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Significances and Outcomes of Mechanical Thrombectomy for Acute Infarction in Very Elderly Patients : A Single Center Experience

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Objective : Mechanical thrombectomy is increasingly being used for the treatment of acute ischemic stroke. The population over 80 years of age is growing, and many of these patients have acute infarction; however, these patients are often excluded from clinical trials, so the aim of this study was to compare the functional outcomes and complication rates in very elderly patients (age ≥80 years) and aged patients (60–79 years) treated with mechanical thrombectomy.

Methods : Between January 2010 and June 2015, we retrospectively reviewed 113 senior patients (over 60 years old) treated at our institution for acute ischemic stroke with mechanical thrombectomy. They were divided into a very elderly (≥80 years) and aged (60–79 years) group, with comparisons in recanalization rates, complications, death and disability on discharge be reported.

Results : The mean age was 70.3 years in the aged group and 83.4 years in the very elderly group. Elderly patients had higher rates of mechanical thrombectomy failure than the younger group (40% vs. 14%; odds ratio [OR] 4.1; 95% confidence interval [CI] 1.4–11.9; p=0.012). Results from thrombolysis in cerebral ischemia and modified Rankin scale at discharge were worse in the older group (p=0.005 and 0.023 respectively). There were no differences in mortality rate or other complications, but infarction progression rates were significantly higher in the very elderly group. (15% vs. 2.2%; OR 8.0; 95% CI 1.2–51.7; p=0.038). The majority (92.3%) of the patients who failed in aged group were not successful after several trials. However, in half (4 of 8) of the very elderly group, the occlusion site could not be accessed.

Conclusion : Patients older than 80 years of age undergoing mechanical thrombectomy for acute infarction were more difficult to recanalize due to inaccessible occlusion sites and had a higher rate of infarction progression, However, mortality and other complications were similar to those in younger patients.

Key Words : Infarction · Aged · Thrombectomy · Aged, 80 and over.

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INTRODUCTION

Although mortality rates have decreased, cerebrovascular disease, including stroke, are still a major cause of death, especially in the elderly in Korea[24]. Mechanical thrombectomy is being used commonly for the treatment of acute ischemic stroke, and recent clinical guidelines recommended endovascular recanalization therapy[10]. After the publication of five clinical trials[2,3,7,11,21], this procedure has been considered the standard treatment for anterior circulation occlusion patients[20], with reported benefits in most patients with acute ischemic stroke, regardless of patient' age, initial stroke severity, and administration of intravenous alteplase[8].

Some studies have investigated treatment with conventional intravenous thrombolysis in the elderly[17,22], however, patients over 80 years of age were mostly excluded from trials, and no large-scale studies distinctly investigated age-specific outcomes of mechanical thrombectomy[4]. The aging population is more susceptible to decreased neuronal plasticity, considerably due to a lack of neurologic restoration, therefore, older infarction patients have poorer overall outcomes[5].

In this study, we compared the functional outcomes and complication rates in very elderly patients (age ≥80 years) versus aged patients (60–79 years) in a single center after treatment with mechanical thrombectomy.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board and we retrospectively reviewed 113 senior patients (over 60 years old) who were treated for acute ischemic stroke with mechanical thrombectomy at our institution between January 2010 and June 2015. The patients were divided into two subgroups : those between 60 and 79 years old and those 80 years of age or over. Variables were compared between these subgroups.

The institutional management criteria for acute ischemic stroke are : 1) imaging evaluation performed immediately after visiting the emergency room (ER) and identifying the presence of hemorrhage, cerebral artery occlusion sites, and perfusion defects with perfusion computed tomography (CT); 2) administration of 0.9 mg/kg (10% bolus and 90% continuous infusion during 1 hour) if eligible for intravenous tissue plasminogen activator (tPA); 3) infarction area verified with magnetic resonance (MR) diffusion weighted imaging and the decision to treat with thrombectomy made by the neurosurgeons and neuro-interventionists considering the perfusion diffusion mismatching; 4) under informed consent from patients or their families, endovascular thrombectomy was carried out regardless of age; and 5) after the procedure, all patients underwent non-contrast CT immediately followed by imaging studies such as non-contrast CT and CT or MR angiography.

Patient data were collected including demographic data (sex and age), infarction risk factors, vascular occlusion sites, the use of intravenous tPA, time from symptom onset to ER visit, procedure time, complications (hemorrhage, progression, brain edema, and mortality) and need for secondary operation. Initial severity was assessed by the National Institutes of Health Stroke Scale (NIHSS). Reperfusion was classified using the modified thrombolysis in cerebral infarction (TICI) scale. Functional outcomes at discharge were measured according to the modified Rankin Scale (mRS). Mechanical thrombectomy was defined as the intra-arterial procedure including stent-retriever systems, the Penumbra system (Penumbra Inc., Alameda, CA, USA), and microwire maceration, with or without the administration of a chemical thrombolytic agent (urokinase or tirofiban), complications were classificated as hemorrhage, infarction progression, and brain edema according to the new lesions in the post-procedural imaging study compared with the initial examination, as well as aggravated neurologic symptoms.

The causes of failure were classified into three categories: first, the procedure was considered unsuccessful if occlusion sites were accessible, but recanalization failed after several attempts. Second, if there was no avenue to the occlusion site, the lesion was classified as inaccessible. Finally, 'guiding failure' was referred to when the guiding system was unable to perform the procedure, despite approaching the lesion.

Statistical analysis was performed using SPSS version 18.0 (IBM Corp., Armonk, NY, USA), continuous variables are presented as means plus or minus standard deviations, and variables were compared between the two subgroups using the Wilcoxon rank sum test for continuous variables and the chi-square or Fisher exact test for categorical variables. Univariate logistic regression models were used for the calculation of the odds ratio and their 95% confidence intervals. A probability value <0.05 was considered statistically significant.

RESULTS

A total of 171 patients were treated with endovascular thrombectomy for acute ischemic stroke in our institution between January 1, 2010 and June 30, 2015. Among these patients, 113 were senior patients, over 60 years of age, who underwent mechanical thrombectomy. Within this group of patients, 20 (17.7%) were very elderly (age ≥80 years) and 93 (82.3%) were aged patients (60–79 years). The mean age of the very elderly group was 83.4±2.3 years (range, 80–87 years), and that of the aged group was 70.3±5.5 years (range, 60–79 years). Baseline characteristics for the two groups are presented in Table 1.

Fifty-five patients (48.7%) were male. In older patients, most of whom were female, the percentage of male patients (20%) was significantly lower compared to younger patients (54.8%, p=0.005). There were no significant differences between the two subgroups in the presence of risk factors (hypertension, diabetes mellitus, dyslipidemia, arterial fibrillation, previous stroke, coronary artery disease, malignancy, and renal disease) or time from onset to ER visit and procedure duration. Most occlusions were identified at the internal cerebral artery in both subgroups (54.8% and 75% respectively).

The data in Table 2 shows rates of recanalization, clinical outcomes, and complications between the two groups. The NIHSS was administered when patients were initially presented to the ER, and the results were not significantly different between the two groups (13.9±6.4 vs. 15.6±6.7; p=0.331). However, very elderly patients were four times more likely to have failed recanalization (8/20 [40%] vs. 13/93 [14%]; p=0.010) and less likely to achieve major reperfusion (TICI score 2B and 3) than the younger group (75.2% vs. 40%; p=0.003) (Table 3).

Treatment outcome was evaluated at discharge using the mRS. There was a trend toward worse outcomes in the older group, with poor outcomes (mRS score 5–6) in 65% of very elderly patients versus 37.6% in aged patients (p=0.023) (Fig. 1, Table 2).

There were no significant differences in the rate of any com-

Table 1. Baseline characteristics of senior patients undergoing mechanical thrombectomy for acute infarction

	Total (n=113)	Aged patient (60–79 years) (n=93)	Very elderly patients (age ≥80 years) (n=20)	*p*-value
Age (years)	72.6±7.2	70.3±5.5	83.4±2.3	<0.001
Male sex	55 (48.7)	51 (54.8)	4 (20.0)	0.005
Hypertension	73 (64.6)	61 (65.6)	12 (60.0)	0.635
Diabetes mellitus	30 (26.5)	28 (30.1)	2 (10.0)	0.065
Dyslipidemia	9 (8.0)	8 (8.6)	1 (5.0)	>0.999
Arterial fibrillation	59 (52.2)	48 (51.6)	1 (55.0)	0.783
Previous stroke	10 (8.8)	9 (9.7)	1 (5.0)	0.688
CAD	8 (7.1)	6 (6.5)	2 (10.0)	0.630
Malignancy	5 (4.4)	5 (5.4)	0 (0.0)	0.584
Renal disease	3 (2.7)	2 (2.2)	1 (5.0)	0.446
Occlusion site				0.334
ICA	66 (58.4)	51 (54.8)	15 (75.0)	
MCA	27 (23.9)	25 (26.9)	2 (10.0)	
ACA	2 (1.8)	2 (2.2)	0 (0.0)	
BA	18 (15.9)	15 (16.1)	3 (15.0)	
IV tPA	47 (41.6)	44 (47.3)	3 (15.0)	0.008
Time from onset to visit ER (min)	149.9±191.1	144.0±18.0	177.3±58.5	0.845
Procedure time (min)	123.4±62.6	123.8±6.5	121.7±14.0	0.979

Values are presented as mean±standard deviation or number (%). CAD : coronary artery disease, ICA : internal carotid artery, MCA : middle cerebral artery, ACA : anterior cerebral artery, BA : basilar artery, ER : emergency room, IV tPA : intravenous tissue plasminogen activator

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Table 2. Comparison of recanalization, clinical outcomes and complications between aged patients and very elderly patients

	Total (n=113)	Aged patient (60–79 years) (n=93)	Very elderly patients (age ≥80 years) (n=20)	*p*-value
Admission NIHSS	14.2±6.5	13.9±6.4	15.6±6.7	0.331
Reperfusion (TICI)				0.005
Fail (0)	21 (18.6)	13 (14.0)	8 (40.0)	
Partial (1–2A)	14 (12.4)	10 (10.8)	4 (20.0)	
Major (2B–3)	78 (69.0)	70 (75.2)	8 (40.0)	
Outcome (mRS)				0.023
Good (0–2)	21 (18.6)	21 (22.6)	0 (0.0)	
Fair (3–4)	44 (38.9)	37 (39.8)	7 (35.0)	
Poor (5–6)	48 (42.5)	35 (37.6)	13 (65.0)	
Complication				
Hemorrhage	15 (13.3)	14 (15.1)	1 (5.0)	0.465
Progression	5 (4.4)	2 (2.2)	3 (15.0)	0.038
Edema	6 (5.3)	6 (6.5)	0 (0.0)	0.589
Mortality	20 (17.7)	16 (17.2)	4 (20.0)	0.752
Operation	10 (8.8)	10 (10.8)	0 (0.0)	0.205

Values are presented as mean±standard deviation or number (%). NIHSS : National institutes of health stroke scales, TICI : thrombolysis in cerebral ischemia, mRS : modified Rankin scale

plication, such as hemorrhage, edema, mortality, or re-operation in the posttreatment period. However, infarction progression was observed eight times more often in the very elderly group than the aged group (3/20 [15%] vs. 2/93 [2.2%]; p=0.038) (Table 2).

DISCUSSION

In this study, several infarction risk factors and occlusion vascular sites were identified, using intravenous tPA, time from symptom onset to ER visit, and procedure time. These results showed a few relevant factors, including male sex and tPA, that differed according to the age-related group. Korean statistics showed that the male to female ratio was 0.68 (2197606 men to 3227031 women) in those over 65 years of age, however this ratio decreased to 0.41 (280744 men to 681374 women) in the elderly group, based on the 2010 population and housing census[24]. It was also reported that the life expectancy of men and women was 79 and 85.5 years, respectively. With increasing age, the size of the male population generally declined, so our study could not avoid a lower percentage of men in very elderly patients. In addition, the Korean Ministry of Food and Drug safety suggested that using tPA in patients over 80 years of age is contraindicated[23]. This would result in only a few cases of IV tPA in the very elderly group, however Mazighi et al.[16] reported that intravenous and intra-arterial combined treatment in octogenarians had a higher recanalization rate and increased neurological improvement.

Research from Loh et al.[14] presented the outcomes of mechanical thrombectomy in patients younger than 80 years of age, but did not state the success rate of recanalization. In another study that analyzed intra-arterial therapy in elderly stroke patients, the authors reported that there were no significant differences in the TICI 2–3 reperfusion rates between those younger than 80 years and 80 years or older (75.4% vs. 71.4%; p=0.57). Still, the major reperfusion rate of TICI 2B to 3 was lower in very elderly patients (40% vs. 25%; p=0.06)[4]. We analyzed the success rate of mechanical thrombectomy as TICI 2A or more between aged patients (60–79 years) and the very elderly (age ≥80 years). Our younger group showed better recanalization results compared to the older group (86% vs. 60%), and the major reperfusion rate (TICI 2B–3) was also

significantly higher (75.3% vs. 40%; p=0.002) (Table 3). Although there were different methods of treatment among these studies[4,14], these results suggest a likely poorer revascularization rate in the elderly compared to younger patients.

When failures after mechanical thrombectomy, including factors such as occlusion site, thrombectomy method and cause of failure was analyzed (Table 4), it was found that the cause of procedure failure was significant in the two subgroups. In the majority (92.3%) of failed cases in patients aged 60–79, multiple approaches and attempts at recanalization were documented. However, in half (4 of 8) of the very elderly group, the occlusion site could not be accessed. Many studies reported age-related changes in the vasculature, including atherosclerosis of the vessel wall, media thickness, and hemodynamic modification[1,9,15]. The mechanical thrombectomy was sometimes difficult due to a tortuous aortic arch or acute angulation of the proximal portion in old patients. Given a lack of research regarding these points in the cerebrovascular field, further investigation regarding age-related vascular changes and failed endovascular treatment is necessary.

Furthermore, when assessing thrombectomy results in the short term, poor outcomes (mRS 5–6) were identified in the very elderly, while good outcomes (mRS 0–2) were shown significantly more often in aged patients (Table 2). Chandra et al.[4] reported that an age of 80 years and over was a substantial predictor of poor outcomes at 90 days. Similarly, several studies[6,12,18] have shown a lower rate of good functional outcomes in patients aged 80 years and older for 3 months after intra-arterial or intravenous treatment. However, Pego et al.[19] pointed out that there was no significant difference in mRS score between older and younger patients who were treated with intravenous thrombolysis. This might suggest that age-related neuronal loss leads to decreased neurological reserve, which influences the poor functional recovery seen in very elderly patients at the time of discharge as well as at 3 months follow-up.

Table 3. Univariate logistic regressions of recanalization, clinical outcomes and complications

	Patient	Unadjusted OR (95% CI)	*p*-value
Reperfusion (TICI)			
Fail vs. partial+major			
Age group (n=93)	13 (14.0)	1	
Very elderly group (n=20)	10 (10.8)	4.1 (1.41–11.96)	0.010
Major vs. fail+partial			
Age group (n=93)	70 (75.3)	1	
Very elderly group (n=20)	8 (40.0)	0.22 (0.08–0.60)	0.003
Outcome (mRS)			
Fair vs. good+poor			
Age group (n=93)	37 (39.8)	1	
Very elderly group (n=20)	7 (35.0)	0.82 (0.30–2.23)	0.691
Poor vs. good+fair			
Age group (n=93)	35 (37.6)	1	
Very elderly group (n=20)	13 (65.0)	3.08 (1.12–8.45)	0.029
Complication			
Hemorrhage vs. none			
Age group (n=93)	14 (15.1)	1	
Very elderly group (n=20)	1 (5.0)	0.30 (0.04–2.40)	0.255
Progression vs. none			
Age group (n=93)	2 (2.2)	1	
Very elderly group (n=20)	3 (15.0)	8.03 (1.25–51.72)	0.028
Mortality vs. none			
Age group (n=93)	16 (17.2)	1	
Very elderly group (n=20)	4 (20.0)	1.20 (0.36–4.08)	0.767

Values are presented as number (%) unless otherwise indicated. OR : odds ratio, CI : confidence interval, TICI : thrombolysis in cerebral ischemia, mRS : modified Rankin Scale

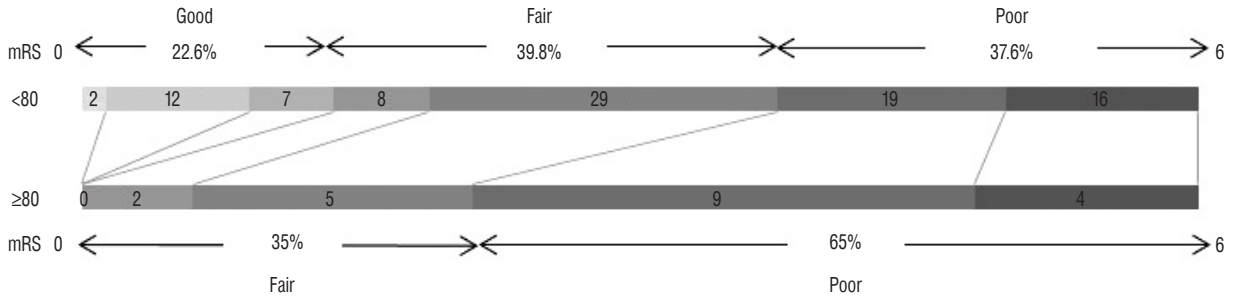

Fig. 1. Discharge modified Rankin Scale (mRS) score in very elderly patients (age ≥80 years) and aged patient (60–79 years).

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Table 4. Analysis of the elderly patients who failed to mechanical thrombectomy

	Total (n=21)	Aged patient (60–79 years) (n=13)	Very elderly patients (age ≥80 years) (n=8)	*p*-value
Age (years)	74.7±8.2	69.7±6.1	82.8±2.7	<0.001
Male sex	9 (42.9)	8 (61.5)	1 (12.5)	0.067
Location				0.368
ICA	7 (33.3)	6 (46.2)	1 (12.5)	
MCA	9 (42.9)	4 (30.8)	5 (62.5)	
BA	4 (19.0)	2 (15.4)	2 (25.0)	
ACA	1 (4.8)	1 (7.7)	0 (0.0)	
Treatment method				0.0867
Stent-retriever systems	9 (42.9)	6 (46.2)	3 (37.5)	
Microwire maceration	7 (33.3)	6 (46.2)	1 (12.5)	
None	5 (23.8)	1 (7.7)	4 (50.0)	
Fail cause				0.0117
Unsuccessful procedure	16 (76.2)	12 (92.3)	4 (50.0)	
Inaccessible lesion	4 (19.0)	0 (0.0)	4 (50.0)	
Guiding failure	1 (4.8)	1 (7.7)	0 (0.0)	

Values are presented as mean±standard deviation or number (%). ICA : internal carotid artery, MCA : middle cerebral artery, ACA : anterior cerebral artery, BA : basilar artery

Many studies have focused on the hemorrhagic transformation of complications after recanalization, and showed that these did not differ significantly in patients over 80 years compared with a younger group[4,6,9,18,19]. In our study, there was no difference in hemorrhage, however infarction progression was observed eight times more frequently in very elderly patients (Table 3). Kim et al.[13] demonstrated that ischemia progression is the most common cause of early neurological deterioration after thrombolysis. It could be suggested that poor results from thrombectomy were manifested in the older age group due to greater infarction progression.

A limitation of this study is that patient data was collected and analyzed retrospectively in a single institution. In addition, the treatment methods and procedure indications for acute ischemic patients were somewhat heterogeneous, including different thrombectomy devices and various agents. In the early part of the study period, wire-based maceration was mainly used. However in the latter part of the study, the use of stent retrievers and balloon guiding catheters due to development of the devices appeared to improve the results of treatment. Finally, the evaluated outcome was discharge mRS, the follow-up period was variable, ranging from two days to several weeks, which could be too short to accurately assess the results.

CONCLUSION

There is little known from previous clinical trials regarding the established treatment for acute ischemic stroke in very elderly patients. Thus, it is necessary to consider the outcomes of various treatments in this group. Although mortality and other complications were similar to those of younger patients, patients over 80 years of age undergoing mechanical thrombectomy for acute infarction were more difficult to recanalize due to inaccessible occlusion sites and a higher rate of infarction progression. Therefore, the procedure recommended should be decided with prudence.

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