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Research Article

Effects of Stroke Severity on Treatment Initiated in the Emergency Department

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Abstract

Aim: Stroke severity depends on the treatments administered from the moment the patient enters the emergency department and the success of patient management. In our study, we aimed to evaluate the effect of National Institutes of Health Stroke Scale (NIHSS) scoring on intervention time and the relationship of qualitative measures with clinical outcome in patients in our stroke center.
Material and Method: The files of patients who underwent iv TPA and/or mechanical thrombectomy in the emergency department who were followed up at the stroke center between 2022 and 2023 were retrospectively reviewed. Patients were divided into 4 groups as NIHSS score 0-5, 5-10, 10-20, ≥21; 3 groups as modified Rankin Scale (MRS) score 0-2, 3-5 and 6. Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in the descriptive statistics of the data. ANOVA (Tukey test), Kruskal-Wallis, Mann-Whitney u test were used in the analysis of quantitative independent data; chi-square test was used in the analysis of qualitative independent data, and fischer test was used when chi-square test conditions were not met.
Results: Symptom puncture, symptom recanalization, puncture recanalization, door imaging, door TPA, door puncture times did not differ significantly ($p>0.05$) between stroke severity groups. The first-pass recanalization rate was significantly ($p<0.05$) higher in the MRS III-IV-V group than in the MRS 0-I-II group, while the first-pass recanalization rate did not differ significantly ($p>0.05$) between the MRS VI group and the MRS 0-I-II, MRS III-IV-V groups. In the group with bleeding at 24 hours, TICI stage was significantly ($p<0.05$) lower, 3rd month MRS score was significantly ($p<0.05$) higher, and tan score was significantly ($p<0.05$) lower than the group without bleeding at 24 hours.
Conclusion: Although there is no correlation between stroke severity and emergency department quality-metrics times, recanalization success has an effect on good outcome. Instroke, the coordination and experience of all components of the neurology and emergency medicine clinics hould be good in terms of diagnosis and timing.

Keywords: Thrombectomy, stroke, iv Tpa, emergency service

INTRODUCTION

Stroke is the leading cause of disability and one of the most prevalent causes of mortality globally (1). Initially, intravenous tissue plasminogen activator (iv tPA) was recommended as the primary treatment option, as per the first published guidelines. However, recent research has demonstrated the effectiveness of mechanical thrombectomy for large vessel occlusions. Notably, mechanical thrombectomy is now included in the guidelines for acute ischemic stroke (AIS) patients presenting within the first six hours, specifically for those with occlusions in the M1 segment of the internal carotid artery (ICA) or the middle cerebral artery (MCA) (2-5). Furthermore, findings from the DAWN and DEFUSE-3 studies have led to an extension of the treatment window for mechanical thrombectomy to 24 hours for AIS patients (6,7).

AIS constitutes a neurological emergency that necessitates prompt and interventional treatment. Given that the initial presentation occurs in the emergency department, the provision of rapid and effective treatment is critically important (5). In both our country and globally, the process of establishing a diagnosis and making a treatment decision should ideally be completed within 45 minutes of presentation. Should thrombolytic therapy and/or mechanical thrombectomy (MT) be deemed necessary, it is imperative that the door-to-needle time remains under 60

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minutes (8). However, factors such as overcrowding in the emergency department, along with delays in the diagnosis and treatment of acute stroke patients, contribute to an extended length of stay in the emergency department (9).

Numerous factors can influence the efficacy and timeliness of treatment in the emergency department, including patient volume, waiting times for triage and ward admission, and disorganized emergency entries resulting from irregular operational procedures. Consequently, the severity of the condition and the physician's ability to identify an acute stroke case that necessitates prompt intervention, appropriate triage, and effective patient management are critical for achieving favorable clinical outcomes. The National Institutes of Health Stroke Scale (NIHSS) is a standardized scoring system that assesses the severity of a patient's neurological deficits on a scale from 0 to 42. This scoring system is instrumental in determining the appropriateness of iv tPA and/or MT in emergency situations. Therefore, the objective of our study was to investigate whether the NIHSS score influences the timing of intervention in patients receiving iv tPA in conjunction with MT or MT alone. Additionally, we aimed to evaluate the clinical outcomes and the incidence of intracerebral hemorrhage among patients treated at our stroke center using qualitative measures.

MATERIAL AND METHOD

This study received approval from the Clinical Studies Ethics Committee of University of Health Sciences Haseki Training And Research Hospital (Decision No: 261-2023) and was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

The medical records of patients who were monitored at the stroke center from 2022 to 2023, underwent MT, and received iv tPA in the emergency department were subjected to a retrospective review. Demographic information, medical history, medication usage, baseline neurologic examination results, time of hospital admission, angiography data, imaging times, and neurologic examination findings at 24 hours and 3 months were extracted from patient records. The demographic data and door duration for the patients are presented in Table 1. Additionally, we aimed to assess the clinical outcomes and intracerebral hemorrhage status of patients at our stroke center using qualitative criteria. The qualitative criteria employed included symptom puncture, symptom recanalization, puncture recanalization, door imaging, door iv tPA administration, and door puncture times.

Patient Selection

The study included patients with occlusion of the P1 segment of the basilar artery (BA), posterior cerebral artery (PCA), ICA (tandem, T, L), or M1 segment of the MCA, as determined by computed tomography (CT) of the brain, provided that there was no evidence of bleeding. Eligible participants had an Alberta Stroke Program Early Computed Tomography (ASPECT) score greater than 6 . Patients with ASPECT scores below 6 were not included in the study because it was thought that this would affect bleeding rates. Since our study was classified according to the NIHSS score, NIHSS limitation was not considered in the inclusion criteria. Additionally, participants had a pre-stroke modified Rankin Scale (MRS) score of 0-1, a symptom-to-door time of less than 4.5 hours, or a symptom-to-door time ranging from 4.5 to 16 hours. There were no ischemic lesions observed on magnetic resonance imaging (MRI) in the FLAIR sequence, and all patients underwent MT. Patients with an ASPECT score of less than 6 or those with bleeding on brain CT were excluded from the study.

Patients were categorized into three groups based on their NIHSS scores, MRS scores, and the presence or absence of intracranial hemorrhage. The NIHSS scores were further subdivided into four categories: 0-5, 5-10, 10-20, and ≥21. The MRS scores were classified into three groups: 0-2, 3-5, and 6. Additionally, patients were divided into two groups based on the presence or absence of intracranial hemorrhage at the 24-hour mark.

Endovascular Treatment

Upon presentation at the emergency department, patients were evaluated by a neurologist. All patients underwent non-contrast brain CT and computed tomography angiography (CTA). Those without contraindications who presented within the first 4.5 hours after the onset of symptoms, as well as those admitted within 16 hours without ischemic lesions evident on magnetic resonance imaging (MRI) FLAIR sequences, were administered alteplase at a dosage of 0.9 mg/kg in the emergency department before being transferred to the angiography unit for MT.

Clinical evaluation scales were employed to assess early ischemic changes on cranial CT using the ASPECT scoring system (10). The modified Tan scoring system was utilized to determine the collateral score on CTA (11). The level of recanalization was assessed according to the modified Treatment in Cerebral Ischemia (mTICI) classification (12). Specifically, mTICI 0 was characterized by the absence of flow, mTICI 1 indicated filling of the distal MCA without blood supply to the cortical branches, mTICI 2a represented filling of less than half of the MCA irrigation area, mTICI 2b denoted filling of more than half of the MCA irrigation area, mTICI 2c indicated filling of the entire MCA irrigation area but at a slower rate than the normal side, and mTICI 3 signified complete recanalization. Following the initial thrombectomy attempt, mTICI 2c-3 recanalization was classified as first-pass recanalization. Intracerebral hemorrhages observed on brain CT at 24 hours post-MT were evaluated according to the criteria established by the European Cooperative Acute Stroke Study (ECASS III). Hemorrhages that resulted in an increase of ≥4 points in the NIHSS score at admission were classified as symptomatic intracerebral hemorrhage (ICH). The disability status at 90 days was assessed using the MR.

Statistical Analysis

Statistical analysis was conducted utilizing various descriptive statistics, including mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was assessed using the Kolmogorov-Smirnov test and the Shapiro-Wilk test. For the analysis of quantitative independent data, ANOVA

(with Tukey's post-hoc test), the Kruskal-Wallis test, and the Mann-Whitney U test were employed. The Chi-square test was utilized for the analysis of qualitative independent data, while Fisher's exact test was applied when the conditions for the Chi-square test were not satisfied. The statistical analyses were performed using SPSS version 28.0.

RESULTS

The mean age of the patients in this study was 69.5 years (standard deviation: 16.7; range: 21.0-96.0). Among the total of 132 patients, 76 (55%) were male and 62 (45%) were female. A total of 57 patients (47%) were identified as smokers, 87 patients (63%) had a diagnosis of hypertension, 75 patients (54%) had atrial fibrillation, 54 patients (39%) had coronary artery disease, 29 patients (21%) had diabetes, and 37 patients (27%) were classified as obese. Additionally, 26 patients (19%) had a prior history of stroke. Thirteen patients (11%) were receiving warfarin, while 23 patients (17%) were on newer generation oral anticoagulants.

The mean admission ASPECT score was 9.3 (standard deviation: 0.9; range: 6.0-10.0), and 59 patients (43%) received iv tPA. Among the 138 patients who underwent thrombectomy, the mean time from symptom onset to puncture was 247.9 minutes (standard deviation: 166.6), the mean time from symptom onset to recanalization was 303.1 minutes (standard deviation: 171.8), and the mean time from puncture to recanalization was 53.3 minutes (standard deviation: 17.9). The mean door-to-imaging time was 18.8 minutes (standard deviation: 16.6), the mean door-to-TPA time was 48.7 minutes (standard deviation: 20.7), and the mean door-to-puncture time was 55.4 minutes (standard deviation: 17.0). Furthermore, successful reperfusion, defined as TICI scores of 2B, 2C, or 3, was achieved in 118 out of 130 patients (85%) (see Table 1).

Table 1. Demographic data and door durations

		Min-Max	Median	Mean±SD/n (%)
Age		21.0-96.0	75.0	69.5±16.7
Sex	**Woman**			76 (55)
	Man			62 (45)
Cigarette smoking	**(-)**			81 (59)
	(+)			57 (41)
Comorbid disease				
Hypertension				87 (63)
Atrial fibrillation				75 (54)
Coronary artery disease				54 (39)
Diabetes mellitus				29 (21)
Obesity				37 (27)
Stroke history	**(-)**			112 (81)
	(+)			26 (19)
Large vessel occlusion	**(-)**			0 (0)
	(+)			138 (100)
Warfarin use	**(-)**			123 (89)
	(+)			15 (11)
NOAC use	**(-)**			115 (83)
	(+)			23 (17)
IV TPA	**(-)**			79 (57)
	(+)			59 (43)
Admission ASPECT		6.0-10.0	10.0	9.3±0.9
Symptom puncture time		30.0-730.0	202.5	248.9±166.6
Symptom recanalization time		90.0-810.0	252.5	303.1±171.8
Puncture recanalization time		10.0-125.0	50.0	53.3±17.9
Door imaging time		5.0-120.0	15.0	18.8±16.6
Door TPA time		20.0-110.0	45.0	48.7±20.7
Door puncture time		15.0-90.0	56.0	55.4±17.0
TICI score	**0**			13 (10)
	2A			7 (5)
	2B			35 (25)
	2C			22 (16)
	3			61 (44)

SD: standard deviation, ASPECT: Alberta Stroke Programme Early CT score, NOAC: new oral anticoagulant, IV TPA: intravenous tissue plasminogen activator, TICI: treatment in cerebral ischemia

The mean NIHSS admission score was 10.4±3.3, while the NIHSS score at the 24th hour was 6.2±5.0. The MRS score at three months was recorded as 2.2±2.1. First-pass recanalization was successfully achieved in 57 out of 138 patients, representing 41.4% of the cohort. The incidence of bleeding at the 24-hour mark was observed in 40 out of 138 patients, equating to a rate of 29%. Antiplatelet therapy was initiated in 54 out of 138 patients (39%), based on the indication-contraindication status following the control CT scan conducted after 24 hours. Among the patients, 71 out of 138 (52%) exhibited good collateral flow (defined as >50% collateral flow), while 11 out of 138 patients (8%) received salvage therapy (refer to Table 2).

Table 2. NIHSS score and other general information

		Min-Max	Median	Mean±SD/n (%)
NIHSS score				
Admission		4.0-22.0	10.0	10.4±3.3
24th hour		0.0-25.0	4.0	6.2±5.0
3rd month MRS		0.0-6.0	2.0	2.2±2.1
First pass recanalization	**(-)**			81 (58.6)
	(+)			57 (41.4)
Distal embolism	**(-)**			78 (57)
	(+)			60 (43)
sICH in 24 hours	**(-)**			98 (71)
	(+)			40 (29)
Antiaggregant therapy	**(-)**			84 (61)
	(+)			54 (39)
Tan score	**(-)**			28 (20)
	<50%			39 (28)
	50-99%			51 (37)
	100%			20 (15)

MRS: Modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, sICH: symptomatic intracranial hemorrhage

Patients were categorized into three groups based on their scores on the NIHSS, the MRS, and the presence or absence of intracranial hemorrhage. Within these categories, the NIHSS scores were further divided into four groups: 0-5, 6-10, 11-20, and ≥21. The MRS scores were classified into three groups: 0-2, 3-5, and 6. Additionally, patients were grouped according to the presence or absence of intracranial hemorrhage at the 24-hour mark. The times for symptom onset and recanalization did not show significant differences (p>0.05) among the groups classified by NIHSS scores of 0-5, 6-10, 11-20, and ≥21. Furthermore, the values for door imaging, door-to-TPA administration, and door puncture did not differ significantly (p>0.05) across the same NIHSS score groups (see Table 3).

Table 3. Relationship of qualitemetric measures with NIHSS score

		NIHSS score 0-5	NIHSS score 6-10	NIHSS score 11-20	NIHSS score ≥21	p
Symptom puncture time	**Mean±SD**	310.8±227.7	223.2±159.6	269.6±176.6	165.0±	0.450[K]
	Median	287.5	170.0	210.0	165.0	
Symptom recanalization time	**Mean±SD**	374.4±232.6	274.6±160.1	333.0±188.3	220.0±	0.258[K]
	Median	349.5	220.0	271.0	220.0	
Puncture recanalization time	**Mean±SD**	63.6±16.4	51.6±18.0	61.1±29.7	55.0±	0.203[K]
	Median	60.0	50.0	52.5	55.0	
Door imaging time	**Mean±SD**	20.9±18.8	18.1±14.6	19.7±16.5	9.0±	0.616[K]
	Median	15.0	15.0	15.0	9.0	
Door TPA time	**Mean±SD**	62.0±27.5	52.9±19.8	43.7±18.7	±	0.056[K]
	Median	55.0	50.0	40.0	0.0	
Door puncture time	**Mean±SD**	65.0±17.6	57.3±17.0	54.0±17.8	50.0±	0.186[K]
	Median	72.5	60.0	52.5	50.0	
First pass recanalization						
First pass	**n (%)**	8 (40.0)	47 (53.4)	44 (69.8)	1 (100)	p>0.05[X²]
Repeating	**n (%)**	4 (20.0)	18 (20.5)	16 (25.4)	0 (0.0)	

K Kruskal-Wallis (Mann-Whitney U test) / X² Chi-squaretest (Fischer test); NIHSS: National Institutes of Health Stroke Scale, TPA: tissue plasminogen activator

The times for symptom puncture and symptom recanalization did not exhibit significant differences (p>0.05) among the groups categorized by MRS scores of 0-I-II, III-IV-V, and VI. Additionally, no significant differences (p>0.05) were observed between the MRS 0-I-II, III-IV-V, and VI groups regarding puncture recanalization, door imaging, door iv tPA administration, and door puncture values. However, the TICI stage was significantly higher (p<0.05) in the MRS 0-I-II group compared to the MRS III-IV-V and VI groups. Furthermore, the first-pass recanalization rate was significantly higher (p<0.05) in the MRS III-IV-V group than in the MRS 0-I-II group. No significant difference (p>0.05) was found in the first-pass recanalization rate between the MRS VI group and the MRS 0-I-II and III-IV-V groups (see Table 4).

Table 4. Comparison of MRS groups

			[1]MRS 0-I-II	[2]MRS III-IV-V	[3]MRS VI	p
Symptom puncture time	**Mean±SD**		256.6±178.9	237.3±156.7	240.4±179.2	0.910[K]
	Median		200.0	185.0	180.0	
Symptom recanalization time	**Mean±SD**		310.9±182.8	310.0±168.1	296.3±194.6	0.792[K]
	Median		230.0	262.5	225.0	
Puncture recanalization time	**Mean±SD**		54.0±18.6	71.9±37.5	52.3±20.3	0.062[K]
	Median		51.0	62.0	45.0	
Door imaging time	**Mean±SD**		18.8±17.3	20.2±12.3	18.4±13.5	0.327[K]
	Median		15.0	15.0	15.0	
Door TPA time	**Mean±SD**		49.9±19.7	59.9±19.7	46.1±24.8	0.061[K]
	Median		45.0	55.0	40.0	
Door puncture time	**Mean±SD**		55.5±16.7	62.0±20.3	54.8±17.0	0.246[K]
	Median		60.0	60.0	50.0	
TICI	**0**	**n (%)**	2 (2.2)	5 (20.8)	6 (26.1)	**0.000[X²]**
	II A	**n (%)**	2 (2.2)	4 (16.7)	1 (4.3)	
	II B	**n (%)**	22 (24.2)	6 (25.0)	7 (30.4)	
	II C	**n (%)**	12 (13.2)	6 (25.0)	4 (17.4)	
	III	**n (%)**	53 (58.2)	3[1] (12.5)	5[1] (21.7)	
First pass recanalization						
First pass	**n (%)**		59[2] (64.8)	23 (95.8)	18 (78.3)	**0.008[X²]**
Repeating	**n (%)**		32 (35.2)	1 (4.2)	5 (21.7)	

K Kruskal-Wallis (Mann-Whitney U test) / X² Chi-square test; [1]Difference with MRS 0-I-II group p<0.05, [2]Difference with MRS III-IV-V group p<0.05; MRS: Modified Rankin Scale, TPA: tissue plasminogen activator, TICI: treatment in cerebral ischemia

At the 24-hour mark, there were no significant differences (p>0.05) in symptom puncture time and symptom recanalization time between the groups with and without bleeding. Additionally, at 24 hours, the parameters of door imaging, door iv tPA, and door puncture value also did not exhibit significant differences (p>0.05) between the two groups. However, within the group that experienced bleeding at 24 hours, the TICI stage was significantly lower (p<0.05) compared to the group without bleeding. Furthermore, the MRS score at three months was significantly higher (p<0.05) in the bleeding group than in the non-bleeding group at the 24-hour assessment. Lastly, the tan score in the bleeding group at 24 hours was significantly lower (p<0.05) than that of the non-bleeding group (see Table 5).

Table 5. Comparison of groups with and without intracranial hemorrhage

		sICH (-)		sICH (+)		p
		Mean±SD/n (%)	Median	Mean±SD/n (%)	Median	
Symptom puncture time		248.1±176.3	180.0	256.3±171.5	197.5	0.609[m]
Symptom recanalization time		306.0±183.0	227.5	313.6±178.9	252.5	0.644[m]
Puncture recanalization time		57.6±24.3	57.5	54.9±23.7	54.5	0.398[m]
Door imaging time		17.6±13.5	15.0	22.9±20.5	15.0	0.127[m]
Door TPA time		50.4±19.3	45.0	53.8±28.3	45.0	0.961[m]
Door puncture time		56.3±18.0	60.0	57.1±16.4	56.5	0.877[m]
TICI	**0**	10 (10.5)		3 (7.1)		**0.000[X²]**
	IIA	3 (3.1)		4 (9.5)		
	II B	21 (21.8)		14 (33.3)		
	II C	15 (15.6)		7 (16.7)		
	III	47 (49.0)		14 (33.3)		
First pass recanalization	**First pass**	66 (68.0)		34 (82.9)		0.074[X²]
	Repeating	31 (32.0)		7 (17.1)		
3rd month MRS		1.6±0.0	1.0	3.2±1.0	2.0	**0.001[m]**

[m]Mann-Whitney U test / X² Chi-square test; sICH: symptomatic intracranial hemorrhage, TPA: tissue plasminogen activator, TICI: treatment in cerebral ischemia, MRS: Modified Rankin Scale

DISCUSSION

This study, conducted at a stroke center that has recently completed its first year of operation, presents novel insights into the relationship between treatment duration and perfusion achieved through endovascular recanalization.

In our study, the cohort of patients who underwent MT predominantly consisted of an elderly population, with a mean age of 69.5 years. The distribution of gender and the prevalence of comorbid conditions varied across the literature; in our study, the proportion of female patients was 45%, which was equal to that of male patients. The following comorbidities were observed: hypertension in 63% of patients, atrial fibrillation in 54%, coronary artery disease in 39%, diabetes in 21%, obesity in 27%, and a history of stroke in 19%. Additionally, 11% of the patients were receiving warfarin, while 17% were on newer generation oral anticoagulants (2-7).

In the study, the durations for door-imaging, door-TPA, and door-puncture were consistent with international quality guidelines as well as the timeline outlined in the quality guidelines published by the Ministry of Health (8,13-15). Compliance with these standards was achieved through frequent in-service training and tailoring emergency department operations to acute stroke management.

Teamwork, experience, and effective coordination are critical components in stroke centers. Chatterjee et al. (16,17) found that the density of the emergency department did not influence imaging and thrombolysis times for patients presenting with acute stroke. In contrast, Reznek et al. reported that increased crowding was associated with prolonged time from patient arrival to imaging. Furthermore, Arrate et al. demonstrated that stroke severity significantly impacted the time from arrival to imaging, identifying stroke severity as the primary determinant of patient management and care timelines (18). Additionally, another study indicated that patients with NIHSS scores ranging from 16 to 25 had a higher likelihood of completing the imaging procedure within 25 minutes, while patients with scores exceeding 25 experienced delays in imaging due to medical complications, such as loss of airway control (19). In our study, which categorized patients based on NIHSS scores of 0-5, 6-10, 11-20, and ≥21, we observed that the NIHSS score did not significantly affect the duration from the patient's presentation in the emergency department to the initiation of effective treatment, consistent with the findings of Sauser et al. (20). This result can be explained by the fact that the same procedures are applied to all patients in the emergency department in case of stroke rather than the severity of the stroke.

In previous studies, the impact of early reperfusion on favorable clinical outcomes has been established; however, due to the limitations associated with patient selection, there is a pressing need for larger, data-driven investigations (13-15,21). It has been observed that patients who undergo early revascularization tend to exhibit improved functional outcomes. Specifically, a shorter duration of vessel occlusion is associated with fewer sequelae, which may contribute to enhanced patient outcomes (22-26). In our study, the time to symptom recanalization did not show a significant difference among the MRS groups 0-I-II, III-IV-V, and VI. Nevertheless, a significant correlation was identified between the modified TICI score and both clinical outcomes and successful recanalization. Furthermore, our findings indicated that the incidence of symptomatic intracranial hemorrhage was significantly lower in patients demonstrating good recanalization, underscoring the critical importance of effective endovascular treatment over merely early intervention. Additionally, consistent with existing literature, the MRS scores were higher, and the tan scores were significantly lower in the hemorrhagic group compared to the non-hemorrhagic group, suggesting that multiple factors influence favorable clinical outcomes (27,28).

CONCLUSION

In our study, we did not identify a correlation between stroke severity and the quality-metric times observed in the emergency department. It is possible that different outcomes may emerge if studies are conducted with larger populations. A well-trained team and effective interdepartmental coordination are essential for more efficient and timely treatment of acute stroke. The coordination of all components within the neurology and emergency medicine departments, which is critical in the context of acute stroke, should be meticulously organized with respect to diagnosis and time management. Acute stroke patients should be treated quickly and effectively regardless of NIHSS intensity. There should be an experienced team and a standardized in-hospital procedure for acute stroke patients.

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