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Original Article

Evaluation of Door-to-Needle Stroke Patients With Thrombolytic Activation Code in Imam Reza Educational Center in Tabriz

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Abstract

Objectives: To investigate the therapeutic process and golden times for treating stroke patients receiving thrombolytic therapy at Imam Reza Hospital in Tabriz.

Design: A cross-sectional descriptive study.

Setting(s): The information for all patients entering the study was extracted from the stroke registry of the Neurosciences Research Center.

Participants: Participants comprised all patients who were referred to Imam Reza Hospital emergency department (ED) in 2018, hospitalized as stroke patients, and had an indication for receiving thrombolytic therapy.

Outcome measures: Data included demographic information, length of stay in the ED, time interval from the onset of symptom to ED arrival, time to CT scan, time to the start of thrombolytic therapy, outcomes (e.g., discharge, hospitalization, or death), and the use of tissue plasminogen activator (tPA) therapy.

Results: A total of 140 patients were studied, with a mean and median age of 66.19 ± 12.68 and 67.5 years, respectively. The mode age was 73 years, with the maximum age being 91 years and the minimum age being 34 years. Moreover, 82 (58.6%) of patients were male, and 58 (41.4%) were female. The mean time interval from ED arrival to the start of thrombolytic injection was 54.49 ± 27.42 minutes, with a median and mode of 51 and 60 minutes, respectively. The minimum time was 17 minutes, and the maximum time was 218 minutes. The modified ranking scale (mRS) score at 7 days was significantly related to the National Institutes of Health Stroke Scale (NIHSS) at arrival, NIHSS 36 hours after treatment, NIHSS at 7 days after treatment, the incidence of intracerebral hemorrhage, and hospitalization duration ($P \leq 0.001$).

Conclusions: Initiating thrombolytic injection within 60 minutes is feasible, and patients' status 7 days after discharge has a significant relationship with NIHSS at arrival, NIHSS 36 hours post-treatment, and NIHSS 7 days post-treatment. Moreover, there is a significant correlation between mRS at 7 days and an interval of less than 60 minutes from ED arrival to the start of thrombolytic injection. In such cases, mRS is lower.

Keywords: Workflow, Stroke, Thrombolytic therapy

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Introduction

Brain vessel diseases are the third leading cause of death after cardiac diseases and cancers in the United States. They are also the most common neurologic disorders causing morbidity and death.[1,2] The term "brain vessel disease" is defined as any kind of brain abnormality resulting from blood vessel damage, with three main processes: vessel thrombotic obstruction, vessel embolic obstruction, and vessel rupture.[1]

Given that brain stroke is a leading cause of mortality in society, studying factors that contribute to the prevention and early recognition of people at risk helps reduce its incidence.[3] Early identification of patients in the emergency department (ED) and rapid determination of their treatment process can reduce the effects and duration of their stay in the ED, decreasing treatment costs, the burden on the hospital, and the emergency rush.[4] Therefore, we conducted this study to investigate

the therapeutic process and golden times for treating stroke patients receiving thrombolytic therapy at Imam Reza Hospital in Tabriz.

Methods

Study Design and Data Collection

This is a randomized antegrade follow-up study, with a descriptive nature. It began after being approved by the research committee of the Medical Sciences Faculty at Tabriz University and the state Ethics Committee of the university.

Inclusion and Exclusion Criteria

All stroke patients referred to the ED of Imam Reza Hospital in Tabriz who had thrombolytic therapy indications were included in the study. Exclusion criteria included patients with malignancies, patients experiencing trauma, patients presenting with any symptoms other than stroke, patients with any contraindications for thrombolytic therapy (e.g., active bleeding, hemorrhagic stroke, and coagulopathy), and patients or their representatives unwilling to receive thrombolytic therapy.

Data and Checklist

For all patients entering the study, the following data were recorded: demographic information, length of stay in the ED, time interval from the symptom onset to ED arrival, time to CT scan, time to the start of thrombolytic therapy, outcomes (e.g., discharge, hospitalization, or death), and use of tissue plasminogen activator (tPA) therapy. All information was extracted from the stroke registry of the Neurosciences Research Center.

Data Analysis

Collected data were analyzed using IBM SPSS statistic version 24, with a significance level set at $P \leq 0.05$. The data were entered into the SPSS 15.0 statistical system. Descriptive statistical method (i.e., mean, median, mode, and standard deviation) was used for and for descriptive data. Pearson correlation was used for assessing the correlation between quantitative data, and logistic regression was used for evaluating the correlation between qualitative and quantitative data.

Results

A total of 140 patients were studied, with a mean age of 66.19 ± 12.68, a median age of 67.5 years, and a mode age of 73 years. The maximum age was 91 years, and the minimum age was 34 years. Furthermore, 82 (58.6%) patients were male, and 58 (41.4%) were female. The mean time interval from the symptom onset to ED arrival was 109.65 ± 52.83 minutes, with a median and mode time of 102 minutes and 138 minutes, respectively. The maximum and minimum time was 240 and 24 minutes, respectively. The mean time interval from ED arrival to activating the SAMA code was 4.23 ± 11.2 minutes, with a median and mode of 2 minutes, a minimum time of 1 minute, and a maximum time of 240 minutes. Moreover, the mean time interval from ED arrival to doing a spiral brain CT scan was 26.59 ± 36.05 minutes, with a median of 16 minutes, a mode of 13 minutes, a minimum time of 5 minutes, and a maximum time of 227 minutes. Additionally, the mean interval time from ED arrival to thrombolytic injection was 54.49 ± 27.42 minutes, with a median of 51 minutes, a mode of 60 minutes, a minimum time of 17 minutes, and a maximum time of 218 minutes.

The mean time interval from symptoms onset to starting thrombolytic therapy was 164.51 ± 50.35 minutes, with a median of 170 minutes, a mode of 120 minutes, a minimum of 75 minutes, and a maximum time of 236 minutes. Furthermore, mean hospitalization duration was 12.52 ± 12.21 days, with a median of 9 and a mode of 8 days. The minimum time was 3 days, and the maximum was 87 days. In addition, the highest thrombolytic injection rate was in June and July (Table 1).

Out of the 140 patients studied, 10 patients died in the hospital. Two of them died from brain hernia, one from a brain hemorrhage, three from pneumonia, one from a heart attack and renal failure combined, one from another brain stroke, one from hernia following a brain hemorrhage, and one from tamponade following digital subtraction angiography. In addition, 12 patients had asymptomatic hemorrhage (8.6%), and 10 had symptomatic hemorrhage (7.1%). The classification of brain hemorrhage according to the European Cooperative Acute Stroke Study (ECASS) is presented in Table 2.

Patients' mean arrival NIHSS was 13.64 ± 6.30, with a median of 13, a mode of 11, a minimum score of 1, and a maximum score of 29. The mean NIHSS for patients 36 hours after treatment was 11.24 ± 9.03, with a median of 9, a mode of 5, a minimum score of 0, and a maximum score of 40. Patients' modified ranking scale (mRS) scores 7 days after treatment are illustrated in Table 3.

After seven days, mRS had a significant correlation with initial NIHSS scores, NIHSS scores 36 hours and 7 days after treatment, brain hemorrhage occurrence, and hospitalization time ($P \leq 0.001$). There was no significant

Table 1. Distribution of Thrombolytic Injection in Different Months

Month	Frequencies	Percent
April	13	9.3
May	8	7.5
June	11	7.9
July	19	13.6
August	13	9.3
September	9	6.4
October	10	7.1
November	12	8.6
December	10	7.1
January	13	9.3
February	9	6.4
March	13	9.3

Table 2. Brain Hemorrhage Frequency According to ECASS

Type	Frequency	Percent
No. Hemorrhage	118	84.3
HI1	5	3.6
HI2	3	2.1
PH1	4	2.9
PH2	9	6.4
PH3	1	0.7

Note. ECASS: European cooperative acute stroke study.

Table 3. Patients' mRS After 7 Days

mRS	Frequency	Percentage
0	18	12.9
1	11	7.9
2	18	12.9
3	22	15.7
4	30	21.4
5	26	18.6
6	7	5
Unknown	8	5.7

Note. mRS: Modified ranking scale.

relationship between the 7-day mRS scores and the time intervals from the ED arrival to injection or symptom onset to injection.

The reasons for the delayed thrombolytic injection were a delay in signing consent by a deputy in two patients, triage error in diagnosis in one case, and emergency medical services (EMS) failure to inform the hospital in one case. Patients who received thrombolytic injections within 60 minutes had significantly lower mRS scores after 7 days compared to those receiving injections after more than 60 minutes ($P=0.048$). However, this does not imply that delays in imaging do not affect patient outcomes as prolonged times can increase the patient's door-to-needle (DTN) time over 60 minutes, which can exacerbate patient outcomes.

Discussion

Sadeghi-Hokmabadi and colleagues' study indicated a significant decrease in door-to-CT (DTC) time in the post-intervention period, which involved performing CT scans and tests for stroke patients immediately upon hospital entry, preparing ICU beds for them, and training nurses exclusively for dealing with stroke patients. In this study, the median DTC time has decreased from 75 minutes to 20 minutes for stroke patients, and the mean DTN time (time interval between the patient's arrival to the hospital and injection of thrombolytic for stroke patients) was 55 minutes in the post-intervention period. Interventions carried out by Sadeghi-Hokmabadi et al decreased DTC time significantly and result in reasonable DTN. These interventions are possible in most hospitals and should be considered for implementation in hospitals.[5] In our study, the interval from ED arrival to injection was under 60 minutes.

Sadeghi-Hokmabadi et al also found that the mean DTC time for the pre-Hospital Notification (PHN) group (the group informed to hospital by EMS) was 6 minutes longer than that for the non-PHN group, which was statistically significant. The result of the study revealed that simple and short training classes for EMS staff and the implantation of PHN by EMS directly calling a neurologist effectively reduced DTC and DTN times for stroke patients.[6] In our study, there was a delay in treatment when EMS did not inform the hospital, while in most cases informed by EMS, the time to start injection was shorter.

A study by Tai et al showed that despite significant improvements in NIHSS scores after thrombolysis of patients with activated stroke code, there was no significant difference in mRS scores at discharge. This can suggest that decreasing the time of the treatment start, both before and after stroke code activation, may not change the classification of patients based on NIHSS and mRS scales. Most patients in this study were treated within 3-4.5 hours, likely because of different patient selection criteria in 3-4.5 hours after coincidence. Although IV-tPA is useful for up to 4.5 hours, this study showed that quick access protocols such as activating a stroke code decrease DTN time and probably increase the use of IV-tPA. However, further studies are needed to create protocols that minimize treatment delay.[7]

In our study, there was no statistically significant correlation between the time from ED arrival to fibrinolytic injection and the one-week mRS scores, but the reduction of this gap can prevent passing golden time (4.5 hours), allowing more patients to receive thrombolytic therapy. This is important for comparing these patients to those who did not receive thrombolytic therapy. Our study suggests that efforts to shorten DTN time focus on increasing the number of patients in the fibrinolytic-receiving group rather than directly reducing their mRS scores. However, one-week mRS outcomes are clearly associated with NIHSS scores at arrival. The study by Sauser K indicated that the door-to- imaging (DTI) time and imaging–to-needle (ITN) time play a significant role in reducing DTN time and are common causes for delaying tPA therapy in acute ischemic brain stroke patients. Therefore, improving ITN time should be an important objective for improving DTN time for thrombolysis in these patients.[8] In our study, the average DTI was 15 minutes, which should be reduced.

In addition, the results of the study by Fonarow et al displayed that lower DTN times for tPA injection are associated with better outcomes in acute ischemic stroke patients. A cross-sectional analysis of 25504 patients with ischemic stroke who received tPA within 60 minutes of arrival at ED showed a significant reduction in-hospital mortality and intracerebral hemorrhage compared to those who received tPA more than 60 minutes after arrival.[9,10]

Conclusions

In our study, patients with a DTN time of less than 60 minutes had significantly lower mRS scores after one week compared to those with a DTN time of more than 60 minutes. However, patients with a DTI of less than 10 minutes did not show significantly different mRS scores one week later compared to patients with a DTI time of more than 10 minutes ($P=0.558$). Nevertheless, this does not imply that prolonged imaging has no effect on outcomes as the total delay can increase DTN time to over 60 minutes, which has negative effects on patient outcomes.

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Data availability statement

Data gathered for the study are available from the corresponding author upon reasonable request.

Ethical approval

Ethical approval was obtained from the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1398.849).

Consent for publication

All authors accept and permit to publish this study

Conflict of interests

The authors declare that they have no conflict of interests.

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