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Feasibility of Mechanical Thrombectomy for Acute Ischemic Stroke Patients Aged 90 Years or Older Compared to Younger Patients

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Abstract

Mechanical thrombectomy (MT) is a proven treatment for acute ischemic stroke (AIS). However, the efficacy of this treatment is uncertain for very elderly patients. This study aimed to investigate the safety and effectiveness of MT in 90 years or older patients compared with younger patients. We retrospectively reviewed AIS patients treated with MT between October 2018 and June 2020 in our institution. Patients were divided into two groups: aged ≥90 and <90 years. We compared the following factors: functional outcome at discharge, in-hospital death, successful recanalization, and complications. Multivariate logistic regression analysis for the good functional outcome was performed. In consideration of pre-stroke basic activities of very elderly patients, we defined the good functional outcome as modified Rankin Scale (mRS) 0–3. In all, 66 patients were included, and 19 patients (28%) were ≥90 years old. Pre-stoke mRS was higher in ≥90-year-old patients (p = 0.01). In ≥90-year-old patients, we achieved successful recanalization in 17 patients (90%), and only one patient experienced hemorrhagic complication related with the procedure. The good functional outcome (mRS: 0–3) at discharge were six patients (32%) in ≥90 years old versus 19 patients (40%) in <90 years old (p = 0.6). Three patients died in hospital in each group (16% versus 6%) (p = 0.3). Only the stroke severity was negatively related with the good functional outcome in a multivariate analysis. In conclusion, for ≥90-year-old patients compared with younger patients, MT is an equally feasible therapy. Patients should not be excluded from MT based on age alone.

Keywords: acute ischemic stroke, large vessel occlusion, mechanical thrombectomy, nonagenarian, 90 years or older

Introduction

Aging is a major risk factor for stroke, and more than 80% of strokes occur in elderly patients over the age of 65. We often encounter patients with elderly strokes. The population of the elderly is growing worldwide; thus, the number of elderly stroke patients is expected to increase in the future.[1)] Disabilities following the stroke of elderly patients are more severe than those of younger patients, and affect the cost of medical and nursing care. Treatments reducing the degree of disabilities in elderly stroke patients are valuable.

Mechanical thrombectomy (MT) is an established treatment for acute ischemic stroke (AIS) due to a large vessel occlusion (LVO).[2)] The HERMES meta-analysis of the five pivotal MT trials showed that MT had beneficial effects in 80 years or older patients over standard treatment. However, only 15% of patients were over 80 years old in this pooled-patient analysis.[3)] Alawieh reported a retrospective multicenter real-world study of elderly patients treated with MT. The good functional outcome was worse in older patients relative to younger patients,

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and the age above 80 years was independently associated with poor outcome.[4] A meta-analysis of 16 studies published between 2014 and 2019 involving 3954 patients also showed that patients over 80 years old had poorer functional outcome and higher mortality rates than younger patients.[5]

We often treat AIS patients over 90 years old. There are insufficient data on the efficacy of MT for over 90-year-old patients in the prospective studies. The latest American Heart Association/American Stroke Association guideline suggested that the benefit of MT over standard care in 90 years or older patients is not clear.[2] Therefore, the decision of MT for patients over 90 years old is questionable. In this study, we analyzed the feasibility and outcome of MT for 90 years or older patients compared with younger patients. This is the first English MT report for patients aged over 90 years from Japan.

Materials and Methods

Patients selection and study design

This is a retrospective observational study. The study protocol was approved by the Seirei-Hamamatsu General Hospital's Ethics Committee. We retrospectively reviewed the electronic medical records of consecutive AIS patients, who were 18 years of age or older, underwent MT from October 2018 through June 2020 at the Seirei Hamamatsu General Hospital. We only included patients who had occluded internal carotid artery, middle cerebral artery, or basilar artery. We divided patients into two groups according to age: 18–89 and ≥90 years old.

Technical procedure

In all patients, MT was performed under conscious sedation. The treatment devices used in MT were Solitaire FR (Medtronic, Minneapolis, MN, USA), Trevo ProVue (Stryker, Kalamazoo, MI, USA), EmboTrapII (Johnson and Johnson, New Brunswick, NJ, USA), Penumbra (Penumbra, Alameda, CA, USA), AXS Catalyst (Stryker), and Sofia Flow Plus (Terumo, Tokyo, Japan). Treating physicians selected the devices and singular (aspiration or stent retriever) or combined approaches.

Patients data collection

We collected the following patients' characteristics: age, sex, pre-stroke modified Rankin Scale (mRS) (mRS measures patients disability and dependence, and ranges from 0 to 6; 0 is no symptom, 5 is complete physical dependence, and 6 is dead),[6] comorbidities related to stroke, pre-stroke antithrombotic therapy, stroke severity with National Institutes of Health Stroke Scale (NIHSS) (NIHSS ranges from 0 to 42; a higher score indicates more severe neurological impairment),[7] early ischemic changes on head computed tomography (CT) according to Alberta stroke program early CT (ASPECT) score (ASPECT score ranges from 0 to 10; a lower score indicates larger ischemic core),[8,9] occluded vessels and stroke etiology according to Trial Org 10172 in Acute Stroke Treatment (TOAST) classification.[10]

Evaluation of outcomes and treatment-related factors

The primary endpoint of this study is the good functional outcome as mRS 0–3 at discharge. In consideration of pre-stroke disabilities of elderly patients, we defined the good functional outcome as mRS 0–3.[11,12] The secondary endpoints are the mortality rate in hospital and the success rate for endovascular treatment. Successful recanalization of occluded vessels is classified as thrombolysis in cerebral infarction (TICI) scores of 2b, 2c, or 3.[13,14] We also assessed the use of intravenous tissue plasminogen activator (tPA), hemorrhagic complications associated with procedures, the causes of in-hospital death, length of hospitalization, disposition at hospital discharge, and the treatment-related times: time from stroke onset to groin puncture and time from groin puncture to recanalization. The stroke onset time involves the last time point of patient's normal condition.

Statistical analysis

We evaluated normality for continuous variables using the Shapiro–Wilk normality test and expressed them as mean and standard deviation or median and interquartile range (P25–P75). Variables were compared between two groups: <90 and ≥90 years old, using either the t-test or the Mann–Whitney U test for continuous variables and the Fisher's exact test for categorical variables. We included the following factors into multivariate analysis models for the good functional outcome: age, sex, pre-stroke mRS, admission NIHSS, tPA administration, procedure-related hemorrhagic complications, and successful recanalization. All analyses were performed with EZR (provided from Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing).[15] A p value less than 0.05 was considered statistically significant.

Results

Patient characteristics

Table 1 shows the demographic and clinical data of the 66 Japanese patients included in this study. In all, 47 patients (71%) were <90 years old, and 19

Table 1 Baseline characteristics of patients

	All	<90 years old	≥90 years old	Test used	p value
n	66	47	19		
Age, years, median [IQR]	82.5 [74.2–91]	79 [70.5–84]	92 [91–95]	U	<0.001
Female, n (%)	40 (61)	23 (49)	17 (90)	Fisher	0.002
Pre-stroke mRS, n(%)				Fisher	0.01
0	25 (38)	22 (47)	3 (16)		
1	11 (17)	9 (19)	2 (11)		
2	15 (23)	9 (19)	6 (31)		
3	13 (20)	5 (11)	8 (42)		
4	2 (3)	2 (4)	0 (0)		
Comorbidities, n (%)					
Atrial fibrillation	49 (74)	34 (72)	15 (79)	Fisher	0.8
Hypertension	46 (70)	33 (70)	13 (68)	Fisher	1
Diabetes mellitus	14 (21)	10 (21)	4 (21)	Fisher	1
Hyperlipidemia	16 (24)	10 (21)	6 (32)	Fisher	0.5
Chronic kidney disease	31 (47)	20 (42)	11 (58)	Fisher	0.3
Prior stroke	14 (21)	8 (17)	6 (32)	Fisher	0.2
Antithrobotic therapy on arrival, n(%)	24 (36)	16 (34)	8 (42)	Fisher	0.6
CT ASPECT score, median [IQR]	9 [7–10]	9 [7–10]	9 [7.7–10]	U	0.9
pc ASPECT score, median [IQR]	9.5 [7.7–10]	10 [8–10]	8	U	0.5
NIHSS, mean (SD)	20.7 (6.7)	21.0 (6.5)	20.1 (7.5)	t	0.7
Occlusion vessel, n (%)				Fisher	0.8
ICA	17 (26)	11 (23)	6 (32)		
MCA M1	28 (42)	20 (43)	8 (42)		
MCA M2	13 (20)	9 (19)	4 (21)		
BA	8 (12)	7 (15)	1 (5)		
Type of infarction, n(%)				Fisher	0.7
Cardiac embolism	48 (72)	33 (70)	15 (79)		
ESUS	7 (11)	6 (13)	1 (5)		
ATBI	9 (14)	7 (15)	2 (11)		
Trousseaus	2 (3)	1 (2)	1 (5)		

ASPECT: Alberta Stroke Programme Early Computed Tomography Score, ATBI: atherothrombotic brain infarction, BA: basilar artery, ESUS: Embolic Stroke of Undetermined Source, Fisher: Fisher's exact test, ICA: internal carotid artery, MCA: middle cerebral artery, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, pc ASPECT: Posterior Circulation Alberta Stroke Program Early Computed Tomography Score, t: t test, U: Mann–Whitney U test.

patients (28%) were ≥90 years old. Age, sex, and the distribution of pre-stroke mRS differed significantly between the two groups. The proportion of female patients was 90% (n = 17) in patients ≥90 years old compared with 43% (n = 23) in patients <90 years old. This was significantly higher in ≥90-year-old patients (p = 0.002). Prior to stroke onset, the number of mRS 3 patients was the highest and 53% (n = 11) were mRS 0–2 in patients ≥90 years old while 85% (n = 40) were mRS 0–2 in patients <90 years old (p = 0.01). The following comorbidities related with stroke were not different between the two groups: atrial fibrillation, hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, and previous stroke. The patients of both groups had taken antithrombotic medications similarly.

Stroke characteristics and treatments outcomes

The NIHSS score, the ASPECT score, the distribution of occluded arteries, and the stroke etiologies

Table 2 Angiographic and clinical outcome of patients

	All	<90 years old	≥90 years old	Test used	p value
n	66	47	19		
IV tPA, n (%)	31 (47)	20 (43)	11 (58)	Fisher	0.3
OtoP time (min), median [IQR]	250 [155–473]	248 [152–441]	282 [162–477]	U	0.7
PtoR time (min) of TICI score 2b-3 patients, median [IQR]	52 [30.5–83]	51.5 [28.7–89]	53 [32–76]	U	1
OtoR time (min) of TICI score 2b-3 patients, median [IQR]	314 [211–552]	310 [205–526]	358 [222–618]	U	0.7
TICI score 2b-3, n (%)	55 (83)	38 (81)	17 (90)	Fisher	0.5
Hemorrhagic complication, n (%)	10 (15)	9 (19)	1 (5)	Fisher	0.3
mRS0-3 at discharge, n (%)	25 (38)	19 (40)	6 (32)	Fisher	0.6
mRS0-2 at discharge, n (%)	9 (13)	8 (17)	1 (5)	Fisher	0.4
Death, n (%)	6 (9)	3 (6)	3 (16)	Fisher	0.3
Length of hospitalization (days), median [IQR]	28 [19–46.2]	28 [19.2–46.2]	27.5 [17–41.7]	U	0.5
Discharge disposition, n (%)					
Home	4 (7)	4 (9)	0 (0)	Fisher	0.03
Rehabilitation hospital	41 (68)	33 (75)	8 (50)		
Care facility	4 (7)	1 (2)	3 (19)		
Chronic hospital	11 (18)	6 (14)	5 (31)		

Fisher: Fisher's exact test, mRS: modified Rankin Scale, OtoP time: onset to puncture time, OtoR time: onset to recanalization time, PtoR time: puncture to recanalization time, tPA: tissue-type plasminogen activator, TICI score: thrombolysis in cerebral infarction score, U: Mann–Whitney U test.

were equal between the two groups (Table 1). There was no significant difference between the two groups in the rate of tPA administration and the time from stroke onset to groin puncture. We achieved successful recanalization in 17 patients (90%) in ≥90-year-old patients. This was similar with <90-year-old patients (p = 0.5). Time from groin puncture to recanalization was also equal (p = 1). Hemorrhagic complications related to procedures occurred in 10 patients (15%), and only 1 patient experienced hemorrhagic event in ≥90-year-old patients (Table 2).

Clinical outcomes

Six patients (32%) aged ≥90 years and 19 patients (40%) aged <90 years were mRS 0–3 at discharge, and there was no statistical difference (p = 0.6). Only one patient in ≥90-year-old group was mRS 2 at discharge, and 8 patients in <90-year-old group were mRS 0–2 at discharge (p = 0.4). Six patients died during the hospital stay, 3 in <90-year-old patients (6%) and 3 in ≥90-year-old patients (16%, Table 2, p = 0.3). Only one 89-year-old female patient died from major subarachnoid hemorrhage due to MT, whereas the others died from pulmonary complication or cancer (Table 3). Most of the patients <90 years old discharged to their home or rehabilitation hospitals, whereas in patients ≥90 years old no patient discharged to their home, and about 69% (11/16) discharged to rehabilitation hospitals or care facilities (Table 2). A multivariate logistic regression analysis for the good functional outcome at discharge demonstrated that only higher NIHSS score was a negative predictor (p = 0.03), and older age was not a significant predictor (p = 0.54) (Table 4).

Discussion

This study showed no difference in the good functional outcome at discharge (mRS 0–3) and in-hospital death between ≥90- and <90-year-old patients treated with MT. Only the severity of stroke (higher NIHSS scores), and not older ages, appeared the predictor for worse outcome. However, mRS 0–3 at discharge was low and death during hospitalization tended to be high in the patients ≥90 years old. There were no discharges to home and fewer transfers to rehabilitation hospitals, suggesting rather poorer outcomes in the patients ≥90 years old. The successful recanalization rates and the procedure time were equal between the two groups, and no hemorrhagic complication related with the procedure

Table 3 Causes of death

Age years old	Sex	Causes of death
79	Male	Respiratory failure with sepsis
95	Female	Aspiration pneumonia
91	Female	Aspiration pneumonia
89	Female	Massive SAH with procedure
94	Female	Pancreatic cancer
74	Female	Pancreatic cancer

SAH: subarachnoid hemorrhage.

Table 4 Multivariate logistic regression model for favorable outcome: mRS0-3

	OR	95% CI	p value
Age ≥90 years	0.6	0.14–2.8	0.54
Female	1.3	0.36–4.3	0.71
Higher Pre-stroke mRS	0.7	0.43–1.2	0.21
Higher NIHSS score	0.9	0.82–0.99	0.03
IV tPA	1	0.34–3.2	0.9
Hemorrhagic complication	0.6	0.11–3.2	0.56
TICI score 2b-3	1.4	0.27–7.2	0.67

mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, TICI score: thrombolysis in cerebral infarction score, tPA: tissue-type plasminogen activator.

occurred in ≥90-year-old patients, which suggested MT was still feasible for very elderly patients.

There are six retrospective studies, including our analysis, investigating the efficacy of MT for patients ≥90 years of age relative to patients <90 years of age.[11,16–19] Sussman et al evaluated 108 patients with AIS treated between 2010 and 2018. Twenty-seven percent of the patients was ≥90 years old, and these patients population was similar to our study. Successful revascularization rate, the favorable outcome (mRS 0–2), and mortality rate at 3 months were not different between nonagenarians (90–99 years old) and octogenarians (80–89 years old).[16] Another three reports also showed comparable effects of MT between patients ≥90 years old and younger patients.[17–19] On the contrary, Khan et al revealed that ≥90-year-old patients had poor functional outcome at 3 months compared with <90-year-old patients.[11] However, the mRS at 3 months was similar in both groups in a stratified analysis according to the pre-stroke mRS. The poor outcome among nonagenarians treated with MT was driven largely by the severity of pre-existing functional deficits rather than by age itself. The past study reported in-hospital death of patients ≥90 years old treated with MT as 7–29%,[12,17–20] which was similar to our present study (16%). The result suggests that the MT procedures do not directly cause patients death in ≥90-year-old group, but management of post-stroke complications, especially respiratory ones, and pre-existing comorbidities is important.

Before this analysis, we suspected poorer rates of successful recanalization, higher rates of hemorrhagic complications, and longer time from stroke onset to recanalization in patients ≥90 years old, because their vessels vulnerability and meandering due to arteriosclerosis might be severer. However, there was no significant difference compared with younger patients, which suggests that MT for very old patients was also feasible. Because the previous studies also demonstrated

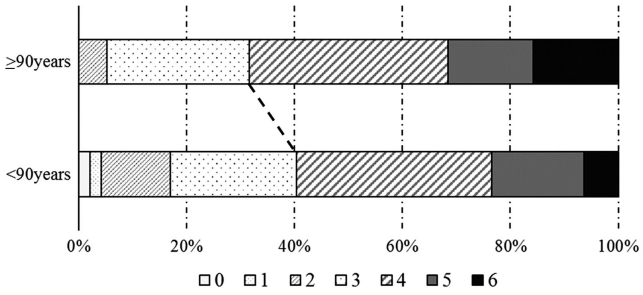

Fig. 1 Distribution of scores on the mRS at discharge between ≥90 years old patients and <90-year-old patients. The good functional outcome was defined as a score of 0–3 on the mRS. mRS: modified Rankin Scale.

that smaller infarct volumes achieved by successful recanalization resulted in the good functional outcome and reduce mortality rate in ≥90-year-old patients,[12,21,22] efforts to minimize treatment time and to successfully recanalize occluded vessels are relevant even in patients over 90 years old.

Elderly people often have disabilities and require some supports in their daily lives even before the onset of the stroke. The treatment goal for these patients is not to become self-reliant but to avoid worsening their conditions. In fact, 42% (n = 8) of patients ≥90 years old already had some disabilities (mRS = 3) before the onset of the stroke (Table 1), but 32% of them achieved mRS 2 or 3 at discharge, which was equivalent to the outcome of younger patients (40%, Table 2). Around two-thirds of over 90-year-old patients discharged to the rehabilitation hospitals or care facilities and they might avoid bed ridden (Table 2), suggesting that MT is an important treatment for very elderly patients with AIS.

MT had been the treatment of choice for AIS patients due to an LVO within 6 hours of the onset until recently. In 2018, two randomized controlled

trials (DAWN and DEFUSE3) demonstrated the benefit of MT up to 16–24 hours from the AIS onset,[23,24] which expanded treatment time windows even for elderly patients. DAWN trial showed that >80-year-old patients benefit from MT equal to younger patients in their subgroup analysis[23] but DEFUSE3 trial excluded over 85-year-old patients.[24] Therefore, the efficacy of MT in patients ≥90 years of age at over 6 hours after the stroke onset has still been controversial. In all, 25 of 66 patients (38%) shown in the present study were treated at more than 6 hours after onset of the symptoms. Although the detailed data are not shown here because of the small number, our real-world data suggested the efficacy and feasibility of MT for very elderly patients under the most current treatment criteria.

Our study has several limitations. The study design is retrospective and non-randomized with a small sample size treated at a single institution. We did not compare patients treated with MT to those with medical management only. The outcomes of our patients were evaluated only at the time of discharge and a longer follow-up is needed, because a previous study indicates that the mortality rate of patients >90 years old treated with MT increased 3 months after discharge.[12] In the next prospective study, we will evaluate the rate of patients with mRS 0–2, as well as mRS 0–3, between the two groups at 3 months after MT and later.

Conclusion

We found a rather poorer trend of functional outcomes at discharge and death in hospital in patients treated with MT ≥90 years of age compared with patients <90 years of age. There were no discharges to home and fewer transfers to rehabilitation hospitals in the patients ≥90 years old. On the other hand, the successful recanalization and the rate of complications related with the procedure were equal between the two groups, suggesting that MT was feasible for ≥90-year-old patients. We conclude that patients should not be excluded from MT because of the age of the patients alone.

Conflicts of Interest Disclosure

All authors have no conflict of interest. All Japan Neurosurgical Society member authors have registered online Self-reported COI Disclosure Statement Forms through the website.

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