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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

INTRAVENOUS THROMBOLYTIC THERAPY IN ACUTE ISCHEMIC STROKE: EXPERIENCES OF ADIYAMAN

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ABSTRACT

INTRODUCTION: Stroke, which poses a huge burden on the health economy all over the world and has negative effects on caregivers, is a serious cause of disability and mortality. The aim of our study was to share the results of intravenous (IV) thrombolytic therapy (tPA) applied to patients with acute ischemic stroke in our neurology clinic in Adıyaman province.
METHODS: Between March 2018 and June 2020, the time of admission to our clinic with the diagnosis of acute ischemic stroke (within the first 4.5 hours) and the application of thrombolytic therapy in our clinic and the responses to treatment of 44 patients who were clinically eligible for IV tPA were analyzed retrospectively. Clinical data and demographic characteristics of the patients were recorded.
RESULTS: A total of 44 patients with acute ischemic stroke, 24 female (54.5%) and 20 male (45.5%) were included in the study. The mean age of the patients was 69.84 ± 12.82 (range, 38-96) years. Intracranial bleeding was observed in 3 patients (6.8%) after treatment. Symptomatic bleeding was detected in only 1 (2.3%) of them. The mean NIHHS and mRS scores of the patients with anterior circulation infarction were 2.78 and 1.09, respectively, at the 3rd month follow-up after treatment, and the mean NIHSS and mRS scores at the 3rd month controls of those with posterior circulation infarction were 3.33 and 1.00, respectively. Three patients with anterior circulation infarction died within 1 week after treatment.
DISCUSSION AND CONCLUSION: In recent years, the number of applications for acute ischemic stroke to our stroke center has been increasing day by day. For patients presenting with acute ischemic stroke, iv tPA therapy is the only treatment option with proven efficacy under appropriate conditions and at the appropriate time.
Keywords: Acute ischemic stroke, thrombolytic therapy, Adıyaman.

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AKUT İSKEMİK İNMEDE İNTRAVENÖZ TROMBOLİTİK TEDAVİ: ADIYAMAN DENEYİMLERİ

ÖZ

GİRİŞ ve AMAÇ: Tüm dünyada sağlık ekonomisi üzerine büyük bir yük oluşturan ve hastaya bakım verenler üzerinde olumsuz etkileri olan inme ciddi derecede sakatlık ve mortalite nedenidir. Çalışmamızın amacı akut iskemik inmeli hastalarda, Adıyaman ilinde nöroloji kliniğimizde uyguladığımız intravenöz (İV) trombolitik tedavi (tPA) sonuçlarını paylaşmaktır.

YÖNTEM ve GEREÇLER: Mart 2018-Haziran 2020 tarihleri arasında akut iskemik inme tanısıyla kliniğimize başvuran zaman (ilk 4,5 saat içerisinde) ve klinik olarak İV tPA uygulamaya uygun olan 44 hastanın kliniğimizde trombolitik tedavi uygulanımı ve tedaviye yanıtları retrospektif olarak incelendi. Hastaların klinik verileri ve demografik özellikler kaydedildi.

BULGULAR: Çalışmaya 24'ü kadın (%54,5) 20'si erkek (%45,5) toplam 44 akut iskemik inme hastası alındı. Hastaların yaş ortalaması 69,84±12,82 (38-96) yıl idi. Tedavi sonrası toplam 3 hastada (%6,8) intrakraniyal kanama gözlendi. Bunlardan sadece 1'inde (%2,3) semptomatik kanama saptandı. Tedavi sonrası 3. ay kontrollerinde anterior sirkülasyon enfarktı olan hastaların ortalama NIHHS ve mRS skorları sırasıyla (2,78), (1,09), posterior sirkülasyon enfarktı olanların 3. ay kontrollerinde ortalama NIHSS ve mRS skorları ise sırasıyla (3,33), (1,00) idi. Tedavi sonrası 1 haftalık sürede anterior sirkülasyon enfarktı olan 3 hasta kaybedildi.

TARTIŞMA ve SONUÇ: Son yıllarda inme merkezimize akut iskemik inme başvurusu gün geçtikçe artmaktadır. Akut iskemik inme ile başvuran hastalara, uygun koşullarda ve uygun zamanda iv r-tPA tedavisi etkinliği kanıtlanmış tek tedavi seçeneğidir.

Anahtar Sözcükler: Akut iskemik inme, trombolitik tedavi, Adıyaman.

INTRODUCTION

Stroke is a condition that develops rapidly due to focal or global impairment of cerebral functions and clinical findings last 24 hours or longer. In addition, more than 80% of strokes are ischemic in origin and fatal (1). Ischemic stroke is the third most common cause of death after heart diseases and malignancy in adults and the most common cause of disability in developed countries (2). A long and expensive rehabilitation process awaits the patients after stroke (1,3). In addition, it is seen that many of the patients need the help of someone else for personal care and daily life activities; the social lives of the patients and their relatives are restricted; they suffer financial damage due to the loss of labor force (4). For these reasons, it is very important to diagnose and treat stroke in the early period. Infarction occurs in the center of the vascular irrigation area within minutes after the occlusion of the cerebral artery. There is an area called "penumbra" in the periphery where irreversible cell death does not occur due to collateral circulation. This is the main goal in the acute treatment of ischemic stroke. The aim is to recanalize the occluded vessel and ensure timely reperfusion. Thrombolytic therapy with intravenous (IV) tissue plasminogen activator (tPA) is clinically beneficial in acute ischemic stroke. The application results are heterogeneous although the positive effect of IV tPA has been demonstrated in many randomized controlled trials (5). IV tPA applications are still not at the desired level even though although it has been approximately 15 years since the license was obtained for the use of IV tPA in acute ischemic stroke in Turkey.

It was planned in our study to examine the clinical results of the patients who were admitted to the emergency department of our hospital within the first 4.5 hours after the acute ischemic stroke and underwent thrombolytic therapy between March 2018 and March 2020 and to discuss the obtained data in light of the literature.

METHODS

The study was conducted in accordance with the Helsinki Declaration ethical standards and approved by the Adıyaman University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Number: 2020/5-36, Date: 18.05.2020).

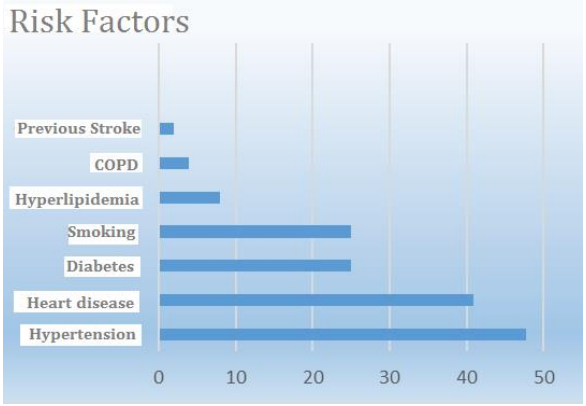
The data of 44 patients who were admitted to our clinic with the diagnosis of acute ischemic stroke between March 2018 and June 2020 and who underwent IV tPA were retrospectively analyzed. 17 stroke patients were admitted to our clinic in 2018, 20 stroke patients in 2019, and 7 stroke patients in the first 6 months of 2020. The

patients were evaluated according to the recommendations of the American Heart Association/American Stroke Association in terms of eligibility and contraindication before IV tPA treatment (6). IVA tPA was not performed in cases such as a history of intracerebral hemorrhage, findings suggestive of subarachnoid hemorrhage, the uncertainty of onset of stroke, rapidly recovering neurological findings, Institutes of Health Stroke Scale (NIHSS) score below 4 and above 25, systolic blood pressure 185 mmHg or diastolic blood pressure above 110 mmHg despite treatment, history of stroke or severe head trauma in the last three months, major surgical intervention in the last two weeks, gastrointestinal or genitourinary bleeding in the last three weeks, vascular intervention in an inaccessible place in the last week, blood sugar above 400 mg/dl or below 50 mg/dl, platelet count less than 100.000/mm3, INR value higher than 1.7, and bleeding in computed brain tomography (CBT) examination. Informed consent was obtained from the patient or their relatives before IV tPA was administered to the patient. 10% of the total dose calculated as 0.9 mg/kg (maximum 90 mg) IV r-tPA (alteplase) was administered as IV bolus and the rest was administered as an infusion in 1 hour. Patients' age, gender, symptom-to-door, door-to-needle, symptom-to-needle time, place of residence (city-countryside), the season of admission, type of admission, front-back system separation, CBT and brain diffusion magnetic resonance imaging (MRI) performed at the time of admission and CBT examinations performed 24 hours after the application, were evaluated. Bleeding in the first 24 hours after treatment was evaluated as an IV tPA complication. The National NIHSS and modified Rankin Scale (mRS) values at the time of admission, at the 1st week, and 3rd month after treatment were examined.

RESULTS

A total of 44 acute ischemic stroke patients, 24 of whom were female (54.5%) and 20 of whom were male (45.5%), were included in the study. The mean age of the patients was 69.84±12.82 (38-96) (Table 1). All patients initially underwent CBT and brain diffusion MRI. No signs of early infarction were observed in any of the acute CBTs. Therefore, the Alberta Stroke Program Early CT Score was evaluated as 10 in all patients. None of the 44 patients who underwent nasogastric and urinary catheter insertion before IV tPA administration in our emergency department developed nasopharyngeal or genitourinary system bleeding during and after the infusion. The mean time from the onset of symptoms to admission (symptom-door), the mean time from the time of admission to the hospital to the onset of IVF tPA (door-needle), and the mean time from the onset of symptoms to IVF tPA administration (symptom-needle) were determined as 114.77±53.079, 37.79±14.86, and 152.56±48.06 respectively. None of the patients had any complications during the infusion (Table 1).

It was determined that 21 patients (47.7%) had hypertension, 18 patients (40.9%) had heart disease, 11 patients (25%) had diabetes mellitus, 11 patients (25%) had a history of smoking, 8 patients (18.2%) had hyperlipidemia, 4 patients (9.1%) had COPD, and 2 patients (4.5%) had a history of stroke when the risk factors for stroke were evaluated. It was also determined that 5 patients (11.4%) had a history of ASA use, 1 patient (2.3%) had a history of clopidogrel use, 11 patients (25%) had a history of oral antidiabetic (OAD) drug use, and 14 patients (31.8%) had a history of antihypertensive drug use. ECG taken in the emergency department revealed normal sinus rhythm in 33 people (75%) and atrial fibrillation in 11 people (25%) (Table 1), (Graphic).



Grafhic. Risk factors for stroke in patients.
COPD: chronic obstructive pulmonary disease.

Postadmission carotid-vertebral artery Doppler USG revealed atherosclerotic changes in 28 people (63.8%), stenosis under 50% in 3 people (6.8%), and stenosis over 70% in 1 person (2.3%). It was found that 27 people (61.4%)

applied to us from the city and 17 people (38.6%) from the countryside. There was no significant difference between the two groups in terms of NIHSS scores at the 3rd month even though there was a statistically significant difference between the symptom-to-door times of rural and urban patients. It was determined that 7 people (15.9%) were farmers, 10 people (22.7%) were retired, 23 people (52.3%) were housewives, one person (2.3%) was a tradesperson, one person (2.3%) was a worker, and 2 people (4.5%) were self-employed when the occupations of the patients were examined. 23 people (52.3%) applied to our emergency department during working hours and 21 (47.7%) applied outside working hours considering the time of admission. 37 people (84.1%) applied to our emergency department with 112 ambulances and 7 people (15.9%) applied to our emergency department with their own means considering the means of transport (Table 1).

The mean mRS of admission to the hospital was found to be 3.23±0.94. The first-week mRS was 1.21±0.93 and the third-month mRS was 1.05±0.93 (Table 2). There was no significant relationship between the admissions of the patients in the first 3 hours and between 3-4.5 hours as well as NIHSS scores at the 1st week and 3rd month (Table 3). Significant improvement was observed in both NIHSS and mRS values at 1 week and 3 months after treatment ($p<0.05$). There was no statistically significant relationship between the NIHSS and mRS scores of the patients in the first week and the duration of symptom-to-door time, door-to-needle time, and symptom-to-needle time ($p>0.05$). Of the treated patients, 39 (88.63%) had anterior circulation infarct, 4 (9.1%) had posterior circulation infarct, and one (2.72%) had both anterior and posterior circulation infarct (Table 1). CBT imaging taken at the end of the first 24 hours after treatment revealed hemorrhagic transformation in 3 patients. Two of these patients had anterior circulation infarct and one patient had posterior circulation infarct. Only 1 (2.3%) of the patients was classified as symptomatic intracerebral hemorrhage due to complaints of nausea, vomiting, and headache whereas 3 (6.8%) of our patients had an intracranial hemorrhage of different sizes. There were no mortalities due to bleeding in our study. Symptomatic intracerebral hemorrhage was defined as a hemorrhagic transformation that occurred within the first 36 hours and caused neurological deterioration. The mean NIHHS and mRS scores of the patients with anterior circulation infarct 1 week after treatment were (4.72) and (1.5), respectively; the mean NIHHS and mRS scores of the patients with posterior circulation infarct one week after treatment were (5.50) and (1.25), respectively. Three (3) patients with anterior circulation infarct died within 1 week after treatment. The mean NIHHS and mRS scores of the patients with anterior circulation infarct were (2.78) and (1.09), respectively; and the mean NIHSS and mRS scores of the patients with posterior circulation infarct were (3.33) and (1.00), respectively, at the 3rd-month follow-up. Three patients with anterior circulation infarct and one patient with posterior circulation infarct died between the first week and the end of the third month. 24 patients were discharged without sequelae (mRS 0-1). It was found that the neurological disability of 25 patients (56.8%) improved (mRS 0-1), 11 patients (25%) were found to be able to survive independently despite their disability (mRS 2-3), 2 patients (4.5%) were found to live their lives dependently, and 7 patients (15.9%) were found to be dead.

DISCUSSION AND CONCLUSION

This study aims to contribute to the literature by evaluating the status of IV tPA applications in the treatment of acute ischemic stroke in the Adıyaman province of the Southeastern Anatolia Region of Turkey. Stroke has an important place in neurological diseases because it is likely to improve with intervention in the early period and ranks first among the causes of morbidity worldwide (2). Stroke is one of the diseases that greatly reduce the quality and duration of life in adults even if follow-up, examinations, and treatments are performed in the best centers. The efficacy of IV tPA administration in the early period in acute ischemic stroke has been demonstrated, paving the way for a new treatment (7). This proves a new breakthrough in the treatment of acute ischemic stroke by demonstrating the effectiveness of IV r-tPA administration in acute ischemic stroke patients within 3.0-4.5 hours after the incidence with NINDS (National Institute of Neurological Disorders and Stroke) studies in 1995 and ECASS3 studies (European Cooperative Acute Stroke Study

Table 1. Demographic and clinical characteristics and risk factors of the patients.

Age, mean±standard deviation (years)		69,84±12,82 (38-96)
Gender	Female/Male, n (%)	24 (%54,5)/20 (%45,5)
Symptom-to-door-to-needle time	Symptom-to-door time, minutes	114.77±53.079
	Door-to-needle time, minutes	37.79±14.86
	Symptom-to-needle time, minutes	152.56±48.06
Risk Factors	Hypertension, n (%)	21 (%47.7)
	Heart disease, n (%)	18 (%40.9)
	Diabetes Mellitus, n (%)	11 (%25)
	Smoking, n (%)	11 (%25)
	Hyperlipidemia, n (%)	8 (%18.2)
	Chronic obstructive pulmonary disease, n (%)	4 (%9.1)
	History of previous stroke, n (%)	2 (%4.5)
History of drug use	Antihypertensive drug, n (%)	14 (%31.8)
	Oral antidiabetic drug, n (%)	11 (%25)
	Acetylsalicylic acid, n (%)	5 (%11.4)
	Clopidogrel, n (%)	1 (%2.3)
ECG	Normal sinus rhythm, n (%)	33 (%75)
	Atrial fibrillation, n (%)	11 (%25)
Infarction type	Anterior circulation infarct, n (%)	39 (%88.6)
	Posterior circulation infarct, n (%)	4 (%9.1)
	Anterior+Pasterior circulation infarct, n (%)	1 (%2.7)
Carotid-vertebral Doppler	Atherosclerotic change, n (%)	28 (%63.8)
	<50% stenosis, n (%)	3 (%6.8)
	>50% stenosis, n (%)	1 (%2.3)
Occupation	Housewife, n (%)	23 (%52.3)
	Retired, n (%)	10 (%22.7)
	Farmer, n (%)	7 (%15.9)
	Tradesperson, n (%)	1 (%2.3)
	Worker, n (%)	1 (%2.3)
	Self-employed, n (%)	2 (%4.5)
Place of residence	City, n (%)	27 (%61.4)
	Countryside, n (%)	17 (%38.6)
Time of Admission	During working hours, n (%)	37 (%84.1)
	Outside working hours, n (%)	21 (%47.7)
Means of transport to the hospital	By 112 Ambulance, n (%)	37 (%84.1)
	By their own means, n (%)	7 (%15.9)

Table 2. NIHSS and mRS changes at admission, 1st week, and 3rd month.

	Admission	1st week	3rd month	p-value
NIHSS	10.8±4.66	3.84±3.15	2.29±2.30	p<0.05
mRS	3.23±0.94	1.21±0.93	1.05±0.93	p<0.05

NIHSS: The National Institutes of Health Stroke Scale. mRS: Modified Rankin Scale

Table 3. Symptom-to-door-to-needle time changes of patients with NIHSS and mRS.

Time of Admission	Admission NIHHS/mRS	1st-week NIHHS/mRS	3rd-month NIHHS/mRS	p-value
0-3 hours	10.78/3.37	4.77/1.48	2.70/1.06	p>0.05
3-4.5 hours	13.71/4	4.83/1.33	3.66/1.16	p>0.05

NIHSS: The National Institutes of Health Stroke Scale, mRS: Modified Rankin Scale.

- III) in 2008 (7,8). The license was granted in 2006 for the use of IV tPA in acute ischemic stroke in Turkey. In our clinic, acute ischemic stroke IV tPA has been applied since 2018. It is important to administer the treatment as early as possible as it is life-saving even though the thrombolytic therapy window is recommended as the first 4.5 hours. It is recommended in this context that early recognition of stroke patients in emergency departments is a must and door-to-needle time should not exceed 60 minutes (9). IV tPA treatment was administered to all patients within 4.5 hours of the onset of symptoms, and the mean symptom-to-needle time was approximately 152.5 minutes, and the mean door-to-needle time was approximately 37.7 minutes in our study. Symptom-to-needle time is 150 minutes and door-to-needle time is 69 minutes according to the data of the Turkish Thrombolytic Therapy Study Group (10). Our door–to-needle time was positively

below the average of Turkey even though our results were similar to the average of Turkey.

NIHSS scores of all patients before treatment, at the 1st week, and 3rd month after treatment were compared and NIHSS scores were found to decrease statistically after treatment in our study ($p<0.05$). In addition, mRS scores of all patients before treatment, at 1 week, and 3 months after treatment were compared and it was found that mRS scores decreased statistically ($p<0.05$). Updates were made with more cases according to the previously published "Turkish National IV Thrombolysis Registry" study. The rate of good prognosis (mRS 0-2) with IV tPA is approximately 60% in the case series published in Turkey (10). Evaluations were made at 1 week and 3 months in our study and mRS was found to be 1.21±0.93 and 1.05±0.93, respectively even though the evaluations of most patients after discharge or less than three months were the majority in this study. The low results of our study can be attributed to the absence of basilar artery involvement.

The anterior system infarct was present in 88.6% of the patients in our study. Our hemorrhage rate was low (6,8%) unlike the literature (11,12%). Different studies investigating the effect of symptom-to-needle time on prognosis have shown that symptom-to-needle time is an important factor in clinical recovery in the following years (13-15). However, there was no correlation between symptom-to-needle time and mRS scores at the end of the third month in a recent study (16). Similarly, no correlation was found between symptom-to-needle time and mRS scores in our study.

Intracranial hemorrhage was reported as the most common and feared complication after IV tPA in the studies conducted (17-19). However, the bleeding rates reported in these studies varied since different definitions were made on intracranial hemorrhages. Intracranial hemorrhage was reported by Kutluk et al. (10) with 22% and by Çabalar et al. (15) with 23.9%. Unlike these studies, the rate of intracranial hemorrhage was 6.8% in our study. It is also possible to find a study that found the rate of intracranial hemorrhage to be as low as 3.8% apart from our study (20). It was observed that the mortality rate was reported by Kutluk et al. (10) with 30% (only due to intracranial hemorrhage) and by Çabalar et al. (15) with 21.7% when the literature was examined. No intracranial hemorrhage-related mortality was observed in our study. In addition, no other complications related to IV tPA treatment were observed in our study. There is also a study showing that thrombolytic therapy increased intracranial hemorrhages but this increase was not associated with an increase in mortality rate (18). The mortality rate was 6.8% (3 patients) in the first week and 15.9% (7 patients) in total after 3 months, none of which was due to hemorrhagic complications in our study. 3 patients with anterior circulation infarct died within 1 week after treatment. 3 patients with anterior circulation infarct and 1 patient with posterior circulation infarct died between the first week and the end of the third month. This mortality rate is reported to be 14.7% in the data of the Turkish Thrombolytic Therapy Study Group (10). The mortality rate was similar to the average in Turkey and mortality was generally observed in those with anterior circulation infarct in our study.

We believe that this treatment, which has a 15-year license in Turkey, is at the desired level in Adıyaman province. It came to our attention that 2 patients were admitted to our hospital in the first 4.5 hours and we were not able to administer IV tPA because there was no Alteplase in the hospital pharmacy. Considering the rates of patients who underwent total IV tPA, thrombolytic administration is considerable in Adıyaman. Information on the rates of thrombolytic administration could not be reached in the studies conducted (15,16,20).

As a result, the rate of acute ischemic stroke admission and thrombolytic therapy is increasing day by day in our clinic. It is a very important treatment option with proven efficacy and safety of IV r-tPA treatment under appropriate conditions and at the appropriate time for patients presenting with acute ischemic stroke. The stroke unit of our hospital strives to be one of the important centers in Turkey administering this therapy. Increasing awareness of thrombolytic therapy among both health personnel and the public and the application of this procedure by an experienced multidisciplinary stroke team will increase the chance of success of this treatment.

REFERENCES

1. Blackham KA, Meyers PM, Abruzzo TA, et al; Society for NeuroInterventional Surgery. Endovascular therapy of acute ischemic stroke: report of the standards of practice committee of the society of neurointerventional surgey. J Neurointerv Surg 2012; 4(2): 87-93.

2. Wolf PA, Kannel WB, Mc Gee DL. Epidemiology of strokes in North America. In: Barnett HJM, Stein BM, Mohr JP, Yatsu FM, (eds). Stroke: Pathophysiology, Diagnosis and Management. New York: Churchill Livingstone, 1986: 19-29.
3. Hacke W, Furlan AJ, Al-Rawi Y, et al. Intravenous desmoteplase in patients with acute ischemic stroke selected by MRI perfusion- diffusion weighted imaging or perfusion CT (DIAS-2): A prospective, randomized, double-blind, placebo controlled study. Lancet Neurol 2009; 8(2): 141-150.
4. Zeumer H, Freitag HJ, Knospe V. Intravascular thrombolysis in central nervous system cerebrovascular disease. Neurol Clin North Am 1992; 2: 359-369.
5. Aguiar de Sousa D, von Martial R, Abilleira S, et al. Access to and delivery of acute ischaemic stroke treatments: A survey of national scientific societies and stroke experts in 44 European countries. Eur Stroke J 2019; 4(1): 13-28.
6. Jauch EC, Saver JL, Adams HP Jr, et al.; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke. A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2013; 44(3): 870-947.
7. Hache W, Kaste M, Bluhmki E, et al; ECASS investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008; 359(13): 1317-1329.
8. NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N. Engl J Med 1995; 333(24): 1581-1587.
9. Bock BF. Proceedings of a National Symposium Rapid Identification and Treatment of Acute Stroke: Response System for Patients Presenting With Acute Stroke. Accessed: 23.08.2011
10. Kutluk K, Kaya D, Afsar N, et al; Turkish Thrombolysis Study Group. Analyses of the Turkish National Intravenous Thrombolysis Registry. J Stroke Cerebrovasc Dis 2016; 25(5): 1041-1047.
11. Okada Y, Sadoshima S, Nakane H, et al. Early computed tomographic findings for thrombolytic therapy in patients with acute brain embolism. Stroke 1992; 23(1): 20-23.
12. Brandt T, von Kummer R, Müller-Küppers M, et al. Thrombolytic therapy of acute basilar artery occlusion: variables affecting recanalisation and outcome. Stroke 1996; 27(5): 875-881.
13. Wardlaw JM, Murray V, Berge E, et al. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev 2009; 4: Cd000213.
14. Azzimondi G, Bassein L, Fiorani L, et al. Variables associated with hospital arrival time after stroke: effect of delay on the clinical efficiency of early treatment. Stroke 1997; 28(3): 537-542.
15. Çabalar M, Taşdemir N, Erdogan HA, et al. Akut İskemik İnmede İntravenöz Trombolitik Tedavi Deneyimlerimiz. Bakırköy Tıp Dergisi 2018; 14(1): 71-75
16. Oruç S, Demirtaş H, Yaman M, ve ark. Akut iskemik inmeli olgularda Kocatepe Üniversitesi Nöroloji Kliniği'nin intravenöz trombolitik tedavi deneyimleri. Türk Beyin Damar Hastalıkları Dergisi 2015; 21(3): 189-193.
17. Chapman SN, Mehndiratta P, Johansen MC, et al. Current perspectives on the use of intravenous recombinant tissue plasminogen activator (tPA) for treatment of acute ischemic stroke. Vasc Health Risk Manag 2014; 10: 75-87.
18. Hacke W, Donnan G, Fieschi C, et al. ATLANTIS Trials Investigators; ECASS Trials Investigators; NINDS rt-PA Study Group Investigators. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet. 2004; 363(9411): 768-774.
19. Wahlgren N, Ahmed N, Eriksson N, et al. Safe Implementation of Thrombolysis in Stroke-Monitoring STudy Investigators. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: Safe Implementation of Thrombolysis in Stroke-MOnitoring STudy (SITS-MOST). Stroke 2008; 39(12): 3316-3322.
20. Çetiner M, Canbaz Kabay S, Aydın H. Akut İskemik İnmede İntravenöz Trombolitik Tedavi: Kütahya Deneyimleri. Turk J Neurol 2017; 23(4): 193-198.

Ethics

Ethics Committee Approval: The study was approved by the Adıyaman University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Number: 2020/5-36, Date: 18.05.2020).

Informed Consent: The study is an retrospective data analysis, there is no need to obtain an informed from the patients.

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