Factors Affecting Length of Stay in a Stroke Unit After Intravenous Thrombolytic Therapy: A Retrospective Study

İntravenöz Trombolitik Tedavisi Sonrası İnme Ünitesinde Kalış Süresini Etkileyen Faktörler: Retrospektif Bir Çalışma

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ABSTRACT

Objectives: This study aimed to examine the hospitalization duration in the stroke unit after IV thrombolytic therapy in acute ischemic stroke and the affecting factors.

Methods: The research was designed as a retrospective study. From 334 patients admitted to a state hospital in Istanbul's stroke unit with a stroke diagnosis, 152 patients who received IV thrombolytic therapy constituted the study's sample. The hospital registry system, nurse observation notes, and patient files in the hospital archive were examined by the researcher to access the patients' socio-demographic and clinical data. Pearson correlation analysis was used to analyze the relationships between parameters conforming to a normal distribution, along with descriptive statistical methods.

Results: The mean length of stay in the stroke unit was 3.2±3 days(2). Complications developed in 44.1% (67) of the patients during hospitalization. Among these complications, respiratory-related complications were the highest at 19.5% (13), followed by cerebral hemorrhage and cerebral edema at 18% (12). The most common reason for transferring patients was routine transfer at 82.3% (125). A statistically significant positive correlation was found (r=0.261; p<0.05) between the duration of stay in the stroke unit and the severity of the stroke. A positive (r=0.026; p<0.05) relationship was found between the stroke unit stay duration and the patient's age, and a negative relationship (r=-0.220; p<0.05) was found with the Glasgow Coma Scale before IV thrombolytic therapy.

Conclusion: Short hospital stays and low mortality rates demonstrate the benefit of close observation of IV tPA patients. Complication development during stroke unit stay, stroke severity, age, as well as history of smoking and alcohol use in patients receiving IV thrombolytic therapy affect the length of hospital stay.

Keywords: Acute ischemic stroke; Intravenous thrombolytic therapy; Length of stay.

ÖZET

Amaç: Bu çalışmada, akut iskemik inmede IV trombolitik tedavi sonrası inme ünitesinde yatış süresi ve etkileyen faktörler incelenmiştir.

Yöntem: Retrospektif tipinde tasarlanan bu çalışmada, İstanbul'da bir devlet hastanesinin inme ünitesine inme tanısı ile kabul edilen 334 hastadan IV trombolitik tedavi uygulanan 152 hasta örneklemi oluşturmuştur. Hastaların sosyodemografik ve klinik verilerine erişmek için hastane kayıt sistemi, hemşire gözlem notları ve hastane arşivindeki hasta dosyaları araştırmacı tarafından incelenmiştir. Normal dağılıma uygun parametreler arasındaki ilişkiler Pearson korelasyon analizi ile analiz edilmiş; tanımlayıcı istatistiksel metodlar kullanılmıştır.

Bulgular: İnme ünitesindeki ortalama yatış süresi 3.2±3(2) gün olarak bulunmuştur. Hastalarda yatış sürecinde %44.1 (67) oranında komplikasyon gelişmiştir. Bu komplikasyonlar arasında solunumla ilişkili komplikasyonlar %19.5 (13) ile en yüksek oranda olup, bunu beyin kanaması ve beyin ödemi %18 (12) takip etmiştir. Hastaların transfer edilme sebepleri arasında en sık rastlananı %82.3 (125) ile rutin transfer olmuştur. İnme ünitesinde kalış süresi ile inme şiddeti arasında pozitif yönlü bir korelasyon (r=0.261; p<0.05) bulunmuştur. Ayrıca, inme ünitesinde kalış süresi ile hastanın yaşı arasında pozitif bir ilişki (r=0.026; p<0.05) ve IV trombolitik tedavi öncesi Glasgow Koma Skalası ile negatif bir ilişki (r=-0.220; p<0.05) tespit edilmiştir.

Sonuç: IV tPA hastalarının yakın gözlemi sayesinde kısa hastanede kalış süreleri ve düşük ölüm oranları elde edilmiştir. IV trombolitik tedavi alan hastalarda inme ünitesinde kalış süresi boyunca komplikasyon gelişimi, inme şiddeti, yaş, sigara ve alkol kullanımı gibi faktörler hastanede kalış süresini etkilemektedir.

Anahtar sözcükler: Akut iskemik inme; İntravenöz trombolitik tedavi; Kalış süresi.

Stroke is defined by the World Health Organization as "a disease lasting longer than 24 hours or leading to death, typified by rapidly developing signs of focal cerebral dysfunction".[1] Stroke is a common cause of disability and death with a significant influence on the population of the world and is a major global health problem.[2-4] According to 2018 data, 22.4% of deaths in Türkiye were caused by stroke, which ranks second among the causes of death.[5] Ischemic and hemorrhagic are two types of stroke. It is known that 87% of stroke patients in the United States are of ischemic origin.[6]

Acute treatment of ischemic stroke is important for the prevention of many complications, including disability and death.[7] In the acute period, intravenous thrombolytic therapy (intravenous tissue plasminogen activator - IV tPA) is widely used and provides significant improvement.[8,9] Tissue plasminogen activator is administered as a fibrinolytic, IV bolus followed by infusion within 4.5 hours of the stroke symptoms onset in the treatment of recombinantly produced ischemic stroke. It shows its effect by providing the conversion of plasminogen to plasmin and dispersing the thrombus with the fibrinolytic property of plasmin.[6,10] For this reason, because of the symptomatic intracranial bleeding risk, IV tPA treatment requires close monitoring about 24 hours after treatment.[11] This follow-up should be done in units developed specifically for stroke patients. Stroke units use a multidisciplinary approach in the application of a variety of functions such as bedside monitoring, physical therapy practices, evaluation of swallowing and nutritional status, and appropriate tests for secondary stroke prophylaxis in the acute period.[12] It has been stated that the application of stroke treatment in stroke units contributes significantly to providing effective treatment and care management, providing early treatment, reducing the rate of mortality and shortening the length of hospital stay (LOS).[4,8,13,14] Although the determination of LOS due to stroke is an important indicator of the care quality, the prolongation of LOS increases the risk of complications in patients, delayed mobilization, and deterioration of patient mental health.[15-17] Prolongation of LOS may also be an indicator of poor prognosis and mortality.[18,19] It has been reported that LOS after ischemic stroke is affected by several factors such as socio-demographic characteristics, stroke severity, and chronic diseases.[1,17,20] Knowing which stroke patients will receive long-term inpatient treatment is important both for the treatment and care process and for responding to the emotional expectations of patients and families.[20,21] It is not known to what extent the factors reported to affect LOS in acute ischemic stroke affect the average length of stay. It is thought that the determination of these rates will contribute to the planning and meeting of treatment, care, rehabilitation, and discharge needs, including the psychological needs of acute stroke patients, and will also significantly affect the cost of treatment and care.[1,22]

Since a few studies are available examining the factors affecting the duration of hospital stay after IV tPA in Türkiye, this study would make a significant contribution to the literature. In this study, the aim was to examine the stay duration in the stroke unit and the affecting factors of patients with acute ischemic stroke treated with IV tPA.

Research Questions

- What is the hospital stay length for stroke patients receiving IV tPA treatment?

- Is there an association between the length of stay of stroke patients receiving IV tPA treatment and socio-demographic and clinical characteristics?

Methods

For this retrospective, single-center study, scientific research permission was obtained from the Fatih Sultan Mehmet Training and Research Hospital of the University of Health Sciences

(decision 17073117-050.06) and was conducted in accordance with the requirements of the Declaration of Helsinki. This retrospective study was conducted with 152 patients out of a total of 334 patients who met the inclusion criteria, were treated with IV tPA, and hospitalized with the acute ischemic stroke diagnosis in the stroke unit of a state hospital in Istanbul between January 2017 and December 2019.

The study included patients admitted to the emergency department with a pre-diagnosis of stroke or were referred to the hospital where the study was conducted with a pre-diagnosis of stroke from an external center. Generally, patients who are pre-diagnosed with stroke by emergency physicians during admission are consulted by neurologists. Along with a rapid neurological examination, blood samples are taken for hematology tests and biochemical analysis. Vital signs (oxygen saturation, body temperature, pulse, blood pressure, respiratory rate) are checked, the patient is monitored, and the capillary blood sugar level is measured. The definitive diagnosis of the patient is made using magnetic resonance (MR) or computerized tomography (CT) imaging of the brain. After considering the time elapsed from the stroke symptoms onset, the maximum benefit from the treatment, and the approval of the patient or their relatives, the type of treatment is quickly decided. Patients who will be treated with IV tPA are quickly transferred to the stroke unit from the emergency department. These patients are prepared for IV tPA treatment. This preparation includes patient monitoring and insertion of a bladder tube (BT) and nasogastric tube (NGT) to monitor for post-treatment bleeding complications.

A stroke unit is the second-level neurology intensive care clinic of the hospital where IV tPA and/or mechanical thrombectomy treatment is applied and where patients are followed up for at least 24 hours. The stay length for the purpose of the present study was determined by calculating the time from the patient's admission to the stroke unit to their transfer to any clinic or discharge. The severity of the stroke was classified under the National Institutes of Health Stroke Scale Score (NIHSS) before, during, and after treatment. The NIHSS before IV tPA was used to express stroke severity.

Inclusion Criteria for the Study

- Having had an ischemic stroke for the first time,
- Having received the entire planned IV tPA treatment.

Exclusion Criteria from the Study

- Having a previous neurological defect,
- Having had a transient ischemic attack,
- Having had a hemorrhagic stroke.

The study did not include patients with a history of previous ischemic stroke, which can affect the length of stay. Considering the socio-demographic data of the patients and the literature, a data collection form including variables related to ischemic stroke and length of stay was used. These variables included socio-demographic data such as patients' gender, age, marital status, alcohol use and smoking, chronic diseases, the presence of recent surgical procedures, the presence of complications during hospitalization, and the reason for transfer from the stroke unit. Clinical features such as the National Institutes of Health Stroke Scale (NIHSS) before, during, and after IV tPA, Glasgow Coma Score (GCS) before IV tPA, and stay length in the stroke unit were also included in the data collection.

As the research was retrospective in nature, the hospital registry system, nurse observation notes, and patient files in the hospital archive were examined by the researcher after obtaining necessary permissions to acquire the necessary socio-demographic and clinical data.

The IBM SPSS Statistics 22 (IBM SPSS, Türkiye) program was used to analyze the obtained data statistically. Along with descriptive statistical methods such as frequency, median, mean, and standard deviation, the Shapiro-Wilk test was used to evaluate the conformity of the parameters to the normal distribution. The Mann-Whitney U test was used to compare parameters with no normal distribution. The relationships between parameters conforming to the normal distribution were analyzed using Pearson correlation analysis. The relationships between the parameters not conforming to the normal distribution were analyzed using Spearman's rho correlation analysis. The significance level of statistical data was accepted as $p < 0.05$.

Results

Of the patients who underwent IV tPA, 50.7% were female and 49.3% were male. It was observed that 44.5% of the patients had a history of cigarette/alcohol use and 44.1% developed complications during hospitalization. Routine transfer was the most common reason for transfer from the stroke unit at 82.3%, while the other transfer reasons were distributed as seen in Table 1.

Table 1. Distribution of study parameters for patients who underwent IV tPA		
Sociodemographic Characteristics	(n=152)	%
Sex		
Female	77	50.7
Male	75	49.3
Marital status		
Married	86	56.6
Single	66	43.4
Presence of cigarette or alcohol use		
No	83	54.6
Cigarettes only	68	44.7
Cigarettes and alcohol	1	0.7
Alcohol only	0	0
Presence of chronic disease		
No	17	11.2
Yes	135	88.8
Presence of recent surgical procedures		
No	130	85.5
Yes	22	14.5
Presence of complications developing during hospitalization		
No	85	55.9
Yes	67	44.1
Transfer Reason		
Exitus (Death in stroke unit)	3	2.1
Need for surgical procedure/ 3rd level intensive care	23	15.4
Transfer to routine neurology service	125	82.3
Discharge	1	0.7
IV tPA (n=152)	**Min-Max**	**Mean±SD**
Age	35-94	70.9±13.31
IV tPA administration time (min)	60-270	176.45±57.6
Pre-NIHS score	2-27	8.79±4.76 (8)
Rank NIHS score	0-27	6.82±4.56 (5)
Post NIHS score	0-27	5.98±4.82 (5)
GCS before IV tPA	10-15	14.39±1.34 (15)
Length of stay (days)	0.5-23	3.2±3 (2)

The mean age of patients who underwent IV tPA was 70.9±13.31 years. The mean Glasgow Coma Scale (GCS) score before IV tPA was 14.39±1.34,[15] and the mean time (days) spent at the stroke unit was 3.2±3(2).

Complications developed in 67 of the patients who underwent IV tPA (44.1%). Considering the types of complications, respiratory-related complications were seen in 19.5%, cerebral hemorrhage in 18%, and death in 3% (Table 2).

Table 2. Distribution of complications during hospitalization in patients who underwent IV tPA		
Type of Complication	n	%
Acute kidney failure	4	6
Cerebral hemorrhage	12	18
Brain edema	12	18
Bleeding signs other than cerebral hemorrhage	9	13.5
Gastrointestinal system bleeding	5	7.5
Nose bleeding	2	3
Gum bleeding	2	3
Urinary tract infection (UTI)	4	6
Cardiac complications	5	7.5
Respiratory complications	13	19.5
Pneumonia	5	7.5
Acute respiratory failure	8	12
Death	3	4
Other (knee pain and swelling)	5	7.5

When the stay duration within the stroke unit according to the gender of those who underwent IV tPA was examined, no significant difference was observed (p>0.05). The duration of stay in the stroke unit for patients with cigarette-alcohol use was statistically significantly lower than those with no history of use (p<0.05). Additionally, the duration of stay was statistically significantly higher in patients who developed complications during hospitalization (p<0.05) (Table 3).

A significant and positive correlation was found between the duration of stay in the stroke unit and patient age (r=0.026; p<0.05). A significant and positive correlation was also seen between the duration of stay and the National Institutes of Health Stroke Scale (NIHSS) score before treatment (r=0.261; p<0.01). A significant and negative relationship was found between the duration of stay and the GCS score before IV tPA administration (r=-0.220; p<0.01) (Table 4).

Discussion

This study examined the duration of hospitalization in the stroke unit of acute ischemic stroke patients treated with IV tPA and the affecting factors. Identifying socio-demographic and clinical factors that prolong the stay length is valuable for healthcare planning and is important as it will help manage discharge planning by developing a simple evidence-based estimation equation.[23]

The study determined that, when the duration of hospital stay according to gender was examined, although women

Table 3. Comparison of the duration of stay in the stroke unite according to the sociodemographic and clinical characteristics of the patients who underwent TPA

Variables	n	Min-Max	Mean±SD (median)	p
Gender				
Male	75	0.5-20	3.04±2.86 (2)	0.329
Famele	77	0.5-23	3.36±3.15 (3)	
Marital status				
Married	86	0.5-23	3.11±3.45 (2)	0.083
Single	66	1-11	3.32±2.31 (3)	
Cigarette/Alcohol Use				
No	83	0.5-23	3.7±3.65 (3)	0.030*
Yes	69	0.5-11	2.59±1.82 (2)	
Presence of chronic disease				
No	17	1-4	2.18±1.13 (2)	0.116
Yes	135	0.5-23	3.33±3.14 (2)	
Presence of recent surgical procedures				
No	130	0.5-20	3.15±2.57 (2)	0.204
Yes	22	0.5-23	3.48±4.93 (2)	
Presence of complications during hospitalization				
No	85	1-6	2.48±1.19 (2)	0.048*
Yes	67	0.5-23	4.11±4.16 (3)	

Mann Whitney U Test; *p<0.05.

Table 4. Correlation between the duration of stay at the stroke unite and age, duration of IV tPA administration, NIHS score before, during and after IV tPA, GCS score of patients who underwent IV tPA

Variables	r	p
Age	0.181	0.026*
IV tPA administration time (min)	0.07	0.406
NIHS score before IV tPA+	0.261	0.001*
IV tPA Rank NIHS score+	0.155	0.056
Post IV tPA NIHS score+	0.146	0.074
GCS Score before IV tPA administration	-0.22	0.006*

Pearson Correlation Analysis; + Spearman Rho Correlation Analysis *p<0.05.

stayed in the hospital longer than men, no statistically significant difference was found between gender and length of hospital stay. This result is compatible with the literature.[1,18,24,25] Gaughan et al.[19] reported positive aspects of being married and the number of children in their study. However, as in the study of Majidi et al.,[1] the present study concluded that while hospitalization was longer for single patients, it was not statistically significant.

The stay duration in the stroke unit for patients with cigarette-alcohol use was statistically significantly lower. While

some studies[8,24,26] reported complications with smoking and prolongation of hospital stay, Appelros[27] stated that smokers might be motivated to access cigarettes more quickly. Thus, a shorter stay in the stroke unit for cigarette-alcohol/substance users may be related to this motivation.

88.8% of the patients in the present study had a history of chronic disease. There was no effect of the presence of chronic disease or the presence of a recent surgical procedure on the length of stay. Although it is known that the presence of chronic disease affects functional independence,[7,28] no significant relationship was found between the presence of major chronic disease and the length of stay, similar to the present study.[1,23,27]

Numerous studies have shown that the severity of stroke is the most important condition affecting both the acute period and the overall length of hospital stay.[1,7,25,27,28] According to the present findings, the NIHSS score before IV tPA was 8.79±4.76, while the mean post-treatment NIHSS score was 5.98±4.82. Consistent with this information, it was observed that the duration of hospitalization was shorter in line with the low NIHSS scores of the patients. At the same time, since low NIHSS scores are associated with shorter hospital stays and therefore lower complication rates, acute ischemic

stroke treatments are expected to have a significant effect on the NIHSS score. The fact that there was a mean decrease of 3 points in NIHSS scores with treatment in the current study shows that this expectation was met. There was a significant and positive relationship between the duration of stay in the stroke unit and the pre-treatment NIHSS score. However, a negative and statistically significant relationship between the duration of stay and the Glasgow Coma Scale (GCS) score before IV tPA application was seen. The fact that patients with low GCS scores require longer close follow-ups can explain this result. The study of Saxena et al.[18] was also consistent with this finding.

The study of Appelros[27] reveals that stroke severity is a critical factor affecting both the acute period and the overall length of hospital stay. It has been determined that each 1-point increase in the NIHSS score prolongs the acute period hospitalization by 0.8 days and the total hospitalization period by 3.4 days.[27] The statistical significance of the NIHSS score and low GCS on the length of stay in our study is consistent with these results.

The duration of stay in the stroke unit was statistically significantly higher in patients who developed complications during hospitalization (p<0.05). The rate of complication development among patients was 44.1% during hospitalization, with cerebral hemorrhage occurring in 18% and cerebral edema in 18%. Intracranial hemorrhage and edema rates were low compared to the literature,[1,29] which can be explained by the fact that NIHSS scores were not high after treatment. Bleedings that are considered minor such as gingival bleeding, vascular leakage, and hemoptysis, are among the common complications in stroke treatment.[29] In this study, the rate of minor bleeding was found to be 13.5%.

Ahangar et al.[26] stated that the prevalence of dysphagia in acute stroke varies between 28-65%. Failure to manage dysphagia directly causes aspiration and pneumonia.[29] Pneumonia is a serious complication that occurs with a rate of 15% in the first 48-72 hours after acute ischemic stroke.[29,30] Stroke-associated pneumonia increases the hospital stay length, thus the cost, and also mortality.[29] In this study, it was concluded that respiratory-related complications developed in 19.5% of the patients and, among these, pneumonia was 7.5%. According to this finding, the rate of pneumonia development was lower than the literature. NGT is inserted in the stroke unit before IV tPA application (to prevent invasive procedures after treatment and to monitor possible gastrointestinal bleeding). However, the possibility of developing aspiration cannot be excluded from the onset of stroke symptoms until admission to the stroke intensive care unit. Further research examining the relationship between NGT, pneumonia, and respiratory complications is needed. UTI was observed in 6% of the patients. This situation can be associated with BT insertion (to prevent invasive procedure after treatment and to follow up possible urinary system bleeding). The studies in the literature reported a post-stroke UTI at a rate of 15% to 60%.[29,31] In the present study, the rate of UTI was lower than the literature. When the reason for transfer from the stroke unit was examined, routine transfer to neurology service was the most common reason at 82.3%. The need for a level 3 intensive care unit (ICU) arose in 15.4% of the patients. In other words, a high NIHSS score may increase the rate of referral to a higher-level intensive care unit or death, leading to a shorter length of stay.[32] Kim et al.[28] found that the most transferred patients were those with inoperable intracerebral hemorrhage. These findings were consistent with the patient's characteristics in the present study who were transferred to the 3rd level ICU. In this study, similar to the literature, it was concluded that there was a significant and positive relationship between the duration of stay in the stroke intensive care unit and the patient's age who received IV tPA treatment.[7,18,26,28,33,34] Compared to general service, admission to a stroke unit provides an increase in the rate of independent discharge with a decrease in the "alone" death rate and hospital stay in acute stroke cases.[12] This benefit is more important in patients with ischemic stroke compared to patients with hemorrhagic stroke and has no dependency on gender, age, and comorbidities.[12,13] Neurological death usually occurs within the first several days following a stroke, leading to a shorter hospital stay.[13] On the other hand, Lau et al.[35] compared the stroke intensive care unit with the internal ICU and showed that patients in stroke units had a shorter length of stay. The mean duration of stay in the stroke unit for patients in the present study was 3.2±3 days, which was quite low. Gattringer et al.[7] identified the stroke unit mortality's independent predictors, including stroke severity (NIHSS), pre-stroke functional status (mRS score >0), age, previous heart disease, diabetes mellitus, non-lacunar stroke, and posterior circulation stroke syndrome. As expected, the severity of the initial stroke and age had the most substantial influence on the early mortality of stroke. The mortality rate of patients within the present research was 4%. In the case of this study, early death may be attributable to baseline stroke severity and unchangeable predictors.[7] This study's main

limitations are its single-center conduction and retrospective design. The strengths of the study are that the stroke unit where the study was conducted is located in the most dense and accessible area of Istanbul and has a wide patient profile. In addition, the inclusion of each consecutive patient meeting the study criteria is another strength.

Conclusion

The present study concluded that the development of complications during hospitalization significantly impacts the duration of hospitalization. Most of these complications are preventable, highlighting the importance of close monitoring and follow-up of the patient during hospitalization. It is noteworthy that patients with severe neurological status may experience prolonged hospital stays after receiving IV tPA. The inability to evaluate the discharge time after leaving the stroke unit and the absence of discharge records from the home, rehabilitation center, or nursing home present limitations in determining the impact of socio-demographic factors and complications on the length of stay. Despite these limitations, the short length of stay and low mortality rate observed in the stroke unit of this study underscore the benefits of close observation of IV tPA patients.

Disclosures

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