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Research Article,

Comparison of Treatment Methods in the Management of Acute Ischemic Stroke.

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Abstract:

Aim: Acute ischemic stroke is an emergency clinical condition that occurs as a result of acute intracranial arterial occlusion and neural tissue destruction. In this study, we aimed to evaluate the treatment outcomes in patients who were performed intravenous thrombolysis (IVT), mechanical thrombectomy (MT), or both.

Materials and Methods: In this retrospective study, 131 patients who underwent IVT, MT or both who has the diagnosis of AIS in our hospital between June 1, 2018, and February 1, 2019, were assessed. Age, sex, concomitant chronic diseases, NIHSS score, treatment-related complications, the time between disease presentation and hospital arrival, the duration of treatment, the one-month mortality rates and modified Rankin scores (MRS) were recorded. One-month mortality, NIHSS, and MRS were compared with treatment modalities and other factors.

Results: The mean age of 131 patients included in the study was 71.79±12.67. The MRS did not differ significantly in the groups with IVT, MT, and IVT+MT ($p > 0.05$). In the IVT and MT groups, the NIHSS score increased significantly after the treatment ($p < 0.05$). In the MT+IVT group, the NIHSS score after treatment did not change significantly ($p > 0.05$).

Conclusion: No significant relationship between mortality rates and MRS with treatment method was found. Complication rates were also not different among three treatment groups.

Key words: ischemic stroke, treatment, thrombolysis.

Introduction:

Acute ischemic stroke (AIS) is an emergency clinical condition that occurs as a result of acute intracranial arterial occlusion and neural tissue destruction. The incidence in the United States is 795000. Approximately 80% of stroke cases arise from ischemic stroke and hemorrhagic stroke accounts for 20% of the cases. Stroke is the second most common cause of mortality in the world [1]. Treatment methods for ischemic stroke include intravenous or intraarterial thrombolysis and mechanical thrombectomy (MT)[1-3]. While mechanic thrombectomy is the standard endovascular treatment method that provides successful results in cases with large vessel occlusion, intravenous or intraarterial thrombolysis

may be applied in patients before MT or those whom MT is contraindicated[1, 4-6].

Other factors that affect treatment success in stroke cases can be listed as the time of treatment, age, concomitant other chronic diseases, localization of the occlusion vessel and length of the occluded arterial segment, treatment-related complications, and affected cerebral tissue volume [7-10]. The most appropriate treatment method should be selected, considering these factors. In this study, we aimed to evaluate the treatment outcomes in patients who were performed intravenous thrombolysis (IVT), MT, or both.

Materials and Methods:

Study design:

In this retrospective study, 137 patients who underwent IVT, MT or both who has the diagnosis of AIS in our hospital between June 1, 2018, and February 1, 2019, were assessed. Six patients were excluded due to lack of enough clinical information and transfer of the patient to a different health center due to their own request. Remaining 131 patients were included in the study. Local ethics committee approval was obtained before the study. Since the study was designed retrospectively, informed consent was not obtained from the patients.

Age, sex, concomitant chronic diseases, NIHSS score [11], and treatment-related complications were recorded. The time between disease presentation and hospital arrival and the duration of treatment also noted. The one-month mortality rates and modified Rankin scores (MRS)[12] were obtained six months after the treatment by telephone. MRSs of the patients with mortality were noted as six. One-month mortality, NIHSS, and MRS were evaluated with treatment modalities and other factors.

Diagnosis:

In addition to clinicaal findings, radiologic imaging methods were used in diagnosis. CT and CT angiography were used in the patients who arrived in first three hours. Diffusion MRI, MR angiography and perfusion MRI is performed in the cases who arrived between 3-4.5 hours after the first onset of the clinical symptoms. Diffusion-perfusion mismatch was used to assess penumbra.

Treatment

In the treatment of IVT, 0.9 mg/kg tissue plasminogen activator (TPA) with a maximum dose of 90 mg was used. The 10% of the total dose was given as intravenous bolus and remaining dose was given in infusion over one hour. All MT procedures were performed under general anesthesia via femoral artery approach using Solitaire stent retriever.

Statistical Analysis

In the statistical analysis, IBM SPSS 22.0 (Armonk, New York) software was used. Mean, standard deviation, median, maximum, minimum, frequency, and ratio values were used in descriptive statistics of the numeric data. The distribution of numeric variables was evaluated by the Kolmogorov Smirnov test. Kruskal-Wallis, Mann-Whitney U test was used to compare the independent quantitative data between the groups. For the analysis of independent qualitative data, the chi-square test was used. Fischer's exact test was used when chi-square test conditions were not met. In cases where the p-value was less than 0.05 in a 95% confidence interval, the results of statistical analysis were considered as significant.

Table 1. Descriptive data of the patients-I

		number and percentage	
Age	≤ 65	37	28.2%
	65	94	71.8%
Gender	female	52	39.7%
	male	79	60.3%
Concomitant chronic diseases	absent	16	12.2%
	present	115	87.8%
ICH		56	42.7%
HT		91	69.5%
DM		33	25.2%
Previous stroke		26	19.8%
Other		25	19.1%
Disease presentation			
Speech disorder		98	74.8%
Right hemiparesis		56	42.7%
Left hemiparesis		67	51.1%
Other		6	4.6%
The time between disease onset and hospital arrival			
Less than 1 hour		23	17.6%
1-2 hours		73	55.7%
2-3 hours		26	19.8%
More than 3 hours		9	6.9%
The duration of treatment			
	1 hour	14	10.7%
	2 hours	65	49.6%
	3 hours	36	27.5%
	4 hours	16	12.2%

Results:

Descriptive data:

The mean age of 131 patients included in the study was 71.79±12.67. The minimum and maximum ages were 39 and 96, respectively. In the patients, 52 (39.7%) were female, and 79 (60.3%) were male. There were no known chronic diseases in 16 patients, ICH in 56 patients, HT in 91 patients, DM in 33 patients, and history of a previous stroke in 26 patients. Of the patients, 98 patients (74.8%) presented with a speech disorder, 56 patients (42.7%) with right hemiparesis, 67 patients (51.1%) with left hemiparesis, and six patients (4.6%) with other neurological symptoms. IVT was performed in 71 patients, MT in 21 patients, and both in 39 patients. Descriptive data of the cases are summarized in Table 1 and Table 2.

Table 2. Descriptive data of the patients-II

		Minimum/ Maximum	Median	Mean±standard deviation
MRS		0/6	4	3.52±2.18
NIHSS				
Pre-treatment		4/24	14	13.2±5.6
Post-treatment		0/115	10	11.5±11.3
Tension				number / Percentage
Normal (<120/80 mmHg)				34 / 26%
Grade I (130-139/80-89 mmHg)				36 / 27.5%
Grade II (>140/90 mmHg)				61 / 46.6%
Complication	Absent			113 / 86.3%
	Present			18 / 13.7%
One-month mortality	Present			33 / 25.2%
	Absent			98 / 74.8%

Relationship between treatment methods and clinical informations:

Distribution of age and gender of patients with IVT, MT, and both did not differ significantly (p> 0.05). Also, there was no significant difference among these groups (p> 0.05) in the presence of any accompanying chronic disease and the presence of ischemic cardiac disease (ICH), hypertension (HT), diabetes mellitus (DM), and history of previous stroke. There was no significant difference in the time between disease presentation and patient arrival between the groups (p> 0.05). The duration of treatment was significantly shorter in the MT group than in the IVT and MT+IVT groups (p = 0.043). There was no significant difference in the time between disease presentation and patient arrival between IVT and IVT+MT groups (p> 0.05) (Table 3).

Table 3. Relationship of clinical findings with treatment methods.

		IVT	MT	IVT+MT	p
		Number and percentage	Number and percentage	Number and percentage	
Age	≤ 65	20 / 28.2%	7 / 33.3%	10 / 25.6%	0.819
	65	51 / 71.8%	14 / 66.7%	29 / 74.4%	
Gender	Female	27 / 38%	9 / 42.9%	16 / 41%	0.905
	Male	44 / 62%	12 / 57.1%	23 / 59%	
Concomitant chronic diseases	Absent	9 / 12.7%	1 / 4.8%	6 / 15.4%	0.980
	Present	62 / 87.3%	20 / 95.2%	33 / 84.6%	
ICH		27 / 38%	9 / 42.9%	20 / 51.3%	0.405
HT		52 / 73.2%	15 / 71.4%	24 / 61.5%	0.434
DM		19 / 26.8%	5 / 23.8%	9 / 23.1%	0.902

Previous stroke		15		21.1%		5		23.8%		6		15.4%	0.681
Other		12		16.9%		7		33.3%		6		15.4%	0.190
Disease presentation													
Speech disorder		52		73.2%		17		81%		29		74.4%	0.772
Right hemiparesis		30		42.3%		12		57.1%		14		35.9%	0.282
Left hemiparesis		37		52.1%		8		38.1%		22		56.4%	0.389
Others		4		5.6%		0		0%		2		5.1%	p>0.05
The time between disease onset and hospital arrival													
Less than 1 hour		13		18.3%		5		23.8%		5		12.8%	0.277
1-2 hours		35		49.3%		12		57.1%		26		66.7%	
2-3 hours		17		23.9%		3		14.3%		6		15.4%	
More than 3 hours		6		8.5%		1		4.8%		2		5.1%	
The duration of treatment	1 hour	6		8.5%		6		28.6%		2		5.1%	**0.019**
	2 hours	33		46.5%		11		52.4%		21		53.8%	
	3 hours	19		26.8%		3		14.3%		14		35.9%	
	4 hours	13		18.3%		1		4.8%		2		5.1%	

Outcome comparisons:

The MRS did not differ significantly in the groups with IVT, MT, and IVT+MT (p> 0.05). In the MT group, pre-treatment and post-treatment NIHSS scores were significantly higher than IVT and IVT+MT groups (p <0.05). In the IVT+MT group, pre-treatment NIHSS score was significantly higher than the IVT group (p <0.05). There was no significant difference between IVT and MT+IVT groups after treatment (p> 0.05). In the IVT group, the NIHSS score increased significantly (p <0.05) after the treatment. In the MT group, the NIHSS score showed a significant increase after treatment (p <0.05). In the MT+IVT group, the NIHSS score After treatment did not change significantly (p> 0.05) (Table 4).One-month mortality rates did not differ significantly among groups (p> 0.05) (Table 4).

Complications:

Intracranial hemorrhage was occurred as a complication in 17 of the patients. Out of these patients, two patients were in MT, six patients were in IVT, and nine patients were in MT+IVT groups. In one patient in the MT groups, the occluded segment recanalization was unsuccessful. Complication rates did not differ significantly among groups (p> 0.05) (Table 4).

Table 4. Comparison of applied treatment method with clinical outcome and complications.

		IVT	MT	IVT+MT	p values (comparison between groups)
		mean±standard deviation	mean±standard deviation	mean±standard deviation	
MRS		3.2±2.2	4±2.2	3.9±2	0.243
NIHSS					
Pre-treatment		10.6±5	18.2±3.7	15±5.2	**<0.001**
Post treatment		8.5±5.9	13.8±6.9	16±17.6	**<0.001**
p value (comparison in groups)		**<0.001**	**0.002**	0.057	
		number and percentage	number and percentage	number and percentage	
Complications	Absent	65 91.5%	18 85.7%	30 76.9%	0.102
	Present	6 8.5%	3 14.3%	9 23.1%	
One-month mortality	Present	16 22.5%	7 33.3%	10 25.6%	0.604
	Absent	55 77.5%	14 66.7%	29 74.4%	

Discussion:

Ischemic stroke is one of the leading diseases in morbidity and mortality, and rapid treatment is vital to avoid irreversible neurological damage. For this purpose, thrombolysis with an intravenous or intraarterial application and MT as a vascular interventional procedure are essential in the treatment. According to the results of this study, there was a statistically significant decrease in NIHSS score after the treatment in patients who had only intravenous thrombolytic therapy and who had MT only. However, NIHSS score increased after the treatment when thrombectomy and thrombolytic therapy were applied together, but it was not statistically significant. When the post-treatment NIHSS scores were compared among groups, NIHSS score was found to be significantly lower in patients who had only intravenous thrombolytic therapy than those who had only MT or combined thrombolytic therapy with MT.

MT is known to cause serious complications such as dissection and vascular perforation. In animal experiments, it is shown that MTis more successful in achieving recanalization of occluded arterial segments with a length of 10 mm or less [7]. In the MERCI trial, MT was performed in patients who did not benefit from IVT and was not eligible for intravenous TPA, and there was no significant difference in the complication of intracranial hemorrhage between the groups. It was reported that MT was safe after intravenous TPA use [13]. In the THRACE trial, 26 patients of proximal cerebral artery occlusion performedMTwith or without IVT were evaluated. Although there was no significant difference in the three-month mortality between the two groups, the rate of achieving functional independence was significantly higher in patients who underwent both treatments of intravenous thrombolytic and MTafter three months[6].

There are some studies reported in the literature which shows no statistically significant differences in mortality and post-treatment NIHSS scores between IVT and MT [1-4]. In two reported studies, IVT and MT were compared, and no significant difference was found in three-month mortality. However, the rate of early recanalization and early major improvement was higher in patients with MT. No significant difference was found between the groups in the procedure-related complication rate [14-15]. However, recent studies have shown that MT is more successful than intraarterial and IVT by shortening the recanalization time [7, 16, 17]. On the other hand, studies are showing more successful results in cases where intravenous thrombolytic and MT are applied together [2, 3, 18, 19]. Although contradictory results are observed in the literature on this subject, in a metanalysis, it has been mentioned that endovascular stroke treatment has not been successful in IMS III [20], MR RESCUE [21], and SYTHESIS Expansion [22] studies. However, large vessel occlusion has not been evaluated before the treatment, and modern endovascular thrombectomy devices have not been used in these trials. On the other hand, MR CLEAN [23], ESCAPE [24], EXTEND-IA [25], SWIFT PRIME [26], REVASCAT [21], THERAPY [27], and THRACE [28] studies showed that MT is useful in the treatment of AIS, and it should be included in patient management as a standard in modern stroke treatment [4]. In this study, one-month mortality and IVT at sixth month were evaluated and no significant difference was found in cases where IVT, MT and both were used. Another controversial issue in the literature is the use of IVTbeforeMT, called bridging therapy. It is reported that bridging therapy does not increase the complication rate during MT [29]. In this study, no increase in complication rate was observed in patients treated with IVTbeforeMT. The effect of bridging therapy on treatment success is also controversial, and some studies are showing that there is no significant effect on treatment response[29] and others are showing that it contributes positively to the success of MT procedure, as well[5]. Mortality, NIHSS score before and after the procedure and Rankin score at the sixth month were not statistically significantly different in patients who underwent bridging therapy and in patients who had MTalone in this study. The time from the onset of symptoms to the application of treatment is also crucial for treatment success. In a prior study, patients who underwent MT before and after 60 minutes were compared, and the IVT and complication rates were found to be lower in patients who underwent early MT [9]. There are some limitations in our study. First, the clinical scores and mortality of the patients such as Rankin and NIHSS were compared with treatment options, not the development of recanalization. Another limiting factor is that the cases were not randomly distributed, and the study was designed retrospectively. Besides, large vessel occlusion was not evaluated in this study, which may affect the results. In conclusion, when evaluated with the

literature, we know that in AIS cases, medical treatments such as IVT as well as endovascular treatment methods constitute the only treatment methods we have in the AIS treatment. To prevent irreversible neural parenchymal damage, it is essential to use these treatments alone or together in accordance with patients' clinical situation [30]. In our study, although there was no significant difference in mortality rates in patients who had IVT, MT and combined treatment, the lower post-treatment NIHSS score of the patients with thrombolytic therapy compared to those with MT and combined therapy may indicate the superiority of the MT treatment.

Data Availability:

The SPSS/Excel data are used to store the findings of this study. Data are available from Ertugrul Altinbilek, Department of Emergency Medicine, University of Health Sciences Sisli Etfal Training and Research Hospital, Istanbul, Turkey. Please mail us on ertugrulaltinbilek@gmail.com for researchers who meet the criteria for access to confdential data.

Conflicts of Interest:

The authors declare that they have no conflicts interests.

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