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Evaluation of clinical characteristics and treatment data of acute ischemic stroke patients follow-up in a stroke center with a retrospective cohort study: Two-years analysis

İnme merkezinde takip edilen hastaların klinik özelliklerinin ve tedavi verilerinin retrospektif kohort çalışması ile değerlendirilmesi : İki yıllık analiz

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Abstract

Objective: It was aimed to examine the clinical features and treatment aspects of the patients who were hospitalized and treated with the diagnosis of ischemic stroke in the stroke center of our hospital.
Materials and Methods: This study was conducted by retrospectively analyzing the information recorded with standard data forms of inpatients treated in our stroke center between March 1, 2019 and March 1, 2021.
Results: Of the 125 patients in the study, 56.8% were female and 43.2% were male. The most common risk factor detected in patients was Hypertension. 76% of the patients were using at least one drug for thromboembolism prophylaxis. The anterior part of the brain was affected in 72.8% and the posterior part in 27.2% of the patients. Symptom onset to door time was 180 minutes or less in 84.8% of the patients and door-to-needle time average: calculated as 52 minutes. 71 patients only i.v. tPA treatment, 42 patients both i.v. tPA and mechanical thrombectomy were applied, and only mechanical thrombectomy was applied to 12 patients. The average length of stay in the intensive care unit was 9 days, with an average of 8.6 days for women and 9.4 days for men. The need for a mechanical ventilator developed in 39 patients. Death occurred in a total of 26 patients, including 16 female patients and 10 male patients.
Conclusion: The incidence of ischemic stroke has been increasing continuously over the years. According to our study, considering that more than 80% of acute ischemic stroke patients apply to healthcare institutions in the first 3 hours, it is necessary to increase the number of stroke centers where intravenous TPA and mechanical thrombectomy treatments will be applied and to ensure that more patients benefit from acute stroke treatments.

Keywords: Acute ischemic stroke, thrombolytic therapy, symptom onset to door time, door to needle time.

Öz

Amaç: Hastanemiz inme merkezinde iskemik inme tanısıyla yatıp tedavisi yapılan hastaların klinik özellikleri ve tedavi açısından incelenmeleri amaçlandı.
Gereç ve Yöntem: Bu çalışma 1 Mart 2019 -1 Mart 2021 tarihleri arasında inme merkezimizde yatarak tedavi edilen hastaların standart veri formları ile kayıt altına alınmış olan bilgileri retrospektif olarak analiz edilerek yapılmıştır.
Bulgular: Çalışmada yer alan 125 hastanın %56,8' i kadın, %43.2' si erkek idi. Hastalarda en sık tespit edilen risk faktörü hipertansiyondu. Hastaların %76' sı tromboemboli profilaksisine yönelik en az bir ilaç kullanmaktaydı. Hastaların %72,8' de anterior dolaşım alanı, %27,2' de ise posterior dolaşım alanı etkilenmişti. Hastaların %84,8' inde semptom-kapı zamanı 180 dk ve daha kısa idi, kapı-iğne zamanı ortalama 52 dk olarak hesaplandı. 71 hastaya sadece i.v. tPA tedavisi, 42 hastaya hem i.v. tPA hem de mekanik trombektomi uygulanmış, 12 hastaya ise sadece mekanik trombektomi uygulaması yapılmıştı. Hastaların yoğun bakımda kalış süreleri ortalama 9 gün olup kadınlarda ortalama 8,6 gün, erkeklerde ise 9,4 gün olarak tespit edildi. 39 hastada mekanik ventilasyon ihtiyacı gelişti. 16'sı kadın, 10' u erkek hasta olmak üzere toplam 26 hastada ölüm gerçekleşti.
Sonuç: İskemik inme insidansı yıllar içerisinde sürekli artmaktadır. Çalışmamıza göre akut iskemik inme hastalarının %80'den fazlasının ilk 3 saatte sağlık kuruluşlarına başvurduğu dikkate alınırsa iv. TPA ve mekanik trombektomi tedavilerinin uygulanacağı inme merkezlerinin sayısının arttırılması ve daha fazla hastanın akut inme tedavilerinden faydalanmalarının sağlanması gerekmektedir.

Anahtar Kelimeler: Akut iskemik inme, trombolitik tedavi, semptom başlangıcından kapıya kadar geçen süre, kapıdan iğneye kadar geçen süre.

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Introduction

Acute ischemic stroke (IS) is defined as a cerebrovascular disease that starts suddenly, usually causes focal neurological findings, occurs due to non-traumatic causes and lasts longer than twenty-four hours or may result in death during this period (1). It is an important cause of morbidity and mortality especially in the older age group as it usually affects the middle and older age group. Stroke is the third leading cause of death and the most common cause of disability in developed countries. Stroke affects fifteen million people in the world every year. In this group, one out of every three patients dies due to stroke-related complications and one out of every three patients lives with permanent neurologic disability (2).

According to the data of the American Stroke Association, 87% of stroke patients are diagnosed with ischemic stroke (IS) and 13% with hemorrhagic stroke (HS) (3). In our country, 71.2% of all strokes are IS and 28.8% are HS according to the data of the Turkish multicenter stroke study of the Turkish Society of Cerebrovascular Diseases (4). Stroke incidence is variable according to different regions of the world and may also vary among people in the same country according to racial characteristics and residential areas. In the studies covering the last 20 years, stroke incidence was found as 1-3/1000 and stroke prevalence as 6/1000 (5).

The use of intravenous (i.v.) tissue plasminogen activator (tPA) in the treatment of acute IS has never reached the targeted prevalence despite nearly twenty-five years of experience. In the United Kingdom, i.v. tPA could be administered to only 15% of patients with an indication for i.v. tPA, which constituted 12% of all stroke cases in 2013 (1). In a retrospective cohort study, 55% between 2003-2005 and 18% between 2010-2011 could not be administered i.v. tPA among patients who reached the health center within the first 2 hours and had no contraindication for i.v. tPA in the USA between 2003-2011. According to the result of this analysis, tPA could not be administered to one fourth of the acute IU patients with an indication for i.v. tPA between 2003 and 2011. This study showed that the habit of administering i.v. tPA has increased significantly over the years (6). In another study, i.v. tPA could be administered to only 3.5% of all acute II cases evaluated in the USA in 2008 (7). These findings prove that the use of i.v. tPA varies significantly even between different centers in the same country. Although we cannot know the situation in Turkey with the current data, it is believed that i.v. tPA administration has not become widespread at the desired level and more awareness studies are required (8,9).

Despite the increase in the mortality and morbidity rates due to acute IS in our country, the number of studies on these patients is limited. In this study, we aimed to share the socio-demographic and clinical characteristics of patients who were diagnosed with acute IS in the stroke center of our hospital within a two-year period and our clinical experience with i.v. tPA treatment.

Materials and Methods

The study was conducted in accordance with the Helsinki Declaration Principles. This study is a retrospective cohort study. In the study, the data of a total of 125 patients at the age of 18 years and above diagnosed with acute IS, who were hospitalized and followed up and treated in the stroke center of our hospital between March 1, 2019 and March 1, 2021, were analyzed retrospectively. From the data of all patients which was recorded on standard data collection forms from the first day of admission to the stroke center; their gender, age, time from the onset of the first symptom to the emergency department (symptom-door time), time from the emergency department to the first intervention (door-needle time), accompanying risk factors for IS, medications used for atherothrombosis prophylaxis before IS, glucose and HbA1c levels checked on the first day of admission to the stroke center, localization of the affected cerebral artery, treatments applied, duration

of stay in intensive care unit, mechanical ventilation needs and discharge status were analyzed. The results were compared statistically.

Statistics

(SPSS) 23.0 package program was used in the analysis of the data. Average, percentage distribution, t-test in independent groups were used in the evaluation of the data and chi-square test was used in the comparison of the qualitative data. The results were evaluated at $p<0.05$ significance level.

Results

Of the 125 patients in our study, 71 were female (56.8%) and 54 were male (43.2%). The mean age of female patients was: 72.36±12.86, and the mean age of male patients was: 68.77±12.07. 84 (67.2%) of the patients were at the age of 65 and above and 41 (32.8%) of the patients were younger than 65 years (Table 1).

Table 1. Age and gender data of the patients

Gender	Number / Ratio of Patients	Age Average	Below 65 years old	Above 65 years old
Female	71(56.8%)	72.36±12.86	25.35%	74.65%
Male	54(43.2%)	68.77±12.07	42.59%	57.41%

When the patients were analyzed in terms of IS risk factors, hypertension (HT) ranked first. HT was detected in 98 patients (78.4%), coronary artery disease (CAD) in 61 patients (48.8%), diabetes mellitus (DM) in 45 patients (36%) and atrial fibrillation (AF) in 32 patients (25.6%). 8 patients had none of these risk factors, 21 patients had only one risk factor, 56 patients had two risk factors and 48 patients had three or more risk factors.

Among the patients included in the study, 95 (76%) were using at least one drug for thromboembolism prophylaxis. Of these, 60 patients were using acetylsalicylic acid (ASA), 23 patients were using new generation oral anticoagulants (NGAs) and 12 patients were using warfarin sodium.

When the time from the onset of the first symptom to the arrival to the emergency department (symptom-door time) was analyzed, 41 patients were identified within the first 60-120 minutes (min.), 65 patients between 120-180 min. and 19 patients 180 min. or above. The time between arrival to the emergency department and the interventional procedure (door-needle time) was within the first 30 minutes in 72 patients (57.6%) and 30-60 minutes in 53 patients (42.4%) (Figure 1).

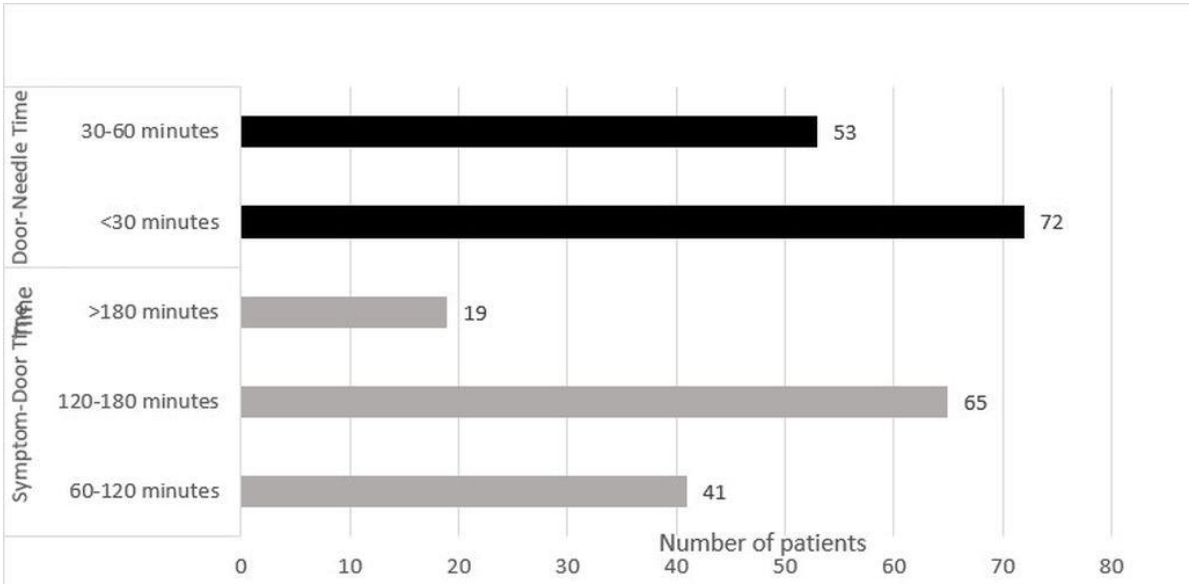

Figure 1.

When the localization of the involved vascular areas in the brain was analyzed according to imaging data obtained using diffusion magnetic resonance imaging, brain computed tomography and contrast-enhanced brain and carotid-vertebral artery angiography, digital subtraction brain and carotid-vertebral angiography after the interventional procedure, 91 patients (72.8%) had middle cerebral artery (MCA) and/or anterior cerebral artery (ACA) occlusion (in the anterior circulation area of the brain), while 34 patients (27.2%) had vertebral artery (VA) and/or basilar artery (BA) and/or posterior cerebral artery (PCA) occlusion (in the posterior circulation area of the brain). In addition, stenoses of the internal carotid artery (ICA) of various degrees were detected in 14 patients.

DM was detected in 45 of the patients included in the study. Of these patients, 28 patients had HbA1C levels between 6 and 8, 7 patients had levels between 8 and 10, and 10 patients had levels 10 and above. When the first glucose values of the patients after hospitalization were analyzed, it was found as between 150-250 mg/dl in 26 patients, 250 mg/dl and above in 13 patients, and 85-150 mg/dl in 6 patients.

When the treatments applied to the patients included in the study were analyzed, it was observed that 71 patients were administered only i.v. tPA, 42 patients were administered both i.v. tPA and mechanical thrombectomy, and 12 patients were administered only mechanical thrombectomy (Figure 2). It was observed that intracranial hemorrhage developed in 10 patients (8%) after thrombolytic therapy.

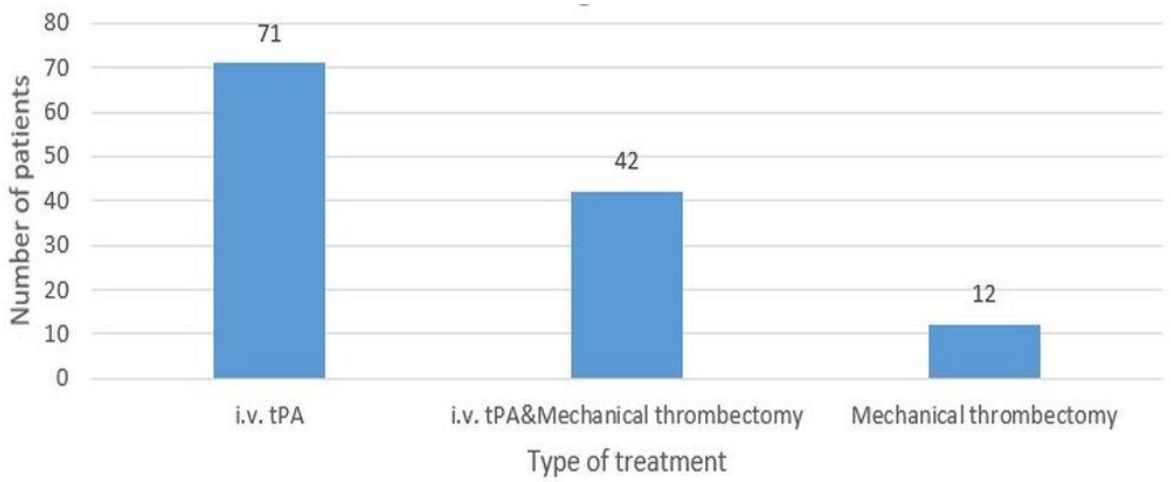

Figure 2.

The mean duration of stay in intensive care unit of the patients included in the study was calculated as nine days, which was 8.6 days in the female gender group and 9.4 days in the male gender group. 39 patients, 23 of whom were female and 16 were male, required mechanical ventilation. Death occurred in a total of 24 patients, 14 of whom were female and 10 were male (Figure 3).

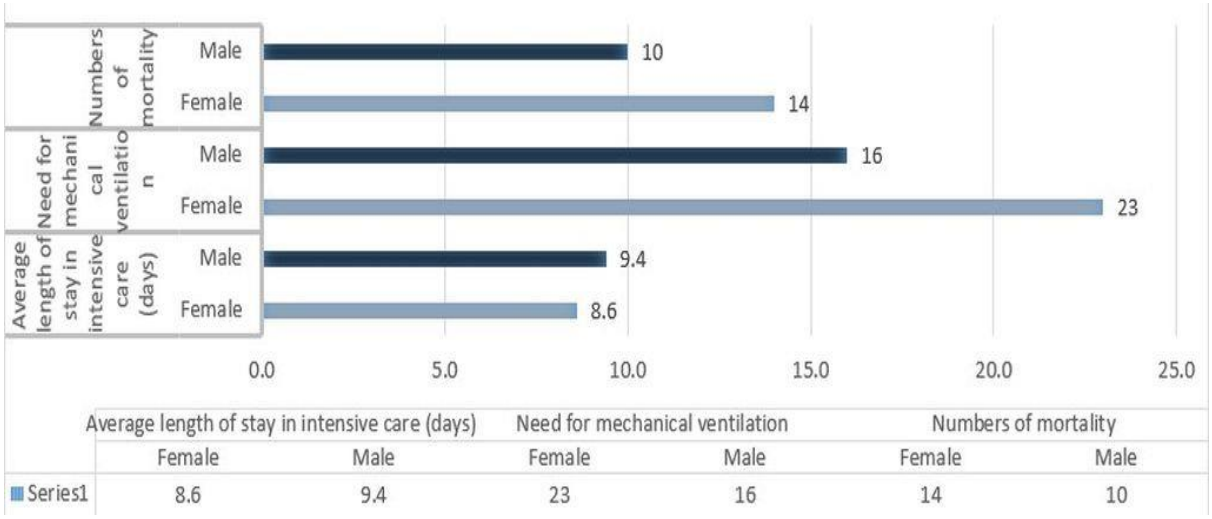

Figure 3.

Discussion

Stroke is a frequently encountered disease group in neurology practice. It is the third most common cause of mortality in the world after heart diseases and cancer (10). Among the causes of morbidity, it ranks first in the world and second in Turkey (11). Even in patients who receive appropriate treatment in specialized centers, there is a significant decrease in the quality and duration of life of the affected person after stroke (11).

Although cerebrovascular diseases are reported to be slightly more common in men, there is no significant difference between the genders. Kumral et al. reported a male rate of 55.6% and a female rate of 44.4% in their study, and this rate was reported as 53% for men and 47% for women in the study by Laskowitz et al. (12, 13). In our study, 56.8% of the patients were female and 43.2% were male. Distribution according to age groups: 0-44 years: 3 males and 1 female, 45-64 years: 16 females and 12

males, and 54 females and 39 males above the age of 65 (Table 1). In our study, it was observed that men under the age of 65 had a numerical superiority over women, and women over the age of 65 had a numerical superiority over men. This data is similar to the data of the study conducted by Ozdemir et al. in 2000 (4).

Age is the strongest determinant of stroke and stroke doubles every decade above the age of 55 (14). Ischemic stroke is most common in people who are above the age of 65 and 70% of patients are in this age group (15-17). Reganon et al. (18) reported the age average for IS as 65.3 ± 8.2, Gurger et al. (19) as 68.6 ± 14, and Altun et al. as 70.24 (20). In our study, approximately 67.2% of the patients with IS were at the age of 65 or above and the age average for IS was 70.81 ± 12.53. These results were similar to the previous reports in the literature. Strokes occurring at early ages (under the age of 45) constitute 3-5% of all ischemic strokes (21). In our study, we found that the frequency of all ischemic stroke in this age group was 3.2% (4 patients) , which is consistent with the previous studies.

Risk factors for stroke include HT, DM, high blood cholesterol, cardiovascular diseases, AF, smoking and alcohol consumption (22). In this study, the risk factors for IS were similar in both men and women and were HT (78.4%), CAD (48.8%), DM (36%) and AF (25.6%), respectively. HT is the most important of the established modifiable risk factors for IS and it is also the risk factor with the highest prevalence in the society (23). HT was the most common risk factor in our study. There was one risk factor in 21 patients, two risk factors in 49 patients and three or more risk factors in 53 patients.

In the study of Framingham, atherosclerotic brain strokes were found as 2.5 times higher in diabetic male patients and 3.6 times higher in diabetic female patients (24). 45 patients (36%), 27 of whom were female and 18 were male, who were included in this study had diagnosed with DM. In the study of ARIC, HbA1c was shown to be an independent risk factor for stroke in diabetic patients (25). In our study, 12 of 26 patients who died had DM. Of these, 4 patients had HbA1c between 6-8%, 5 patients had HbA1c between 8-10% and 3 patients had HbA1c 10 and above.

In our study, 95 patients (76%) were using at least one antithrombotic drug for thromboembolism prophylaxis. Of these patients, 60 (48%) were using ASA only, 23 (18.4%) were using non-vitamin K antagonist oral anticoagulants (NOACs) and 12 (9.6%) were using warfarin sodium. 16 patients had a previous medical history, all of these 16 patients were receiving anticoagulant therapy, 10 of them were using NOACs and 6 of them were using warfarin sodium. Literature studies have reported a 1.5-2.0 times decrease in atherothrombosis rates in the use of anticoagulant drugs for thromboembolism prophylaxis (24). The possible reasons for the development of IS despite the use of anticoagulants for thromboembolism prophylaxis in 76% of the patients in this study include the fact that the patients did not use NOACs agents at the appropriate dose and/or regularly, the target INR level could not be reached in the use of warfarin, which requires INR monitoring, and therefore the protective effect did not occur. In addition, it has been reported in the literature that the use of ASA alone may not be sufficient for antithrombotic effect in some patients and therefore combination therapy should be provided (25). Most of the patients in our study (60 patients) were using ASA alone, and therefore, adequate prophylaxis for atherothrombosis may not have been provided.

When the patients included in the study were analyzed in terms of symptom-door time, it was determined that 84.4% of the patients applied to the emergency department within the first three hours. 19 patients applied to the emergency department 180 minutes or longer after the onset of the first symptom (Figure 1). It is known how important especially the first 4 hours are for thrombolytic treatment in IS (26). When compared with the literature studies, the symptom-door time was shorter in the patients in our study (27, 28). The reason for the shorter symptom-door time in this study was that the IS cases in our province and

surrounding provinces were directed to our hospital without losing time because our hospital has a stroke center. For this, emergency ambulance unit and stroke center should work in coordination with public and private hospitals. It is uttermostly important to provide the necessary trainings to the health personnel on IS. Furthermore, the public should also be informed about IS through meetings, mass media and family physicians and awareness should be raised on this issue. For this reason, increasing the number of stroke centers throughout the country is of critical importance in terms of stroke diagnosis and treatment.

The primary purpose of thrombolytic therapy is to dissolve the thrombus and ensure the continuity of cerebral blood flow by recanalization. In the American Heart Association (AHA) 2010 guide, the period of providing i.v. thrombolytic therapy is recommended as the first 4.5 hours. Although this period is recommended as 4.5 hours, treatment should be provided as soon as possible. Therefore, early recognition of stroke patients in emergency services and door-to-needle time not exceeding 60 minutes are recommended (29). In this study, door-to-needle time was within the first 30 minutes in 57 patients and between 30-60 minutes in 78 patients. According to the data of the "Thrombolytic Therapy Study Group of Turkey", this time was determined as 69 minutes on average (30). In this study, the mean door-needle time was 52 minutes and this time was found to be shorter when compared with the average of Turkey.

When the affected brain localizations of the patients were examined, it was found that 91 patients (72.8%) had MCA and/or ACA occlusion (brain anterior circulation area) and 34 patients (27.2%) had VA and/or BA and/or PCA occlusion (brain posterior circulation area). Moreover, ICA stenoses of various degrees were detected in 14 patients. In a recent study, infarcts were detected in the anterior circulation area of the brain in 63%, in the posterior circulation area in 30%, in both the anterior and posterior circulation areas in 3%, and in the border zone areas in 4% of patients followed up in a stroke center with a diagnosis of acute IS (31).

71 patients included in this study were administered i.v. tPA, 42 patients were administered both i.v. tPA and mechanical thrombectomy, and 12 patients were administered only mechanical thrombectomy. Intracranial hemorrhage developed in 8% of patients after thrombolytic therapy. In a recent study carried out by Kunt and Aslan, the rate of hemorrhage in patients who were administered i.v. tPA was 13% (31).

The average length of stay in the intensive care unit was calculated as 9 days (1-93), which was 8.6 days in women and 9.4 days in men. No significant correlation was found between the length of stay in the intensive care unit and gender ($t=-.372$, $p=0.711$, $p>0.05$). Although there is no quality criterion for the length of stay in the stroke unit, the optimal length of stay was calculated as 3 days. However, post-stroke care period was not included in this period (32). The length of time in this study was due to the inclusion of the post-stroke care period in the stroke hospitalization period. Requirement of mechanical ventilation developed in a total of 36 patients, and the NIHSS average of these patients was 13.46. It was observed that of these patients, 22 were female patients and 14 were male patients, and that the age average was 64.8 in men and 70.12 years in women. In this study, death occurred in a total of 24 patients (19.2%), 14 of whom were female (58.33%) and 10 of whom were male (41.67%). No statistically significant difference was found in the distribution of mortality rates according to gender ($p=0.014$; 6.567; $p<0.05$). In a study carried out in Thailand in which stroke patients were evaluated for 13 years, the mortality rate in acute stroke patients was found between 10.24-14.77%, while this rate was found between 3.97-10.53% in acute IS patients who were administered thrombolytics (33). In the study carried out by Kunt and Aslan, it was reported that mortality developed in 13% of IS patients followed up in a stroke center (31).

The incidence of ischemic stroke increases continuously over the years. In order to reduce the morbidity and mortality that may develop due to IS,

it is necessary to increase the number of stroke centers throughout our country so that thrombolytic therapy can be started to patients without wasting time. In addition, raising awareness of the public through mass media and informative meetings and raising social awareness will shorten the duration of admission to stroke centers and contribute positively to morbidity and mortality after thrombolytic therapy.

The limitation of our study include the lack of patient data on hyperlipidemia, metabolic syndrome, obesity and smoking, which are modifiable risk factors for IS.

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