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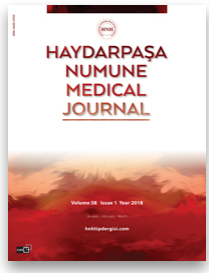

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ORIGINAL ARTICLE

Low NIHSS Stroke due to Large Vessel Occlusion: What is the Prognosis?

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Abstract

Introduction: The benefit of mechanical thrombectomy (MT) vs. medical therapy in mild stroke (NIHSS <6) is still being investigated. In this study, we evaluate the prognosis of low NIHSS patients with large vessel occlusion (LVO) who did not undergo MT at admission.

Methods: This was a retrospective study. Thirty-nine patients with acute ischemic stroke due to large vessel occlusion with mRS 0-2, NIHSS 0-6, were included in the study between 2021-2023. The outcome was evaluated by the modified Rankin Scale score at 90 days.

Results: The mean age of patients was 68.4 (32-97). Twenty-four of them were male, and 15 were female. The median NIHSS score at admission was 3. The most common occlusion site was the M2 segment. Nineteen patients received bridging IVT. Only three patients experienced clinical deterioration and underwent MT during hospitalization. The outcomes between the clinical deterioration and non-deterioration groups did not differ statistically.

Discussion and Conclusion: MT can be performed in low NIHSS stroke patients, especially those with ICA occlusions. To define the exact candidate, the results of ongoing trials such as ENDOLOW and MOSTE are needed.

Keywords: Large vessel occlusion; low NIHSS; prognosis.

Current guidelines recommend mechanical thrombectomy (MT) for acute ischemic stroke (AIS) patients with large vessel occlusion (LVO) and National Institutes of Health Stroke Scale (NIHSS) ≥6, Alberta Stroke Program Early Computed Tomography Score (ASPECT) of ≤6, up to 6 hours from symptom onset as Class 1A quality[1,2]. One in 25 patients with AIS presenting with an NIHSS score <6 and up to 20% of this population experience early neurological deterioration and poor outcomes[3,4].

It is still unclear which patients with low NIHSS scores are candidates for MT[5,6]. Occlusion site, such as in cases of internal carotid artery (ICA) and the first segment of the middle cerebral artery (M1), may have a tendency toward neurological worsening[6]. Collateral circulation, thrombus length, initial infarct core, and metabolic problems (uncontrolled glycemic indexes and elevated blood pressures) may be mechanisms underlying early deterioration[5-7].

Here, we studied the prognosis of low NIHSS patients with LVO who did not undergo MT at admission.

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Materials and Methods

Patient Population

The local Ethics Committee (13.07.23/104) approved this single-center, retrospective study. This study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each patient or their statutory representative. Thirty-nine patients with acute ischemic stroke due to LVO with a modified Rankin Scale (mRS) score of 0-2 and NIHSS 0-6 were included in the study between 2021-2023 at the neurology department of a tertiary stroke center. Demographic data were obtained from the hospital and the national health registry. Age, sex, comorbidities, pre-stroke treatment, vital signs, laboratory tests, time of onset at admission, initial stroke severity, arterial occlusion site, and symptomatic intracranial hemorrhage (sICH) as well as other complications such as hemorrhagic transformation (HT) and malignant infarction were recorded. The inclusion criteria were age ≥18 years, underwent non-contrast computed tomography (CT) or CT angiography at the time of admission, having LVO and neurological deficits ≥0 according to the NIHSS. Patients with mRS>2, NIHSS>6, and those with sustained infarction at admission were excluded. Patients with low NIHSS but the presence of motor or language symptoms were accepted as a vulnerable population and underwent MT.

Treatment Methods

Intravenous thrombolysis (IVT) was initiated in all eligible patients. For patients who received IVT, the t-PA dosage was 0.9 mg/kg, with a maximum dose of 90 mg over 1 hour. MT was performed when early neurological deterioration (defined as an increase in NIHSS score ≥4 at 24 hours) occurred.

Definitions of Outcomes

The primary functional outcomes were good prognosis (mRS 0-2) and mortality (mRS 6) on Day 90. Patients were seen during their routine clinical check-up in the outpatient setting or were reached by telephone. The safety outcome was the absence of sICH. In general, sICH was defined as a new intracranial hemorrhage associated with an increase in the NIHSS score (>4 points) from the score immediately before the exacerbation. Hemorrhage was graded according to the method used in the European Cooperative Acute Stroke Trials. The NIHSS score at admission and at 24 hours was used to assess the severity of neurological deficits. Asymptomatic intracranial

Table 1. Demographic Characteristics of Patients

	All Patients (n=39)
Age (year) Med±SD	68.44±14.80
Gender, n (%)	
Female	15 (38.5)
Male	24 (61.5)
Comorbidities, n (%)	
HT	25 (64.1)
DM	14 (35.9)
CAD	12 (30.8)
AF	9 (23.1)
Admission Time, n (%)	
0-60 min	8 (20.5)
61-120 min	9 (23.1)
121-180 min	11(28.2)
181-240 min	5 (12.8)
>240 min	6 (15.4)
NIHSS Mean±SD	2.87±2.26
Occlusion Site, n (%)	
ICA Terminal	10 (25.6)
Tandem	3 (7.7)
ICA Proximal	2 (5.1)
M1	5 (12.8)
M2	15 (38.5)
P1	4 (10.3)
tPA, n (%)	
No	20 (51.3)
Yes	19 (48.7)
Clinical Deteriotation and Underwent MT, n (%)	
No	36 (92.3)
Yes	3 (7.7)
24. Hour NIHSS Mean±SD	2.79±3.77
Symptomatic ICH, n (%)	
No	39 (100)
Yes	0 (0.0)
Hemorrhagic Transformation, n (%)	
No	34 (87.2)
Yes	5 (12.8)
Malignant Infarction n (%)	
No	38 (97.4)
Yes	1 (2.6)
Decompression, n (%)	
No	39 (100)
Yes	0 (0.0)
Extracranial Complication, n (%)	
No	37 (94.9)
Yes	2 (5.1)
Toast, Etiology, n (%)	
Large-vessel Atherosclerosis	13 (33.3)
Cardioembolism	11 (28.2)
Small vessel atherosclerosis	1 (2.6)
More than one reason	3 (7.7)
Undetermined	11 (28.2)
90. Day mRS Mean±SD	0.49±1.17
Length of Stay (Day) Mean±SD	5.44±5.26

Table 2. Clinical Deteriotation and Underwent MT Comparison

	Clinical Deteriotation and Underwent MT			
	No (n=36) Mean±SD Median (Min-Max)	Yes (n=3) Mean±SD Median (Min-Max)	Test Statistics	
			Z; X^2	p
Age (year)	68.53±15.31 67.0 (32.0-97.0)	67.33±7.51 63.0 (63.0-76.0)	z=0.422	0.709
Gender, n (%)				
Female	14 (38.9)	1 (33.3)	-	0.674*
Male	22 (61.1)	2 (66.7)		
Comorbidities, n (%)				
HT	24 (66.7)	1 (33.3)	-	0.289*
DM	14 (38.9)	0 (0.0)	-	0.252*
CAD	10 (27.8)	2 (66.7)	-	0.219*
AF	8 (22.2)	1 (33.3)	-	0.556*
Admission Time, n (%)				
0-60 min	8 (22.2)	0 (0.0)	χ^2=8.262	0.082
61-120 min	9 (25.0)	0 (0.0)		
121-180 min	8 (22.2)	3 (100.0)		
181-240 min	5 (13.9)	0 (0.0)		
>240 min	6 (16.7)	0 (0.0)		
NIHSS	2.92±2.32 3.0 (0.0-6.0)	2.33±1.53 2.0 (1.0-4.0)	z=0.348	0.746
Occlusion Site, n (%)				
ICA Terminal	8 (22.2)	2 (66.7)	-	-
Tandem	3 (8.3)	0 (0.0)		
ICA Proximal	2 (5.6)	0 (0.0)		
M1	5 (13.9)	0 (0.0)		
M2	14 (38.9)	1 (33.3)		
P1	4 (11.1)	0 (0.0)		
tPA, n (%)				
No	19 (52.8)	1 (33.3)	-	0.480*
Yes	17 (47.2)	2 (66.7)		
24. Hour NIHSS	2.64±3.69 2.0 (0.0-20.0)	4.67±5.03 4.0 (0.0-10.0)	z=0.755	0.497
Hemorrhagic Transformation, n (%)				
No	32 (88.9)	2 (66.7)	-	0.345*
Yes	4 (11.1)	1 (33.3)		
Extracranial Complication, n (%)				
No	34 (94.4)	3 (100.0)	-	0.850*
Yes	2 (5.6)	0 (0.0)		
Toast, Etiology, n (%)				
Large-vessel atherosclerosis	11 (30.6)	2 (66.7)	-	-
Cardioembolism	11 (30.6)	0 (0.0)		
Small-vessel atherosclerosis	1 (2.8)	0 (0.0)		
More than one reason	2 (5.6)	1 (33.3)		
Undetermined	11 (30.6)	0 (0.0)		
90. Day mRS	0.42±1.05 0.0 (0.0-5.0)	1.33±2.31 0.0 (0.0-4.0)	z=0.747	0.635
Length of Stay (Day)	5.03±4.95 4.0 (1.0-29.0)	10.33±7.57 7.0 (5.0-19.0)	z=1.838	0.069

X^2: Ki square Test; z: Mann Whitney U Test Statistics; *Fisher Exact test results.

Table 3. Parameters according to the hemorrhagic transformation

	Hemorrhagic Transformation			
	No (n=34) Mean±SD Median (Min-Max)	Yes (n=5) Mean±SD Median (Min-Max)	Test statistics	
			Z; X^2	p
Age (year)	68.76±15.21 68.5 (32.0-97.0)	66.20±12.87 63.0 (54.0-88.0)	z=1.030	0.314
Gender, n (%)				
Female	14 (41.2)	1 (20.0)	-	0.351
Male	20 (58.8)	4 (80.0)		
Comorbidities, n (%)				
HT	21 (61.8)	4 (80.0)	-	0.400
DM	11 (32.4)	3 (60.0)	-	0.237
CAD	10 (29.4)	2 (40.0)	-	0.494
AF	8 (23.5)	1 (20.0)	-	0.676
Admission Time, n (%)				
0-60 min	8 (23.5)	0 (0.0)	χ^2=3.223	0.521
61-120 min	7 (20.6)	2 (40.0)		
121-180 min	10 (29.4)	1 (20.0)		
181-240 min	4 (11.8)	1 (20.0)		
>240 min	5 (14.7)	1 (20.0)		
NIHSS	2.79±2.21 3.0 (0.0-6.0)	3.40±2.79 4.0 (0.0-6.0)	z=0.640	0.554
Occlusion Site, n (%)				
ICA Terminal	9 (26.5)	1 (20.0)	-	-
Tandem	3 (8.8)	0 (0.0)		
ICA Proximal	1 (2.9)	1 (20.0)		
M1	5 (14.7)	0 (0.0)		
M2	12 (35.3)	3 (60.0)		
P1	4 (11.8)	0 (0.0)		
tPA, n (%)				
No	20 (58.8)	0 (0.0)	-	0.020
Yes	14 (41.2)	5 (100.0)		
24. Hour NIHSS	2.56±3.89 1.5 (0.0-20.0)	4.40±2.61 6.0 (0.0-6.0)	z=1.698	0.098
Extracranial Complication, n (%)				
No	33 (97.1)	4 (80.0)	-	0.243
Yes	1 (2.9)	1 (20.0)		
Toast, Etiology n (%)				
Large-vessel atherosclerosis	10 (29.4)	3 (60.0)	-	-
Cardioembolism	9 (26.5)	2 (40.0)		
Small-vessel atherosclerosis	1 (2.9)	0 (0.0)		
More than one reason	3 (8.8)	0 (0.0)		
Undetermined	11 (32.4)	0 (0.0)		
90. Day mRS	0.35±1.04 0.0 (0.0-5.0)	1.40±1.67 1.0 (0.0-4.0)	z=2.293	0.107
Length of Stay (Day)	4.50±2.79 4.0 (1.0-14.0)	11.80±11.86 7.0 (2.0-29.0)	z=1.104	0.294

X^2: Ki Square Test; z: Mann Whitney U Test Statistics; *Fisher Exact test results.

hemorrhage (aICH), subarachnoid hemorrhage, malignant infarction, and decompression were also analyzed in the present study. Malignant infarction was defined as a large space-occupying infarction involving massive edema, herniation, or frequent death. Extracranial complications were also assessed. For etiological classification, TOAST was used. The TOAST classification denotes five types of ischemic stroke: 1) large-artery atherosclerosis, 2) cardioembolism, 3) small-vessel occlusion, 4) stroke of other determined etiology, and 5) stroke of undetermined etiology.

Statistical Analysis

Number (n) and percentage (%) values were used to show the distribution of individuals in demographic information such as gender, disease status, and occlusion site. The suitability of the continuous variables in the study to normal distribution was evaluated graphically and with the Shapiro-Wilk test. It was determined that none of the continuous variables followed a normal distribution. Mean±SD (standard deviation) and Median (Minimum-Maximum) values were provided to display the descriptive statistics of the variables.

The Mann-Whitney U test was used to compare the values of age, mRS, admission NIHSS, 24th-hour NIHSS, 90th-day mRS, and hospital stay according to clinical worsening and hemorrhagic transformation. Cross tables were created to compare categorical variables according to clinical deterioration and hemorrhagic transformation, and number (n), percentage (%), and chi-square (χ^2) test statistics were given.

IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS-Excel 2007 programs were used for statistical analyses and calculations. Statistical significance level was accepted as $p<0.05$.

Results

The mean age of patients was 68.4 (32-97). Twenty-four of them were male, and 15 were female. The most common comorbidity was hypertension (n=25). Mean admission time was 157 minutes (30-420). The median NIHSS score at admission was three. The most common occlusion site was the M2 segment. Nineteen patients received bridging IVT. Only three of the patients experienced clinical deterioration and underwent MT during hospitalization. The 24th-hour median NIHSS score was two (0-20). No sICH or decompression was observed. Five patients had hemorrhagic transformation, and one had malignant infarction. Two patients had extracranial complications, which were hematuria. According to the TOAST classification for etiology, 33.3% of patients had large vessel atherosclerosis, and 11% had cardioembolism. At 90-day mRS, 32 patients had an mRS of zero. The mortality rate was zero. The median hospital stay was five days (Table 1).

No statistically significant difference was detected in terms of age, gender, comorbidities, time of admission, mRS, NIHSS, tPA, 24th-hour NIHSS, hemorrhagic transformation, extracranial complications, 90th-day mRS, or length of hospitalization according to clinical deterioration ($p>0.05$) (Table 2).

It was determined that 58.8% (n=20) of the individuals without hemorrhagic transformation did not receive tPA, while 41.2% (n=14) did, and all of the individuals with hemorrhagic transformation (n=5) received tPA. A statistically significant difference was detected in terms of the distribution of tPA administration according to hemorrhagic transformation ($p=0.020$). No statistically significant difference was found in other parameters when comparing the groups according to the presence of hemorrhagic transformation (Table 3).

Discussion

We reported no statistically significant difference between early clinical deterioration and non-deterioration in patients with low NIHSS strokes with LVO. In recent studies, it was shown that MT was comparable to medical management, but the risk of sICH seemed to be higher[3], or MT was associated with a poor prognosis[7,8]. In contrast, early MT without clinical worsening had similar or even better mRS scores at day 90[9-11]. Individual factors may play a role in these varied results. Collateral status, initial stroke volume, and thrombus length were related to clinical deterioration[5-7]. Older age, female gender, smoking, diabetes, atrial fibrillation, and prior stroke were associated with worse clinical outcomes[12].

Three patients (7.7%) experienced clinical deterioration and underwent MT in our study. In previous studies, the rates of clinical deterioration were 8-9%, and these patients underwent rescue MT[5,6]. We found no statistically significant association between clinical worsening and age, gender, comorbidities, NIHSS scores, complications, and day 90 mRS scores. The importance of the arterial occlusion site was highlighted in clinical deterioration[3,5,6]. Mazya et al.[5] reported that non-hemorrhagic early neurological worsening was seen in 30% of patients with terminal internal carotid

artery (ICA) or tandem occlusions (ICA+middle cerebral artery (MCA)). In our series, two patients had terminal ICA occlusions, and one had an M2 segment MCA occlusion, but no significant difference was detected between arterial occlusion site and clinical worsening.

sICH and other hemorrhagic events are additional factors in clinical deterioration[3,7,12]. In our study, we grouped the patients according to hemorrhagic transformation. We found no statistically significant difference between groups except for the administration of tPA. In the hemorrhagic transformation group, the rate of tPA administration was higher (p=0.020).

Most of the patients in our study had M2 occlusions. A recently published meta-analysis and the MINOR-STROKE collaboration showed that M2 occlusions were independently associated with a reduced risk of early neurological deterioration and were not suitable candidates for MT[6,13]. Recent studies claimed that early MT for low NIHSS showed better prognosis[9,14]. We performed MT on patients with aphasia and pure monoparesis despite low NIHSS scores, and early MT for these patients might have contributed to better clinical outcomes. However, we excluded this group, so the exact role of early MT in the outcome of low NIHSS stroke could not be identified.

There are several limitations in this study. It had a retrospective design and a small sample size. Patients with aphasia or pure monoparesis were considered strategic cases and underwent MT despite low NIHSS scores.

Conclusion

MT can be performed in low NIHSS stroke patients, especially those with ICA occlusions. To define the exact candidate, the results of ongoing trials such as ENDOLOW and MOSTE are needed.

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Fatih Sultan Mehmet Training and Research Hospital (dated 13/07/2023, numbered 104). This study was conducted in accordance with the Declaration of Helsinki.

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