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Retrospective Analysis of the Treatment of Patients with Acute Stroke in a Training and Research Hospital

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Abstract

Aim: This study aimed to evaluate the indications for intravenous recombinant tissue plasminogen activator (IV r-tPA) and/or mechanical thrombectomy in patients with acute stroke and the research intended to determine why these treatments were not applied in some cases.

Materials and Methods: This study included 300 stroke patients treated between January 2018 and June 2019 for whom the data were accessible. The patients with acute stroke were retrospectively examined with regards to demographic and clinical information.

Results: Of the 300 patients, 142 (47%) were females and 158 (52%) were males and 214 patients (71%) were admitted to the hospital within the first 4.5 hours. The mean age of the patients was 68.11±13.15 years (34-94 years). Moreover, 58 (19%) patients did not receive IV r-tPA and/or undergo mechanical thrombectomy owing to contraindications.

Conclusion: In this study, we determined that the most common reason for not applying IV r-tPA and/or mechanical thrombectomy was the inability of some patients to reach the hospital within the treatment window. Multi-centre studies are needed to investigate the various factors contributing to the delay in accessing treatment for patients with acute ischaemic stroke. Addressing these issues may increase the proportion of patients receiving thrombolytic therapy and/or undergoing mechanical thrombectomy.

Keywords: Acute stroke, thrombolytic therapy, mechanical thrombectomy

Introduction

Acute ischemic stroke is the third most common cause of mortality after coronary artery diseases and cancer (1). It is a severe neurological problem that ranks first worldwide in terms of morbidity. Approximately 6 million people die due to a stroke and 17 million people have a stroke each year (2,3). Ischemic strokes constitute more than 85% of all strokes (4). In our country, this rate was reported to be 71% (5).

In the treatment of acute ischemic stroke, intravenous recombinant tissue plasminogen activator (iv r-tPA) is the only approved medical treatment option for patients admitted in the treatment window (6,7). Endovascular treatment is recommended in patients with major vascular occlusion (8). Unfortunately, the most important obstacle to these treatments is the limited duration. 1.9 million neurons are lost in every minute of the brain until reperfusion is achieved (9).

However, despite the efficacy of iv r-tPA in acute ischemic stroke patients iv r-tPA, due to numerous limiting factors, it has been reported that only 3.0-8.5% of patients with ischemic stroke were applied iv r-tPA (10-12). The aim of this study was to evaluate the iv r-tPA and/or mechanical thrombectomy indications in the patients with acute stroke admitted to our emergency department and/or hospitalized at the neurology department and in case these treatments were not applied, to determine reasons why these treatments were not applied in our patients and to correct these issues.

Materials and Methods

Bursa Yüksek İhtisas Training and Research Hospital is a tertiary care hospital. In our hospital, periodic training on stroke is being provided to healthcare personnel since 4 years. A number of awareness programs have been organized to increase public awareness about stroke.

This study was presented as an oral presentation at the 15th International Emergency Medicine Congress (April 25-28, 2019).
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In our stroke centre, iv r-tPA was first administered to patients with acute ischemic stroke in 2016. Since 2017, mechanical thrombectomy is being performed in our hospital.

The study included 300 patients with accessible data who had been admitted to the emergency department of our hospital for the diagnosis of stroke and/or hospitalized in the neurology department due to stroke between January 2018 and June 2019. The study was approved by the ethics committee of Bursa Yüksek İhtisas Training and Research Hospital, decision numbered and dated: 2011-KAEK-25, 2019/06-28, and the requirement of informed consent was waived off because of the retrospective nature of the study. The patients with acute stroke were retrospectively examined with regards to demographic (age, sex) and clinical information (the time of stroke, admission time, risk factors for stroke, neurological examination findings, stroke severity, and radiological findings), whether iv r-tPA and/or mechanical thrombectomy treatment was applied, and the reasons why these treatments were not applied. Stroke severity at admission was determined using the National Institutes of Health Stroke Scale (NIHSS). In the case of wake-up strokes, the onset of the symptom was accepted as the last point in time when the patient appeared normal.

Statistical Analysis

The consistency of continuous variables to normal distribution was examined with the Kolmogorov-Smirnov test. According to the normality test result, continuous variables are expressed with mean, standard deviation, minimum and maximum values. Categorical variables were given as n (%) values as indicative statistics. SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) program was used for statistical analysis.

Results

Of the 300 patients, 142 (47%) were females and 158 (52%) were males; all the patients had been admitted between January 2018 and June 2019 to the emergency department of our hospital with the diagnosis of stroke and/or hospitalized in the neurology department due to stroke.

The mean age of the patients was 68.11±13.15 years (34-94 years). The time between the onset of stroke symptoms and admission to the emergency department varied from 15 minutes to 10 days, and the mean time was 5 (0.42:420) hours. NIHSS scores ranged between 0 and 32. Of the 259 (86%) patients diagnosed with ischemic stroke, 11 (3.6%) and 30 (10%) were diagnosed with intracerebral haemorrhage and transient cerebral ischemic attack, respectively.

Total 137 (45%) patients had been admitted to the hospital in the first 1.5 hours; 53 (17%), between 1.5 and 3 hours; 24 (8%), between 3 and 4.5 hours; 54 (18%), between 4.5 and 24 hours; and 32 (10.6%), after 24 hours. A total of 214 (71%) patients had been admitted to the hospital within the first 4.5 hours; 58 (19%) of the patients admitted to the hospital during the window period had contraindications for iv r-tPA.

When the patients were evaluated in terms of risk factors of stroke, it was found that 191 (63%), 64 (21%), 86 (28%), 104 (34%), 78 (26%), 86 (28%), and 57 (19%) of the patients had hypertension, hyperlipidemia, coronary artery disease, Diabetes mellitus, were smokers, history of stroke, and history of atrial fibrillation, respectively.

There were 64 (21%) patients with NIHSS of ≥6 who could not reach the hospital within the treatment window.

Ninety-seven (32%) patients with NIHSS of ≥6 who had been admitted to the hospital in the first 4.5 hours (treatment window) were examined, and it was found that 27 of these patients underwent iv r-tPA, three underwent iv r-tPA and mechanical thrombectomy, and nine underwent only mechanical thrombectomy. Fifty-eight (19%) of the patients did not undergo iv r-tPA and/or mechanical thrombectomy due to contraindications (Table 1).

Table 1. Reasons for non-treatment in patients with NIHSS of ≥6 who had been admitted to the hospital within the first 4.5 hours

Reason	Number	Percentage
Blood pressure could not be lowered	5	8.6%
Hypodensity >1/3 of the cerebral hemisphere	4	6.8%
Wake-up stroke	6	10.3%
Due to advanced age and other concomitant diseases	9	15.5%
Use of NOAC in the last 48 hours	1	1.7%
Thrombocytopenia	1	1.7%
Previous stroke in last 3 months	1	1.7%
Disability that prevents mobility	4	6.8%
Lack of consent	2	3.4%
Intracerebral giant aneurysm	1	1.7%
Major surgery performed within the previous 14 days	1	1.7%
Rapid recovering stroke	6	10.3%
Oral anticoagulant use and INR >1.7	2	3.4%
Suitable time window had passed before the examinations were completed	6	10.3%
Intracerebral haemorrhage	9	15.5%
Total	58	100%

NIHSS: National Institutes of Health Stroke Scale, NOAC: Non-vitamin K antagonist oral anticoagulant, INR: International normalized ratio

Of the 27 patients over the age of 80 years who had been admitted within the first 4.5 hours, eight underwent iv r-tPA, one underwent iv r-tPA and mechanical thrombectomy, and one underwent only mechanical thrombectomy.

Discussion

The license for the use of iv r-tPA in acute ischemic stroke was obtained in Turkey in 2006. Although the application of iv r-tPA in Turkey is not yet at the desired level, its use is gradually increasing (13). It has been shown that in the case of acute ischemic stroke, 15-minute decrease in the door-to-needle time leads to 5% decrease in mortality in iv r-tPA application (14).

It has been determined that the annual rate of stroke-related deaths has decreased by 34% in the 10-year period between 1997 and 2007 owing to the efforts conducted to combat stroke and the fact that treatments applied in the acute period are becoming increasingly common (15).

Unfortunately, previous studies have found the rates of patients treated with iv r-tPA to be far below the desired level owing to many factors (10-12), this is caused by different reasons in different countries (11,16).

Many patients are unable to reach the hospital within the treatment window. One of the most important reasons for the inability of patients to reach the hospital within the treatment window may be society's low level of knowledge on this subject (17).

In terms of treatment window, in this study, 63% and 71% of the patients were admitted to the hospital within the first 3 hours and 4.5 hours, respectively. This ratio was found to be higher compared with that in previous studies (18-23). This may be the result of the training and awareness-raising efforts regarding acute stroke that have been conducted over the past 3 years for healthcare professionals and the public.

In our study, there were 64 (21%) patients with NIHSS of ≥6 who could not reach the hospital within the treatment window, missing the opportunity for acute stroke treatment. In other words, had these patients arrived within the appropriate timeframe, these treatments could have been applied. A significant portion of these delays was due to the prolonged examination times within the hospital. There were six (2%) patients who reached the hospital within the treatment window, but they could not receive treatment as the treatment period was exceeded by the time their tests were completed.

There were 97 (32%) patients with NIHSS of ≥6 who admitted to our hospital within the treatment window. Of these patients, 27 received iv r-tPA, three received iv r-tPA and mechanical thrombectomy, and nine received mechanical thrombectomy. Fifty-eight (19%) of the patients could not be treated due to contraindications.

iv r-tPA and/or mechanical thrombectomy were not considered for six of the patients who arrived at the appropriate time, because these patients had rapid recovery and no significant deficits remained. The administration of iv r-tPA is recommended for patients who improve noticeably but continue to have significant deficits (24,25).

It has been reported that iv r-tPA can be administered in aneurysms with a diameter of <10 mm (26). Thrombolytic therapy was not performed in one of our patients due to a giant aneurysm with a diameter of >10 mm in the intracerebral artery.

Although the risk of intracerebral haemorrhage is higher in elderly patients, the use of iv r-tPA is recommended in patients over 80 years old unless there are other exclusion criteria (27,28). In nine patients, iv r-tPA was not administered due to the increased risk of intracerebral haemorrhage associated with advanced age and other accompanying risk factors. Of the 27 patients who were ≥80 years old and arrived at the hospital in the first 4.5 hours, eight received iv r-tPA, one received iv r-tPA + mechanical thrombectomy, and one received only mechanical thrombectomy.

Patients do not benefit adequately from iv r-tPA when they have a mobility-preventing disability that develops before the stroke. However, iv r-tPA is still recommended moderate disability or in patients who can remain standing with assistance (27-30). In our study, four bed-ridden patients were not treated due to their mobility-preventing disability.

Before initiating iv r-tPA treatment, blood pressure must be below 185/110 mmHg to reduce the risk of intracerebral haemorrhage (27,31). In five of our patients, iv rt-PA was not administered due to blood pressure that could not be reduced below 185/110 mmHg despite antihypertensive treatment.

Two patients did not receive iv r-tPA treatment due to warfarin use and an international normalized ratio (INR) value of >1.7. IV r-tPA is administered in patients using oral anticoagulants if their INR is <1.7 (31).

Study Limitations

The limitations of the present study include the limited number of patients, the inclusion of a single centre, and the lack of access to certain data owing to the retrospective nature of the study. This study investigated and presented the reasons why current treatment modalities for acute stroke treatment, such

as thrombolytic treatment and mechanical thrombectomy, were not applied in some of our patients.

Conclusion

In our study, we determined that the most common reason for not applying iv r-tPA and mechanical thrombectomy treatments out of contraindications to patients was the fact that these patients could not reach the hospital within the treatment window and loss of time that occurred during the examinations and tests performed in the hospital.

To ensure the application of treatments, such as r-tPA and mechanical thrombectomy, which are life-saving and prevent disabilities, it is necessary to prepare algorithms in the hospital so that the processes after a patient is admitted to the emergency department can be managed rapidly. Addressing these factors may increase the ratio of patients who can receive thrombolytic therapy or undergo mechanical thrombectomy.

Ethics

Ethics Committee Approval: The study was approved by the ethics committee of Bursa Yüksek İhtisas Training and Research Hospital, decision numbered and dated: 2011-KAEK-25, 2019/06-28.

Informed Consent: The requirement of informed consent was waived off because of the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

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References

1. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:517-84.
2. Blackham KA, Meyers PM, Abruzzo TA, Albuquerque FC, Fiorella D, Fraser J, 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;4:87-93.
3. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet. 2014;383:245-54.
4. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee Heart disease and stroke statistics—2008 update: a report from the American Heart Associations Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008;117:e25-146.
5. Özdemir G, Özkan S, Uzuner N, Özdemir Ö, Gücüyener D. Türkiye'de beyin damar hastalıkları için major risk faktörleri. Türk çok merkezli stroke çalışması. TBDHD. 2000;6:31-5.
6. NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N. Engl J Med. 1995;333:1581-7.
7. Hache W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. ECASS investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359:1317-29.
8. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et al. American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guidelinefor Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015;46:3020-35.
9. Saver JL. Time is brain–quantified. Stroke. 2006;37:263-6.
10. Reeves MJ, Arora S, Broderick JP, Frankel M, Heinrich JP, Hickenbottom S, et al. Coverdell Prototype Registries Writing Group. Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry. Stroke. 2005;36:1232-40. [Epub 2005 May 12].
11. Eissa A, Krass I, Bajorek BV. Barriers to the utilization of thrombolysis for acute ischaemic stroke. Journal of Clinical Pharmacy and Therapeutics. 2012;37:399-409.
12. Hills NK, Johnston SC. Why are eligible thrombolysis candidates left untreated? Am J Prev Med. 2006;31:S210-6.
13. Kutluk K, Kaya D, Afsar N, Arsava EM, Ozturk V, Uzuner N, et al. Turkish Thrombolysis Study Group. Analyses of the Turkish National Intravenous Thromboliysis Registry. J Stroke Cerebrovasc Dis. 2016;25:1041-7.
14. Fonarow GC, Smith EE, Saver JL, Reeves MJ, Bhatt DL, Grau-Sepulveda MV, et al. Timeliness of tissue-type plasminogen activator therapy in acute ischemic stroke: Patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes: Circulation. 2011;123:750-8.
15. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. Circulation. 2011;123:e18-e209.
16. Baatiema L, Otim ME, Mnatzaganian G, de-Graft Aikins A, Coombes J, Somerset S. Health professionals' views on the barriers and enablers to evidence-based practice for acute stroke care: a systematic review. Implement Sci. 2017;12:74.
17. Kim YS, Park SS, Bae HJ, Heo JH, Kwon SU, Lee BC, et al. Public awareness of stroke in Korea: a population-based national survey. Stroke. 2012;43:1146-9.
18. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke: influence on time to presentation. Stroke.1997;28:912-5.
19. Lacy CR, Suh DC, Bueno M, Kostis JB. Delay in presentation and evaluation for acute stroke: stroke time registry for outcomes knowledge and epidemiology (S.T.R.O.K.E.). Stroke. 2001;32:63-9.
20. Azzimondi G, Bassein L, Fiorani L, Nonino F, Montaguti U, Celin D, et al. Variables associated with hospital arrival time after stroke: effect of delay on the clinical efficiency of early treatment. Stroke. 1997;28:537-42.
21. Chen CH, Tang SC, Tsai LK, Hsieh MJ, Yeh SJ, Huang KY, et al. Stroke code improves intravenous thrombolysis administration in acute ischemic stroke. PLoSOne. 2014;9:e104862.
22. Tekin B, Yatmazoğlu M, Acar E, Senadim S, Çoban E, Dayan C, et al. Pre-hospital Obstacles in Thrombolytic Therapy and Suggested Solutions. Turk J Cerebrovasc Dis. 2015;21:194-7.
23. Ashraf VV, Maneesh M, Praveenkumar R, Saifudheen K, Girija AS. Factors delaying hospital arrival of patients with acute stroke. Ann Indian Acad Neurol. 2015;18:162-6.
24. Re-examining Acute Eligibility for Thrombolysis Task Force; Levine SR, Khatri P, Broderick JP, Grotta JC, Kasner SE, Kim D, et al. NINDS rt-PA Stroke Trial Investigators. Review, historical context, and clarifications of the NINDS rt-PA stroke trials exclusion criteria: Part 1: rapidly improving stroke symptoms. Stroke. 2013;44:2500-5.
25. Topçuoğlu MA, Arsava EM, Özdemir AÖ, Gürkaş E, Necioğlu Örken D, Öztürk Ş. Intravenous thrombolytic therapy in acute stroke: Problems and solutions. Turk J Neurol. 2017;23:162-75.

26. Kim JT, Park MS, Yoon W, Cho KH. Detection and significance of incidental unruptured cerebral aneurysms in patients undergoing intravenous thrombolysis for acute ischemic stroke. J Neuroimaging. 2012;22:197-200.

27. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, et al. Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016;47:581-641.

28. Topçuoğlu MA, Arsava EM, Özdemir AÖ, Gürkaş E, Necioğlu Örken D, Öztürk Ş. Intravenous Thrombolytic Therapy in Acute Stroke: Frequent Systemic Problems and Solutions. Turk J Neurol. 2018;24:13-25.

29. Foell RB, Silver B, Merino JG, Wong EH, Demaerschalk BM, Poncha F, et al. Effects of thrombolysis for acute stroke in patients with pre-existing disability. CMAJ. 2003;169:193-7.

30. Merlino G, Corazza E, Lorenzut S, Gigli G, Cargnelutti D, Valente M. Efficacy and safety of intravenous thrombolysis in patients with acute ischemic stroke and pre–existing disability. J Clin Med. 2019;8:400.

31. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. American Heart Association Stroke Council. 2018 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. 2018;49:e46-110.