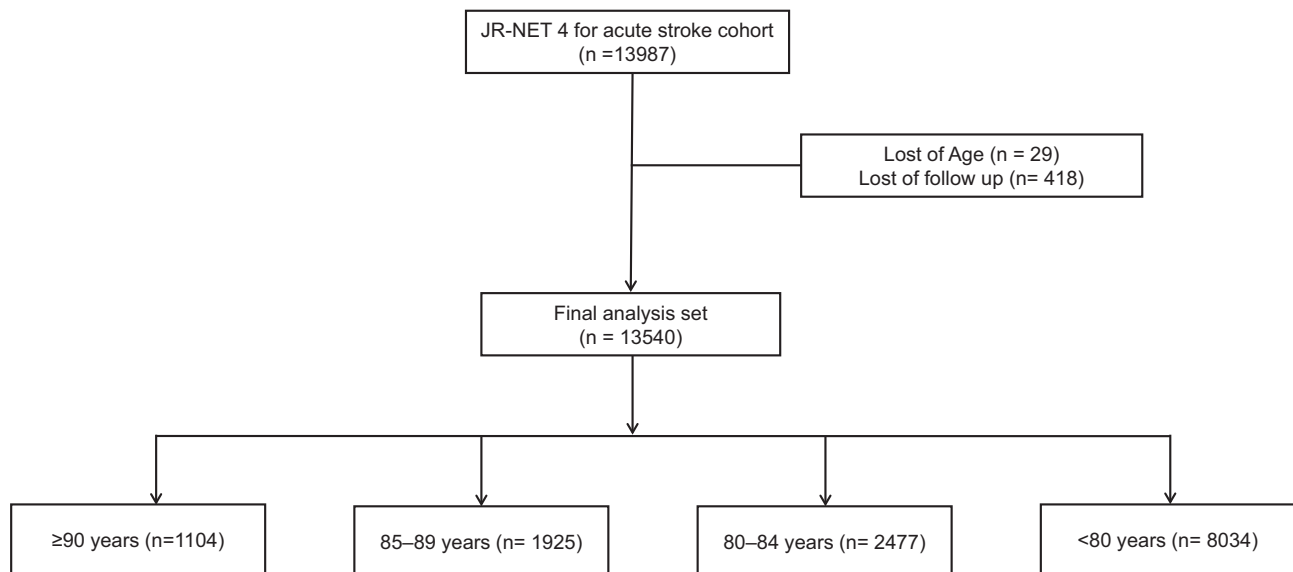
### Outcomes

The primary outcome was the rate of return of the mRS to at least the pre-mRS after 30 days. Secondary outcomes were the incidences of symptomatic intracranial hemorrhage (ICH), any ICH, and mortality within 30 days.

### Statistical analysis

We compared patient characteristics and outcomes between the patients aged over 90 ( $\geq 90$  years), 85-89 years, 80-84 years, and under 80 years of age ( $< 80$  years). Categorical variables were presented as numbers and percentages and were compared using the chi-square test. Continuous variables were expressed as the median and interquartile range (IQR) and compared using the Wilcoxon rank sum test. For variables that showed significant differences among the 4 groups, pairwise comparisons were performed between the  $\geq 90$  years group and each of the other groups. Chi-square tests were used for categorical variables, while pairwise Wilcoxon tests were employed for continuous variables. To account for multiple comparisons, the Bonferroni correction was applied, setting the significance level at  $\alpha = 0.05/3 = 0.0167$ . The p-values below this threshold were considered statistically significant and were marked with an asterisk (\*). There was no plan for imputation of the missing data. The number of cases analyzed for each observed variable is presented. We showed the distribution of both pre-mRS and mRS at 30 days after the procedure in each group. Then, we also indicate the rate of return of the mRS to at least the pre-mRS after 30 days.

We constructed the multivariate logistic regression models to estimate the adjusted odds ratio (OR) of patients aged  $\geq 90$  years for primary and secondary outcomes by adjusting the following variables: sex, pre-mRS, NIHSS score before EVT, ASPECTS ( $< 6$  or  $\geq 6$ ), onset to puncture time ( $< 6$  or  $\geq 6$  hours), anterior or posterior circulation (if there were both anterior and posterior occlusion, we regarded as posterior occlusion), and administration of rt-PA. Those adjusters were selected based on previous reports of their influence on outcomes.<sup>1)</sup> For intracerebral hemorrhage, if a significant difference was found in the groups compared with those aged 90 years and over, a multivariate analysis was performed using factors considered to be clinically relevant. The effects were expressed as ORs and 95% confidence intervals (CIs). All statistical analyses were conducted using JMP 16.0 (SAS Institute Inc., Cary, NC, USA). All reported p-values were 2-tailed, and  $p < 0.05$  were considered to be statistically significant.



**Fig. 1 Study flowchart.**

**JR-NET4: Japanese Registry of NeuroEndovascular Therapy 4**

## Results

### Patient characteristics

A total of 13,987 patients were enrolled in the study. After excluding 447 patients due to missing age information ( $n = 29$ ) and loss to follow-up ( $n = 418$ ), 13,540 patients were included in the final analysis. The cohort was stratified into 4 age groups:  $\geq 90$  years ( $n = 1,104$ ), 85–89 years ( $n = 1,925$ ), 80–84 years ( $n = 2,477$ ), and  $< 80$  years ( $n = 8,034$ ). The median age (IQR) for each group was 92 (91–94), 87 (86–88), 82 (81–83), and 71 (64–75), respectively (Fig. 1, Table 1).

The proportion of female patients and those with ASPECTS scores  $< 6$  was highest in the  $\geq 90$  years group ( $n$  [%]: 819 [74.2%], 1,155 [60.0%], 1,178 [47.6%], 2,613 [32.5%],  $p < 0.0001$ ; 195 [17.7%], 305 [15.8%], 361 [14.6%], 1,170 [14.6%],  $p = 0.004$ ). Additionally, the pre-mRS and NIHSS scores were significantly higher in the  $\geq 90$  years group, with median (IQR) values of 2 (0–3), 1 (0–3), 0 (0–2), and 1 (0–0) ( $p < 0.0001$ ), and 21 (15–26), 20 (14–25), 19 (13–24), and 17 (11–23) ( $p < 0.0001$ ), respectively.

In the  $\geq 90$  years group, occlusions of the internal carotid artery or the M1 segment of the MCA were more frequently observed than in the 80–84 and  $< 80$  age groups ( $n$  [%]: 794 [74.0%] vs. 1,669 [69.6%],  $p = 0.008$ ; 794 [74.0%] vs. 5,353 [70.3%],  $p = 0.013$ ). Conversely, basilar artery occlusions and posterior circulation strokes were less common in the  $\geq 90$  years group than in the  $< 80$ , 80–84, and  $< 80$  years age groups ( $n$  [%]: 67 [6.2%] vs. 688 [9.4%],  $p = 0.002$ ; 80 [7.5%] vs. 246 [10.3%],  $p = 0.009$ , 80 [7.5%] vs. 903 [11.9%],  $p < 0.0001$ ). EVT for MeVOs showed a significant difference among the 4 groups ( $n$  [%]: 199 [18.6%], 382 [20.5%], 484 [20.2%], 1,361 [17.9%],  $p = 0.01$ ); however, no

significant difference was observed between the  $\geq 90$  years group and the other groups. Notably, the use of general anesthesia was lower in the  $\geq 90$  years group than in the 85–89 and  $< 80$  years groups ( $n$  [%]: 12/1,103 [1.1%] vs. 45/1,925 [2.3%],  $p = 0.015$ , 12/1,103 [1.1%] vs. 285/8,020 [3.6%],  $p < 0.0001$ ). Regarding technical procedures, the use of combined techniques was more prevalent in the  $\geq 90$  years group than the  $< 80$  age group ( $n$  [%]: 451 [41.8%] vs. 2,661 [34.8%],  $p < 0.0001$ ). However, percutaneous transluminal angioplasty and stenting were less frequently employed in this group compared to others ( $n$  [%]: 32 [3.0%], 93 [5.0%], 187 [7.8%], 796 [10.4%],  $p < 0.0001$ ; 21 [1.9%], 62 [3.3%], 119 [4.9%], 489 [6.4%],  $p < 0.0001$ ) except between the  $\geq 90$  years group and the 80–84 years group in stenting. The achievement of mTICI  $\geq 2b$  recanalization was higher in the  $< 80$  years group than the  $\geq 90$  years group ( $n$  [%]: 868/1,084 [80.0%] vs. 6,373/7,602 [83.8%],  $p = 0.0019$ ). Post-procedural antiplatelet therapy was less common in the  $\geq 90$  years group than in the 80–84 years group and  $< 80$  years group ( $n$  [%]: 166/1,089 [15.4%] vs. 508/2,364 [21.5%],  $p < 0.0001$ , 166/1,089 [15.4%] vs. 2,254/7,525 [30.0%],  $p < 0.0001$ ). In terms of stroke etiology, cardioembolic stroke was the most frequently observed subtype in patients aged  $\geq 90$  years ( $n$  [%]: 1,538/1,885 [81.6%], 1,860/2,421 [76.8%], 4,809/7,695 [62.5%],  $p < 0.0001$ ). No significant differences were observed between the groups for other clinical variables (Table 1).

### Outcomes

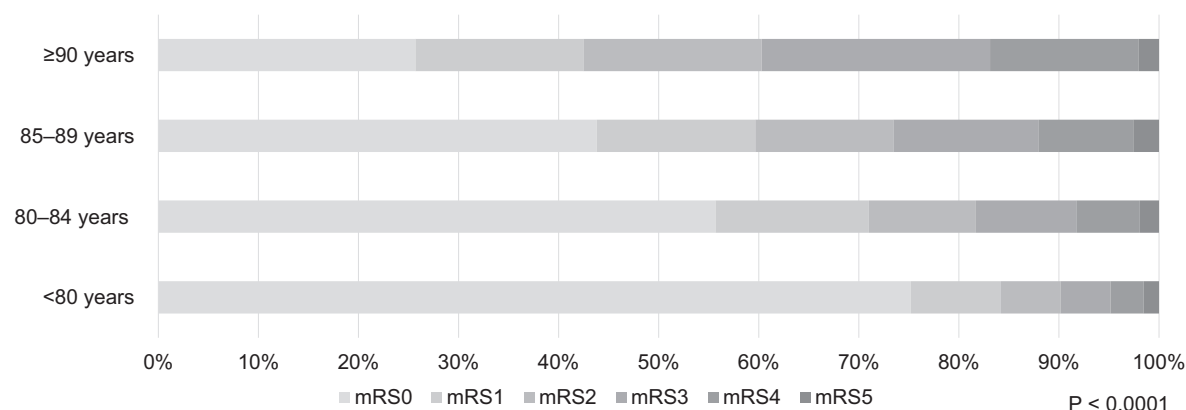
The distribution of both pre-mRS and mRS at 30 days was significantly worse in patients aged  $\geq 90$  years compared to younger groups (Figs. 2 and 3). The proportion of patients who returned to at least their pre-morbid mRS at

**Table 1 Patient characteristics**

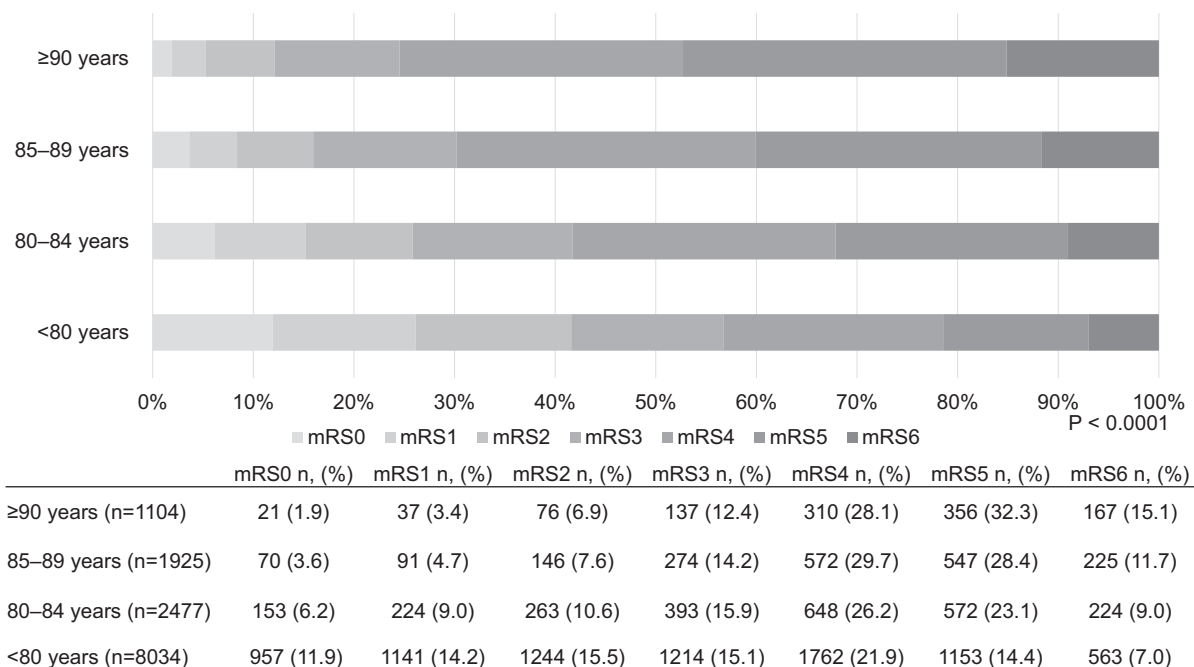
| Variables                                    | Age ≥ 90<br>(n=1104) | 85-89<br>(n=1925)    | p value   | 80-84<br>(n=2477)    | p value   | Age < 80<br>(n=8034) | p value   | p value<br>between<br>4 groups |
|--|----------------------|----------------------|-----------|----------------------|-----------|----------------------|-----------|--------------------------------|
| Age - years, median [IQR]                    | 92 [91-94]           | 87 [86-88]           | < 0.0001* | 82 [81-83]           | < 0.0001* | 71 [64-75]           | < 0.0001* | < 0.0001                       |
| Female, n (%)                                | 819 (74.2)           | 1155 (60.0)          | < 0.0001* | 1178 (47.6)          | < 0.0001* | 2613 (32.5)          | < 0.0001* | < 0.0001                       |
| Premorbid mRS, median [IQR]                  | 2 [0-3]              | 1 [0-3]              | < 0.0001* | 0 [0-2]              | < 0.0001* | 1 [0-0]              | < 0.0001* | < 0.0001                       |
| NIHSS score before EVT, median [IQR]         | 21 [15-26]           | 20 [14-25]           | < 0.0001* | 19 [13-24]           | < 0.0001* | 17 [11-23]           | < 0.0001* | < 0.0001                       |
| ASPECTS, median [IQR]                        | 9 [7-10]<br>(n=756)  | 9 [7-10]<br>(n=1299) | NA        | 9 [7-10]<br>(n=1574) | NA        | 9 [7-10]<br>(n=4983) | NA        | 0.996                          |
| DWI-ASPECTS, median [IQR]                    | 8 [6-9]<br>(n=722)   | 8 [6-9]<br>(n=1286)  | 0.91      | 8 [6-9]<br>(n=1664)  | 0.03      | 8 [6-9]<br>(n=5161)  | 0.16      | 0.04                           |
| All ASPECTS < 6, n (%)                       | 195 (17.7)           | 305 (15.8)           | 0.19      | 361 (14.6)           | 0.018     | 1170 (14.6)          | 0.0067*   | 0.04                           |
| Site of occlusion                            | n = 1073             | n = 1861             |           | n = 2399             |           | n = 7612             |           |                                |
| IC or M1, n (%)                              | 794 (74.0)           | 1326 (71.3)          | 0.11      | 1669 (69.6)          | 0.008*    | 5353 (70.3)          | 0.013*    | 0.049                          |
| Medium vessel, n (%)                         | 199 (18.6)           | 382 (20.5)           | 0.19      | 484 (20.2)           | 0.26      | 1361 (17.9)          | 0.59      | 0.01                           |
| Basilar artery, n (%)                        | 67 (6.2)             | 126 (6.8)            | 0.58      | 204 (8.5)            | 0.02      | 688 (9.4)            | 0.002*    | 0.0007                         |
| Posterior circulation, n (%)                 | 80 (7.5)             | 158 (8.5)            | 0.32      | 246 (10.3)           | 0.009*    | 903 (11.9)           | < 0.0001* | < 0.0001                       |
| Administration of rt-PA, n (%)               | 414/1090<br>(38.0)   | 740/1884<br>(39.3)   | NA        | 943/2421<br>(39.0)   | NA        | 2937/7691<br>(38.2)  | NA        | 0.77                           |
| Onset to puncture time ≥ 6 hours, n (%)      | 212/1058<br>(20.0)   | 365/1807<br>(20.2)   | NA        | 479/2310<br>(20.7)   | NA        | 1554/7398<br>(21.0)  | NA        | 0.81                           |
| General anesthesia, n (%)                    | 12/1103<br>(1.1)     | 45/1925<br>(2.3)     | 0.015*    | 53/2473<br>(2.1)     | 0.029     | 285/8020<br>(3.6)    | < 0.0001* | < 0.0001                       |
| Technical characteristics                    | n = 1078             | n = 1870             |           | n = 2410             |           | n = 7640             |           |                                |
| Stent retriever, n (%)                       | 412 (38.2)           | 709 (37.9)           | NA        | 911 (37.8)           | NA        | 3015 (39.5)          | NA        | 0.36                           |
| Aspiration catheter, n (%)                   | 201 (18.7)           | 417 (22.3)           | 0.019     | 511 (21.2)           | 0.083     | 1771 (23.2)          | 0.0009*   | 0.004                          |
| Combined, n (%)                              | 451 (41.8)           | 729 (39.0)           | 0.13      | 919 (38.1)           | 0.039     | 2661 (34.8)          | < 0.0001* | < 0.0001                       |
| Percutaneous transluminal angioplasty, n (%) | 32 (3.0)             | 93 (5.0)             | 0.010*    | 187 (7.8)            | < 0.0001* | 796 (10.4)           | < 0.0001* | < 0.0001                       |
| Stenting, n (%)                              | 21 (1.9)             | 62 (3.3)             | 0.032     | 119 (4.9)            | < 0.0001* | 489 (6.4)            | < 0.0001* | < 0.0001                       |
| Local intra-arterial fibrinolysis, n (%)     | 42 (3.9)             | 57 (3.7)             | NA        | 102 (4.2)            | NA        | 282 (3.7)            | NA        | 0.24                           |
| TICI ≥ 2b                                    | 868/1084<br>(80.0)   | 1481/1875<br>(79.0)  | 0.48      | 1972/2408<br>(81.9)  | 0.20      | 6373/7602<br>(83.8)  | 0.0019*   | < 0.0001                       |
| Postprocedural antiplatelet therapy, n (%)   | 164/1067<br>(15.4)   | 312/1837<br>(17.0)   | 0.26      | 508/2364<br>(21.5)   | < 0.0001* | 2254/7525<br>(30.0)  | < 0.0001* | < 0.0001                       |
| Stroke etiology                              | n = 1089             | n = 1885             |           | n = 2421             |           | n = 7695             |           |                                |
| Cardioembolic, n (%)                         | 957 (87.9)           | 1538 (81.6)          | < 0.0001* | 1860 (76.8)          | < 0.0001* | 4809 (62.5)          | < 0.0001* | < 0.0001                       |

Abbreviation; IQR: interquartile range; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; EVT: endovascular treatment; ASPECTS: Alberta Stroke Program Early CT score; IC or M1: Internal carotid artery or M1 segment of Middle cerebral artery; rt-PA, recombinant tissue plasminogen activator; TICI: thrombolysis in cerebral infarction

\* Significantly different between the Age ≥ 90 group and other groups.



**Fig. 2** Distribution of premorbid modified Rankin Scale.  $p < 0.0001$ .



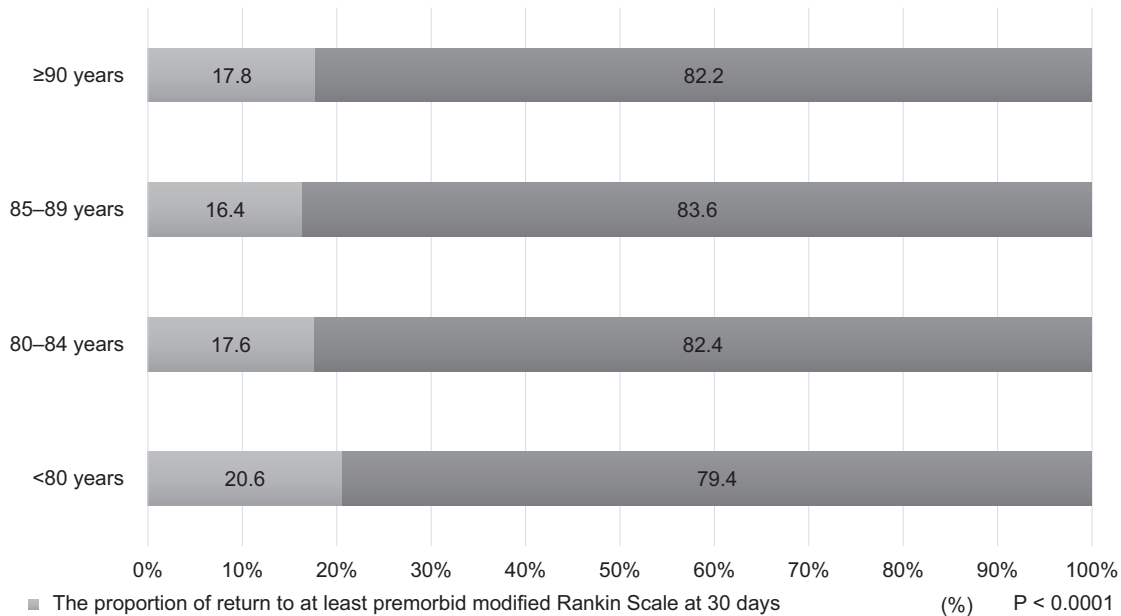
**Fig. 3** Distribution of modified Rankin Scale at 30 days after the procedure.  $p < 0.0001$ .

30 days differed significantly between groups (Fig. 4). However, the adjusted ORs (aOR) (95% CIs) for the 85–89, 80–84, and <80 years groups, compared with the ≥90 years group, were not statistically significant: 0.89 (0.72–1.10), 0.95 (0.77–1.16), and 1.07 (0.89–1.28), respectively. Interestingly, the incidence of symptomatic ICH was lower in the ≥90 years group compared to the 85–89 years and <80 years groups (aOR [95% CI]: 1.86 [1.16–2.98] and 1.71 [1.11–

2.64], respectively). However, the 30-day mortality was significantly higher in the ≥90 years group compared to the 80–84 and <80 years groups (aOR [95% CI]: 0.65 [0.48–0.88] and 0.46 [0.35–0.61], respectively).

No significant differences were observed in the incidence of any ICH between the ≥90 years group and the other age groups (Table 2).





**Fig. 4** Proportion of return to at least pre-morbid modified Rankin scale at 30 days.  $p < 0.0001$ .

### Predictors of symptomatic intracranial hemorrhage

The multivariate analysis showed that 85–89 years and <80 years for ≥90 years, NIHSS score before EVT, All ASPECTS <6, and MeVO were independently associated with higher odds of symptomatic ICH (Table 3).

### Discussion

Based on the largest registry from real-world practice with retrospective, nationwide, multicenter, and observational studies on neuroendovascular treatments for AIS with LVO in Japan, we found that patients aged 90 years and older accounted for 8.2% of all individuals who underwent EVT for LVO. The proportion of these patients whose mRS returned to at least their pre-morbid level at 30 days showed no significant difference compared to younger age groups. Furthermore, while the incidence of symptomatic ICH was lower in patients aged 90 years and older, the mortality rate was higher.

There are very limited studies of the efficacy of EVT of AIS due to LVO in patients over 90 years of age. In the prior report from Japan, the EVT group was compared with a conservative treatment group using a nationwide registry of acute LVO. In this report, mRS 0–2 at 90 days in the EVT group was about 20%,<sup>2)</sup> which compares favorably with 12.1% in the present study. This may have been influenced by the difference in the timing of evaluation of treatment outcomes between 90 and 30 days and may also be because the results were from a more realistic clinical data set. However, all-cause death was like the previous study (15.1% vs. 16.3%). The results showed no significant difference between the ≥90 years patients and the younger

age groups, indicating that performing EVT in patients aged 90 years and older may not be detrimental compared to younger populations. Notably, the incidence of symptomatic ICH was lower in the patients aged ≥90 years compared to the 85–89 years and <80 years groups. This finding may be related to the higher prevalence of atrial fibrillation, a major cause of cardiogenic stroke, which increases with age. Consequently, cardiogenic embolism was likely more common in the oldest patients. In contrast, cases involving atherosclerotic lesions often require multiple passes or the use of percutaneous transluminal angioplasty and stents due to repeated re-occlusion during the procedure, leading to greater procedural complexity. This complexity may have contributed to the lower incidence of symptomatic ICH observed in patients aged ≥90 years.

Furthermore, symptomatic ICH was more frequently observed in cases with higher NIHSS scores before EVT, ASPECTS <6, and MeVO. Therefore, except for these high-risk cases, the decision to avoid EVT solely due to advanced age should be reconsidered.

Based on the present study results, it might appear more important to investigate patient background factors, such as gender, muscle mass, and comorbidities, rather than the risks of the procedure itself.

Additionally, a recent study suggested that EVT was cost-effective for patients over 90 years of age.<sup>15)</sup>

These findings further support the notion that EVT represents a viable therapeutic option for individuals aged 90 years and older.

**Table 2 Outcomes**

| Variables   | Incidence, n (%) | Crude ORs (95% CIs) | P Value   | Adjusted ORs (95% CIs) | P Value  |
|---|------------------|---------------------|-----------|------------------------|----------|
| Return to at least premorbid modified Rankin Scale at 30 days |                  |                     |           |                        |          |
| ≥90 years (n=1090)  | 194 (17.8)       |                     | Reference |                        |          |
| 85-89 years (n=1906)  | 313 (16.4)       | 0.91 (0.75 - 1.10)  | 0.33      | 0.89 (0.72 - 1.10)     | 0.30     |
| 80-84 years (n=2448)  | 431 (17.6)       | 0.99 (0.82 - 1.19)  | 0.89      | 0.95 (0.77 - 1.16)     | 0.60     |
| <80 years (n=7988)  | 1647 (20.6)      | 1.20 (1.02 - 1.41)  | 0.03      | 1.07 (0.89 - 1.28)     | 0.49     |
| Symptomatic intracranial hemorrhage                           |                  |                     |           |                        |          |
| ≥90 years (n=1101)  | 25 (2.3)         |                     | Reference |                        |          |
| 85-89 years (n=1921)  | 81 (4.2)         | 1.89 (1.20 - 2.99)  | 0.006     | 1.86 (1.16 - 2.98)     | 0.01     |
| 80-84 years (n=2472)  | 90 (3.6)         | 1.63 (1.04 - 2.55)  | 0.04      | 1.47 (0.92 - 2.36)     | 0.11     |
| <80 years (n=8022)  | 299 (3.7)        | 1.67 (1.10 - 2.52)  | 0.02      | 1.71 (1.11 - 2.64)     | 0.02     |
| Any intracranial hemorrhage                                   |                  |                     |           |                        |          |
| ≥90 years (n=1101)  | 104 (9.5)        |                     | Reference |                        |          |
| 85-89 years (n=1921)  | 219 (11.4)       | 1.23 (0.96 - 1.58)  | 0.09      | 1.19 (0.92 - 1.53)     | 0.19     |
| 80-84 years (n=2472)  | 237 (9.6)        | 1.02 (0.80 - 1.30)  | 0.89      | 1.02 (0.79 - 1.32)     | 0.87     |
| <80 years (n=8022)  | 775 (9.7)        | 1.03 (0.83 - 1.27)  | 0.82      | 1.13 (0.90 - 1.42)     | 0.29     |
| Mortality at 30-day   |                  |                     |           |                        |          |
| ≥90 years (n=1104)  | 95 (8.6)         |                     | Reference |                        |          |
| 85-89 years (n=1925)  | 131 (6.8)        | 0.78 (0.59 - 1.02)  | 0.07      | 0.85 (0.63 - 1.14)     | 0.28     |
| 80-84 years (n=2477)  | 135 (5.5)        | 0.61 (0.47 - 0.80)  | 0.0004    | 0.65 (0.48 - 0.88)     | 0.006    |
| <80 years (n=8034)  | 317 (4.0)        | 0.44 (0.34 - 0.55)  | < 0.0001  | 0.46 (0.35 - 0.61)     | < 0.0001 |

Abbreviation; OR: odds ratio; CI: confidence intervals

## Limitations

There are several limitations in this study. First, our registry may not have enough variables to adjust confounders between the 2 groups. Because we considered primarily designed to survey the status of EVT throughout the country and to evaluate its safety. Therefore, to increase the response rate from the participating centers as much as possible, the variables collected such as comorbidity might be fewer than other studies of EVT for ischemic stroke due to LVO. Second, this study used a historical cohort treated for ischemic stroke due to LVO. The selection of EVT was dependent on the treating physicians in charge. Therefore, there are inevitable confounding and selection biases in this study. Thus, a multivariate logistic regression model was used to reduce that confounder, but it might still not be sufficient for selection biases. Finally, this registry study was conducted in Japan, where the risk of bleeding events has been reported to differ among ethnicities.<sup>16)</sup> Thus, the generalizability of our findings to the rest of the world should be carefully considered.

## Conclusion

The return of the mRS to at least the premorbid mRS after 30 days in ≥90 years patients with LVO was not significantly different in other groups.

Additionally, while the incidence of symptomatic ICH was lower in patients aged ≥90 years, the mortality rate was higher. These findings suggest that performing EVT in patients aged 90 years and older may not be disadvantageous.

## Acknowledgments

The JR-NET4 Study Group: Principal investigator; Nobuyuki Sakai, Department of Neurosurgery, Seijinkai Shimizu Hospital, Kyoto, Japan; Investigators: Koji Iihara and Hirotochi Imamura, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan, Akira Ishii, Kyoto University, Kyoto, Japan, Yuji Matsumaru, Tsukuba University, Tsukuba, Ibaraki, Japan, Chiaki Sakai, Kobe City Medical Center General Hospital, Kobe, Japan, Tetsu Satow, Kindai University, Osaka-Sayama, Japan, Shinichi Yoshimura, Hyogo Medical University, Nishinomiya, Hyogo, Japan, and

**Table 3 Multivariate Logistic Regression Model for Prediction of symptomatic intracranial hemorrhage**

|                                       | OR (95% CI)       | P Value   |
|---------------------------------------|-------------------|-----------|
| ≥90 years                             | reference         | reference |
| 85-89 years                           | 1.84 (1.15-2.94)  | 0.01      |
| 80-84 years                           | 1.42 (0.89-2.29)  | 0.14      |
| <80 years                             | 1.66 (1.07-2.56)  | 0.02      |
| Female                                | 1.07 (0.88-1.32)  | 0.49      |
| NIHSS score before EVT <sup>a</sup>   | 1.01 (1.001-1.03) | 0.03      |
| All ASPECTS < 6                       | 1.53 (1.20-1.96)  | 0.0007    |
| Medium vessel occlusion               | 1.30 (1.01-1.66)  | 0.04      |
| Posterior circulation occlusion       | 1.31 (0.96-1.78)  | 0.09      |
| Administration of rt-PA               | 0.84 (0.67-1.05)  | 0.12      |
| Onset to puncture time ≥ 6 hours      | 1.18 (0.92-1.51)  | 0.19      |
| Combined technique                    | 0.999 (0.81-1.23) | 0.995     |
| Percutaneous transluminal angioplasty | 1.06 (0.72-1.56)  | 0.77      |
| Stenting                              | 1.14 (0.73-1.78)  | 0.56      |
| Cardioembolic stroke                  | 0.89 (0.70-1.13)  | 0.34      |

<sup>a</sup> Unit OR.

Certified Specialist of Japanese Society of Neuroendovascular Therapy.

## Funding

This study was endorsed by JSNET on November 20, 2019, and partly supported by a research grant from the JSNET in 2019 and 2020, and by the Kobayashi Foundation in 2019.

## Disclaimer

Author Nobuyuki Sakai is one of the Editorial Board members of the Journal. This author was not involved in the peer-review or decision-making process for this paper.

## Conflicts of Interest Disclosure

Dr Uchida has received lecturer fees from Daiichi Sankyo, Bristol Myers Squibb, Stryker, and Medtronic. Dr Imamura has received lecturer fees from Medtronic, Daiichi Sankyo, Stryker, Johnson & Johnson, Terumo, and Asahi Intecc. Dr Shirakawa has received lecturer fees from Stryker, Terumo, Johnson & Johnson, and Medtronic. Dr Yoshimura has received research grants from Medico's Hirata, Medtronic, and Terumo; and has received lecturer fees from Medtronic, Kaneka, Stryker, Daiichi Sankyo, Bristol Myers Squibb, and Johnson & Johnson. Dr N. Sakai has received a research grant from Biomedical Solutions, Medtronic, Terumo, and TG Medical; has received lecturer fees from Asahi-Intec, Biomedical Solutions, Daiichi Sankyo, Kaneka, Medtronic, and Terumo; and has served on the

Advisory Boards for Johnson & Johnson, Medtronic, and Terumo outside the submitted work. Other co-authors have no conflict of interest for this manuscript.

## References

- 1) Yoshimura S, Sakai N, Uchida K, et al. Endovascular therapy in ischemic stroke with acute large-vessel occlusion: recovery by endovascular salvage for cerebral ultra-acute embolism Japan Registry 2. J Am Heart Assoc. 2018;7(9):e008796. doi: 10.1161/JAH A.118.008796
- 2) Fujita K, Tanaka K, Yamagami H, et al. Outcomes of large vessel occlusion stroke in patients aged ≥90 years. Stroke. 2021;52(5):1561-9. doi: 10.1161/STROKEAHA.120.031386
- 3) Bai X, Zhang X, Zhang Y, et al. Mechanical thrombectomy in nonagenarians: a systematic review and meta-analysis. Transl Stroke Res. 2021;12(3):394-405. doi: 10.1007/s12975-021-00894-5
- 4) Karhi S, Nerg O, Miettinen T, et al. Mechanical thrombectomy of large artery occlusion is beneficial in octogenarians. In Vivo. 2018;32(5):1223-30. doi: 10.21873/in vivo.11368
- 5) Sakai N, Fujiwara S, Uchida K, et al. Trends and progress in neuroendovascular treatment in Japan: Japanese Registry of Neuroendovascular Therapy (JR-NET) 4. Main Report. Neurol Med Chir (Tokyo). 2024;64(8):309-15. doi: 10.2176/jns-nmc.2024-0011
- 6) Gumbinger C, Ringleb P, Ippen F, et al. Outcomes of patients with stroke treated with thrombolysis according to prestroke Rankin Scale scores. Neurology. 2019;93(20):e1834-43. doi: 10.1212/WNL.00000000000008468
- 7) Lyden P, Brott T, Tilley B, et al. Improved reliability of the NIH Stroke Scale using video training. NINDS TPA Stroke Study Group. Stroke. 1994;25(11):2220-6. doi: 10.1161/01.str.25.11.2220
- 8) Pexman JH, Barber PA, Hill MD, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. AJNR Am J Neuroradiol. 2001;22(8):



- 1534-42.
- 9) Barber PA, Hill MD, Eliasziw M, et al. Imaging of the brain in acute ischaemic stroke: comparison of computed tomography and magnetic resonance diffusion-weighted imaging. *J Neurol Neurosurg Psychiatry*. 2005;76(11):1528-33. doi: 10.1136/jnnp.2004.059261
  - 10) Tei H, Uchiyama S, Usui T, et al. Posterior circulation ASPECTS on diffusion-weighted MRI can be a powerful marker for predicting functional outcome. *J Neurol*. 2010;257(5):767-73. doi: 10.1007/s00415-009-5406-x
  - 11) Gibo H, Carver CC, Rhoton AL Jr, et al. Microsurgical anatomy of the middle cerebral artery. *J Neurosurg*. 1981;54(2):151-69. doi: 10.3171/jns.1981.54.2.0151
  - 12) Ospel JM, Nguyen TN, Jadhav AP, et al. Endovascular treatment of medium vessel occlusion stroke. *Stroke*. 2024;55(3):769-78. doi: 10.1161/STROKEAHA.123.036942
  - 13) Zaidat OO, Castonguay AC, Linfante I, et al. First pass effect: a new measure for stroke thrombectomy devices. *Stroke*. 2018;49(3):660-6. doi: 10.1161/STROKEAHA.117.020315
  - 14) Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*. 1993;24(1):35-41. doi: 10.1161/01.str.24.1.35
  - 15) Inaba T, Sakuma M, Sakakibara F, et al. Quality-adjusted Life Years and Costs of Mechanical Thrombectomy for Very Elderly Patients with Acute Ischemic Stroke. *Neurol Med Chir*. 2024. in press.
  - 16) Morimoto T, Fukui T, Lee TH, et al. Application of U.S. guidelines in other countries: aspirin for the primary prevention of cardiovascular events in Japan. *Am J Med*. 2004;117(7):459-68. doi: 10.1016/j.amjmed.2004.04.017

---

Corresponding author: Kazutaka Uchida, MD, PhD  
 Department of Neurosurgery, Hyogo Medical University, 1-1  
 Mukogawa, Nishinomiya, Hyogo 663-8501, Japan.  
*e-mail:* kuchidans@gmail.com