



Clinical Results of Mechanical Thrombectomy in Nonagenarians with Acute Ischemic Stroke

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Objective: Multiple randomized trials have demonstrated the efficacy of mechanical thrombectomy (MT), but very elderly patients aged ≥ 90 years were excluded. It remains uncertain whether endovascular therapy is effective for nonagenarians. The objective of this study was to investigate the effectiveness and safety of MT in nonagenarians.

Methods: Between January 2016 and March 2019, acute ischemic stroke patients aged ≥ 80 years who underwent MT at our hospital were retrospectively reviewed. Patients with a baseline pre-stroke modified Rankin Scale (mRS) score ≥ 3 were excluded from the analysis. They were divided into octogenarians (80–89 years old) and nonagenarians (90–99 years old).

Results: Forty-five patients met the inclusion criteria, including 34 octogenarians and 11 nonagenarians. Nonagenarians were more likely to be female (47.0% vs 90.9%; $p < 0.05$). There was a significantly lower rate of a pre-stroke mRS score of 0–1 among the nonagenarians (91.1% vs 63.6%; $p < 0.05$). Revascularization was successful in 71.0% and 81.8% ($p = 0.46$) of octogenarians and nonagenarians, respectively. Functional independence (mRS ≤ 2) at discharge was observed in 26.4% vs 27.2% ($p = 0.95$) of octogenarians and nonagenarians, respectively.

Conclusion: MT in nonagenarians can be considered safe without increasing hemorrhagic complications in comparison with that in octogenarians. One in four patients may have a good outcome and obtain effects equivalent to those in octogenarians if they have a good pre-stroke functional status.

Keywords ► mechanical thrombectomy, acute stroke, nonagenarians

Introduction

A meta-analysis of several randomized controlled trials¹⁻⁵ revealed that the rate of patients with a favorable outcome was higher among those in whom recombinant tissue plasminogen activator (rt-PA) therapy was combined with mechanical thrombectomy (MT). Furthermore, the interval from onset until MT has been increased based on the results of the DAWN⁶ and DEFUSE 3⁷ studies, and this procedure is selected as a standard treatment to be performed in patients with indications.

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In Japan, where the rapid aging of society is advanced, MT has recently been increasingly performed on patients aged ≥ 90 years with large vessel occlusion (LVO). A sub-analysis of the HERMES study demonstrated the efficacy of MT in patients aged 80–89 years.⁸ On the other hand, the number of studies involving patients aged ≥ 90 years is limited, and its usefulness remains to be clarified. In this study, we examined the efficacy and safety of MT for patients aged 90–99 years who had undergone this procedure at our hospital.

Patients and Methods

Of patients aged ≥ 80 years with acute ischemic stroke related to LVO who had undergone MT at our hospital between January 2016 and March 2019, the subjects were those meeting the following criteria: 1) modified Rankin Scale (mRS) score before onset: 0–2, (2) interval from onset or the final onset-free time: ≤ 16 hours (patients with a National Institutes of Health Stroke Scale [NIHSS]⁹ score of < 10 and whose interval of 6–16 hours from the onset was

Table 1 Baseline characteristics

Variables	Octogenarians (n = 34)	Nonagenarians (n = 11)	p-value
Age, median (IQR), years	84.5 (81–88)	92 (91–93.5)	<0.05
Female, n (%)	16 (47.0)	10 (90.9)	<0.05
Pre-stroke mRS 0–1, n (%)	31 (91.1)	7 (63.6)	<0.05
Risk factors, n (%)			
Hypertension	27 (79.4)	8 (72.7)	0.68
Diabetes	3 (8.8)	0 (0)	0.56
Dyslipidemia	8 (23.5)	3 (27.2)	0.80
Atrial fibrillation	22 (64.7)	8 (72.7)	0.62
Stroke subtype, n (%)			
Cardiogenic embolism	21 (61.7)	8 (72.7)	0.50
Large artery atherosclerosis	3 (8.8)	0 (0)	0.30
Unknown	10 (29.4)	3 (27.2)	0.89
Clinical characteristics, median (IQR)			
NIHSS	17.5 (13–23)	18 (14.5–24)	0.63
DWI-ASPECTS	7 (6–9)	8 (7.5–9.5)	0.30
Occlusive artery, n (%)			
ICA	9 (26.4)	4 (36.3)	0.52
MCA M1	14 (41.1)	6 (54.5)	0.43
MCA M2	8 (23.5)	1 (9.0)	0.29
BA	2 (5.8)	0 (0)	0.41
IV-tPA therapy, n (%)	20 (58.8)	7 (63.6)	0.77

BA: basilar artery; DWI-ASPECTS: diffusion-weighted imaging–Alberta Stroke Program Early CT Score; ICA: internal carotid artery; IQR: interquartile range, MCA: middle cerebral artery; mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale; tPA: tissue plasminogen activator

excluded), (3) diffusion-weighted imaging (DWI)–Alberta Stroke Program Early CT Score (ASPECTS)¹⁰: ≥ 5 , and (4) site of occlusion: internal carotid artery, M1–M2 middle cerebral artery, basilar artery (BA), or P1 posterior cerebral artery. We conducted a retrospective study.

MRI was performed as the first-line examination for initial image assessment, and CT/CT angiography was alternatively conducted for patients for whom MRI was contraindicated and when MRI was not available promptly. Intravenous administration of rt-PA was performed on patients who met the indication criteria according to the guidelines.

Informed consent was obtained after a certified neuroendovascular physician or supervisory physician explained the content of treatment to each patient or his/her family.

Mechanical thrombectomy

On all patients, MT was performed under local anesthesia. As to access route, right transfemoral approach was adopted. As a rule, a balloon guiding catheter was used. Stent retrievers, such as a Solitaire FR (Medtronic, Minneapolis, MN, USA) and Trevo ProVue (Stryker, Kalamazoo, MI, USA), were selected as a first-line device, and a Penumbra System (Penumbra, Inc., Alameda, CA, USA) was

combined with each stent retriever when recanalization was not achieved by a single pass or when necessary.

Recanalization was evaluated using the thrombolysis in cerebral infarction (TICI) grade.¹¹ Patients with TICI 2b or 3 were regarded as achieving effective recanalization.

Sorting method and statistical analysis

The subjects were divided into two groups: a group consisting of octogenarians (age: 80–89 years) (Group O) and a group consisting of nonagenarians (age: 90–99 years) (Group N).

Neurological findings were evaluated based on the NIHSS scores on admission and 1 week after onset. Furthermore, patients with an mRS score of 0–2 on discharge from our hospital or referral to another hospital were regarded as achieving a favorable outcome.

Patients' characteristics, mode of MT, and the clinical outcome were compared between two groups using the chi-square test and Mann–Whitney *U*-test. We used JMP 10.0 software for statistical analysis (SAS Institute, Inc., Charlotte, NC, USA). A *p*-value of 0.05 was regarded as significant. The study protocol was approved by the ethics review board of our hospital (Approval No.: Shibyo-hatsu No. 18, Date of approval: August 16, 2019).

Table 2 Endovascular thrombectomy results

Variables	Octogenarians (n = 34)	Nonagenarians (n = 11)	p-value
Devices, n (%)			
Stent retriever	15 (44.1)	7 (63.6)	0.26
Penumbra	3 (8.8)	2 (18.1)	0.39
Both	13 (38.2)	1 (9.0)	0.069
Others	2 (5.8)	1 (9.0)	0.71
TICI, n (%)			
0	3 (8.8)	2 (18.1)	0.39
2a	7 (20.5)	0 (0)	0.10
2b	7 (20.5)	4 (36.3)	0.28
3	17 (50.0)	5 (45.4)	0.79
Successful reperfusion, n (%)	24 (70.5)	9 (81.8)	0.46
Number of passes, median (IQR)	2 (1–2)	2 (1–2)	0.36
Time parameters, median (IQR)			
Puncture to reperfusion time	67.5 (39–84)	48 (36–70)	0.34
Onset to reperfusion time	249 (196–337)	254 (195–368)	0.95

IQR: interquartile range; TICI: thrombolysis in cerebral infarction

Results

Of 57 patients aged ≥ 80 years with LVO who had undergone MT between January 2016 and March 2019, 45 were analyzed, excluding 7 with an mRS score of ≥ 3 before onset, 2 with an NIHSS score of < 10 six hours or more after onset, and 3 with a DWI-ASPECTS of < 5 . Group O consisted of 34 patients, and Group N consisted of 11 patients.

The patients' characteristics are presented in **Table 1**. The proportion of female patients was significantly higher (47.0% vs. 90.9%, respectively, $p < 0.05$) in Group N. The median mRS scores before onset in Groups O and N were 0 (0–1) and 1 (1–2), respectively; the value in the former was significantly lower ($p < 0.05$). There were no differences in the risk factors, type of cerebral infarction, occluded vessels, NIHSS score on arrival, DWI-ASPECTS, or rate of patients in whom IV-rt-PA was administered with MT between the two groups.

Procedure-related factors and outcome are presented in **Table 2**. There were no differences in the rate of patients with TICI 2b or 3 or in the interval from onset to recanalization between two groups. In Group O, the patients in whom a stent retriever was combined with a Penumbra System had a higher tendency despite no significant difference (38.2% vs. 9.0%, respectively, $p = 0.069$). The clinical outcome is presented in **Table 3**. There were no differences in the NIHSS score (1 week after treatment), mRS score on discharge, admission period, or incidence of symptomatic intracranial hemorrhage (sICH).

The mRS scores before onset and on discharge in each group are shown in **Fig. 1**. In Group N, the rate of patients

with an mRS score of 0–1 before onset was significantly lower (91.1% vs. 63.6%, respectively, $p = 0.028$), but there was no difference in the rate of patients with an mRS score of 0–2 on discharge (favorable outcome) between the two groups (26.4% vs. 27.2%, respectively, $p = 0.53$).

The changes in the mRS and NIHSS scores before and after treatment are shown in **Figs. 2** and **3**. There was no difference in the rate of change in the mRS score from admission to discharge (3.5 [2–4] vs. 3 [1.5–4], respectively, $p = 0.32$) (**Table 3** and **Fig. 2**). Furthermore, there was no difference in the rate of improvement in the NIHSS score from admission to 1 week after onset (-4 [–11 to 0] vs. -6 [–11.5 to 3], $p = 0.48$) (**Table 3** and **Fig. 3**).

Discussion

Concerning the results of MT in patients aged ≥ 90 years, only a few retrospective reports have been published and a consensus regarding its usefulness has not been reached. In this study, we examined the results of MT in patients aged ≥ 90 years.

The prognosis of elderly patients with LVO is poorer than that of young patients. On the other hand, a sub-analysis of the HERMES study demonstrated the efficacy of MT for patients aged 80–89 years.⁸⁾ However, another study found that the risk of unfavorable outcome increased by 5.1% with a 1-year increase in age and that this risk in patients aged ≥ 90 years was five times higher than that in young patients (18–89 years).¹²⁾ Age itself may be a prognostic factor for the mRS score at 3 months after MT.¹³⁾

Table 3 Clinical outcomes

Variables	Octogenarians (n = 34)	Nonagenarians (n = 11)	p-value
Clinical outcomes			
mRS 0–2, n (%)	9 (26.4)	3 (27.2)	0.95
mRS 3–5, n (%)	19 (55.8)	7 (63.6)	0.65
mRS 6, n (%)	6 (17.6)	1 (9.0)	0.49
mRS at discharge, median (IQR)	4 (2.2–4.7)	4 (2.5–5)	0.82
mRS shift from baseline, median (IQR)	3.5 (2–4)	3 (1.5–4)	0.32
NIHSS at day 7, median (IQR)	8 (4–20)	9 (4.5–23.5)	0.68
NIHSS shift at day 7, median (IQR)	–4 (–11 to 0)	–6 (–11.5 to 3)	0.48
Length of stay, median (IQR)	22 (10.5–37)	23 (16.5–33)	0.73
Reperfusion hemorrhage			
Any type of hemorrhage, n (%)	9 (26.4)	1 (9.0)	0.22
Symptomatic ICH, n (%)	2 (5.8)	0 (0)	0.41

ICH: intracranial cerebral hemorrhage; IQR: interquartile range; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale

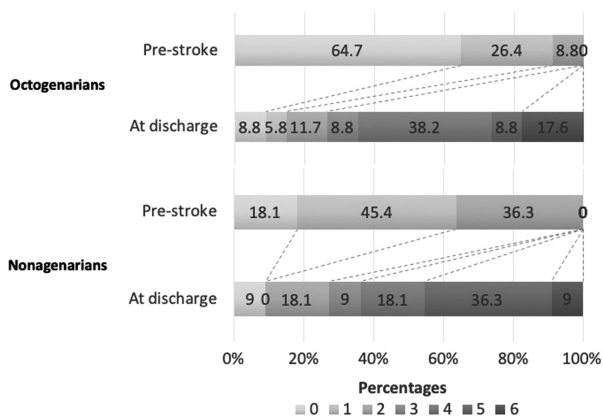


Fig. 1 Distribution of mRS scores at pre stroke and at discharge in octogenarians and nonagenarians. mRS: modified Rankin Scale

In this study, females accounted for 90.9% in Group N. This percentage was significantly higher than that in Group O. This is consistent with the mean life expectancy of females being longer and the rate of females being higher among elderly patients with stroke.¹⁴⁾

In the third version of the guidelines for the adequate use of MT in Japan, it is recommended that this procedure be indicated for patients with an mRS score of 0–1 before onset. However, activities of daily living (ADL) before onset are degraded in many elderly patients, and this study analyzed patients with an mRS score of 0–2 or independency in ADL. Among previous reports of MT for LVO in patients aged ≥90 years, many analyzed those with an mRS score of 0–2 before onset.^{15–18)}

Meyer et al.¹⁵⁾ conducted a similar study and reported the results of treatment in 79 patients aged ≥90 years (mRS score before onset: 0–2). The rate of patients with an mRS score of 0–2 after 90 days was 16.0%. Furthermore,

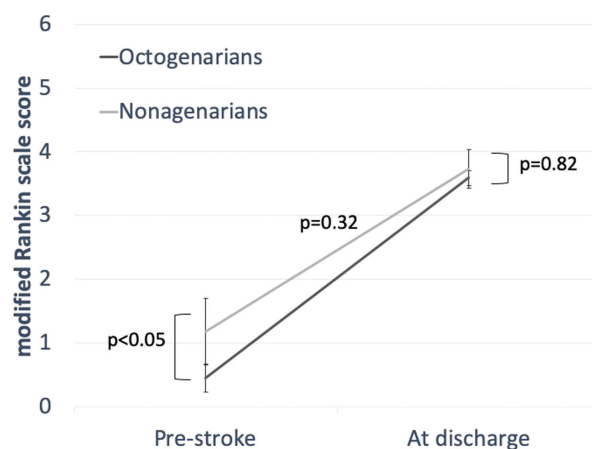


Fig. 2 Comparison of mRS scores at pre stroke and discharge between octogenarians and nonagenarians. mRS: modified Rankin Scale

Sussman et al.¹⁷⁾ noted a favorable outcome in 12.5% of 29 elderly patients (mRS score before onset: 0–2). In this study, 27.3% (3/11) had a favorable outcome. The results were considerably favorable even though the number of patients was small.

On the other hand, a previous meta-analysis involving patients aged 80–89 years reported that the TICI 2b or 3 (effective) recanalization rate ranged from 72% to 85%. The rate of patients with a favorable outcome ranged from 20% to 31%, being similar to that in this study,^{8,19,20)} although the value was slightly lower in Group O.

Furthermore, there were no differences in the changes in the mRS score after the onset of cerebral infarction or rate of improvement in the NIHSS score after treatment between the two groups; in patients aged ≥90 years, therapeutic effects similar to those in patients aged 80–89 years may be obtained.

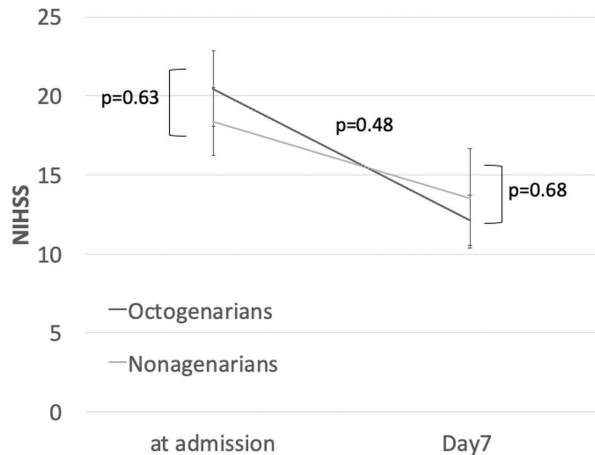


Fig. 3 Comparison of NIHSS scores at admission and day 7 between octogenarians and nonagenarians. NIHSS: National Institutes of Health Stroke Scale

Achieving effective recanalization is an important prognostic factor²¹⁾ although the effective recanalization rate in patients aged 90–99 years ranges from 69% to 79%.^{15–17)} In elderly patients, vessel tortuosity makes it difficult to navigate a guiding catheter to a proper site, requiring a considerable time until the therapeutic device reaching the occluded lesion; therefore, the recanalization rate is lower than that in young patients. In addition, a collateral circulation in elderly patients is less advanced than that in young patients, which may lead to an unfavorable outcome.²²⁾ Regarding IV-rt-PA alone for acute ischemic stroke, only a few studies have presented the results of treatment for patients aged ≥ 90 years. Mateen et al.²³⁾ compared patients aged 80–89 years with those aged 90–99 years and found no differences in the incidence of IV-rt-PA-related sICH or mortality rate.

Several studies reported that the incidence of sICH after MT in patients aged 90–99 years ranged from 5.1% to 21.4%.^{15–17)} One study reported that the risk of hemorrhagic complications in patients aged 90–99 years was double than that in those aged 80–89 years.¹⁷⁾ On the other hand, in this study, rt-PA was used for 63% of patients aged ≥ 90 years, but there was no sICH. Based on the results of this study, MT coupled with intravenous thrombolysis with rt-PA may be relatively safe even for patients aged 90–99 years. However, the number of patients was small, and thus, a larger number of patients should be investigated in the future.

This study has a couple of limitations. First, it was a retrospective, single-center study with small numbers. Second, there were biases in criteria for indicating MT for elderly patients and in the selection of devices.

In the future, a prospective randomized study should be conducted to confirm the efficacy of MT for patients aged 90–99 years.

Conclusions

We examined the results of MT for acute ischemic stroke in patients aged 90–99 years. MT was safely performed without increasing the incidence of hemorrhagic complications in patients aged 90–99 years in comparison with those aged 80–89 years. This study suggests that a favorable outcome is achieved in 25% of patients with independent ADL before onset and that the efficacy of MT for patients aged 90–99 years is similar to that for those aged 80–89 years. A further study with a larger number is warranted to verify the efficacy and safety of MT for nonagenarians.

Disclosure Statement

We declare no conflicts of interest.

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