

Thrombolytic Therapy in Strokes: A Retrospective Clinical Data Analysis of 40 Patients in a 7-Year Period: The Experience of a Greek Internal Medicine Department

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Abstract

Stroke is one of the main causes of mortality and disability in developed countries. In acute ischemic stroke, the standard treatment is recombinant tissue plasminogen activator (rt-PA). The benefits of the treatment depend on the time of administration, the earlier it is administered, the greater its benefit. There are limited studies on the retrospective outcome of thrombolytic therapy in patients with acute ischemic stroke outside of clinical trials. The present retrospective study aimed to analyze the clinical data of 40 patients over 7 years who were hospitalized with acute ischemic stroke at the AHEPA University Hospital in Greece. From January 2013 to December 2020, 40 patients with acute ischemic stroke were admitted and treated. Computed tomography (CT) was performed at 24 h after thrombolytic treatment or earlier in case of neurological worsening. The hospital had 3 months follow-up at the stroke clinic and data consisting of the National Institute of Health Stroke Scale (NIHSS), functional outcome assessed by modified Rankin Scale (mRS) and mortality were reviewed in the medical records from the stroke clinic. The clinical outcome of functional independence defined by the modified Rankin Scale (mRS) ≤ 2 at 3 months was evaluated. Safety outcomes were in-hospital mortality, mortality at 3 months, and symptomatic intracerebral hemorrhage (sICH) defined by the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria. The main finding of the present study, that there was an overall reduction in the NIHSS scale after thrombolysis, proves that the patients showed improvement after performing thrombolysis. Consequently, from the total of 40 thrombolysis performed at the clinic, it can be concluded that most patients had a good outcome.

Keywords: Stroke, thrombolytic therapy, rtPA, NIHSS scale, mRS measurements.

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INTRODUCTION

Stroke is one of the main causes of mortality and disability with enormous subsequent economic and social costs (Hurford R *et al.*, 2020). Therefore, immediate, and effective management of stroke is an important public health goal. In acute ischemic stroke, the standard treatment is recombinant tissue plasminogen activator (rtPA) administration (Powers WJ *et al.*, 2019); and since its introduction stroke treatment has changed dramatically (Dorado L *et al.*, 2014). The American Stroke Association (Powers WJ *et al.*, 2019) guidelines for acute ischemic stroke recommend the immediate (within 4.5 hours from the onset of the episode) provision of Intravenous thrombolytic therapy in eligible patients. The benefits of the treatment depend on the time of

administration, the earlier it is administered, the greater its benefit. However, despite the guidelines and the positive results of standard treatment, the percentage of patients receiving intravenous thrombolysis (IVT) is relatively low (Kepplinger J *et al.*, 2016). Previous randomized controlled trials have found that administration of intravenous thrombolysis within 3 hours of the onset of an acute ischemic episode result in a 10-30% reduction in patient disability and mortality 3 to 6 months after treatment (Wardlaw JM *et al.*, 2014, Emberson J *et al.*, 2014, Turc G *et al.*, 2014). A non-contrast CT scan of the head to rule out intracranial hemorrhage is usually sufficient to make decisions regarding the administration of thrombolysis therapy (Hurford R *et al.*, 2020).

Despite its proven effectiveness of rtPA, limitations, such as the small-time window, the risk of major bleeding, the low arterial recanalization rate, and the moderate effect in unselected patients often result in fewer patients who benefit from and receive thrombolytic therapy (Derex L *et al.*, 2002, Harraf F *et al.*, 2002, Barber PA *et al.*, 2001).

Besides large clinical trials, there are limited studies on the retrospective outcome of thrombolytic therapy in patients with acute ischemic stroke (Tong X *et al.*, 2014). The present retrospective study aimed to analyze the clinical data of patients who received thrombolytic therapy for ischemic stroke in an Internal Medicine Clinic of a University Hospital in Northern Greece.

METHODS

After receiving approval from the committee of medical ethics, we retrospectively analyzed the medical records of all patients with acute ischemic stroke who received thrombolytic therapy from January 2013–December 2020 in the First Propaedeutic Department of Internal Medicine, AHEPA University Hospital, Thessaloniki, Greece. Baseline characteristics including gender, age, initial National Institute of Health Stroke Scale (NIHSS), and underlying diseases were collected. The clinical outcome of functional independence defined by modified Rankin Scale (mRS) ≤ 2 at 3 months was also evaluated and outcomes such as in-hospital mortality, mortality at 3 months, and symptomatic intracerebral hemorrhage (sICH) defined by the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria (IST-3, 2013) were also reviewed.

RESULTS

The sample of the survey was 40 patients: 52.5% (n=21) men and 47.5% (n=19) women; with an average age of 72.23 years (range 41-85 years old). Computed tomography (CT) was performed at 24 h after thrombolytic treatment or earlier in case of neurological worsening.

The mean NIHSS score at admission was 13.625 ± 3.88 (range 5-19), while the mean NIHSS score at discharge was 8.57 ± 10.44 (range 0-39), i.e., a 4.75-point decrease in the mean score. There were four deaths, 6.1% two at the clinic and two after intubation in the ICU. Three of them had a Large Vessel Occlusion (1 VA, 2 MCA). The bad outcome was related to stroke-related respiratory infections. None of them died due to IVT side effects. From the 36 patients that were discharged, the NIHSS was 5.19 ± 1.99 .

The mean mRS score at discharge was 2.87 ± 1.36 (range 0-6). Most of them 55% (22/40) were discharged at home while 35% (14/40) were admitted to a Rehabilitation Facility. The mRS score of the survived discharged patients was 2.53 ± 0.9 .

Complications related to the thrombolysis were hematuria and hemorrhagic conversion and there were also recorded two cases of stroke-related complications of aspiration pneumonia.

Of the total CT examinations performed, 16 revealed ischemic infarction, yet with various localization. A Large Vessel Occlusion was detected in 17 cases while 23/40 had smaller vessel territory infarcts (Table 1).

Table 1: Descriptive measures of the patients with Acute Stroke hospitalized in Internal Medicine Department 2013-2020

N	Age mean \pm sd	Gender	NIHSS-at admission mean \pm sd	NIHSS-at discharge mean \pm sd	mRS at discharge mean \pm sd	Deaths	Stroke Territory	Large Vessel Occlusion	Thrombolysis Side effects
40	72,23 \pm 7,68 Range 42-85	21Male 19 Female	13,625 \pm 3,89 Range 5-19	8,57 \pm 10,44 Range 0-39	2,88 \pm 1,36 Range 0-6	4	ACA 2 MCA 12 VA 2 BA 1 SA 23	17/40	1 Hemorrhagic Transformation 1 Hematuria

ACA: Anterior cerebral Artery, MCA: Middle cerebral Artery, VA: Vertebral Artery, BA: Basilar Artery, SA: Smaller arteries

Vascular ultrasound examinations included atheromatous plaques (20%), atheromatous lesions (22.9%), calcifications (17.1%), vascular stenoses (25.7%), and complete interception syndrome (5.7%). Yet, in 3% of the patient ultrasonographic evaluation was normal and in 5.6% of the cases, there was no ultrasound assessment due to time constraints.

DISCUSSION

There was an overall reduction in the NIHSS scale after thrombolysis, with most patients having a good result. The latter, in combination with the relatively small incidence of serious side effects, suggests proper selection and good therapeutic management.

Unfortunately, the number of patients eligible for rtPA administration was limited.

Like these findings, in the study of Karadeli & Simsekoglu (Karadeli H *et al.*, 2021) on 47 patients with mild stroke who received tPA, the NIHSS scores of patients decreased significantly after the treatment. The mRS scores at the first and third months were significantly decreased according to the mRS scores when they entered the treatment, proving the efficacy of iv-tPA in patients with acute ischemic stroke and mild symptoms and demonstrating the low-risk profile of this therapy. Hemorrhagic transformation was observed in 3 of 40 patients, and only one patient experienced neurological deterioration after treatment.

Our study is in line with previous studies regarding the low mortality and side effects of thrombolytic treatment (Emberson J *et al.*, 2021). It has also demonstrated its efficacy in the cases of LVO that have been questioned previously in the Era of Thrombectomy (Hassan AE *et al.*, 2021). Unfortunately, the percentage of patients that arrive in the appropriate timeframe at hospital, is still limited. From the total of 235 and 242 stroke patients who arrived in the emergency department of our clinic, in 2019 and 2018, only seven and nine respectively were eligible for rescue therapy with IVT. In most of the cases, the exclusion criterion was the admission beyond the time-window. Unfortunately, in-Hospital delays are a common phenomenon in our case and that has a major impact on our performance. Previously reported in-Hospital delays improvement have contributed to less mortality and morbidity (Darehed D *et al.*, 2020). The first assessment of the stroke in all the above cases was made by an internist and the IVT was performed in collaboration with the neurological department. This fact underlines the need for all the physicians in the emergency department to get familiarized with the signs and symptoms of acute stroke and develop protocols for fast and efficient treatment in collaboration with neurologists.

In Greece, it is a common practice to assess first, a possible stroke patient, the internist. Especially when the patient is over 65 years old with a variety of comorbidities. Internists in the ER department should be aware of the symptoms of an acute stroke and act based on specific protocol procedures in collaboration with Neurologists because “Time is Brain”. Previous reports suggest that this practice can be equally effective for patients (Chew SH *et al.*, 2021). Finally, although the increase in the number of performed IVTs in recent years, we still have a long way to reach the number of IVTs performed in other European countries. The training of the physicians along with the public information regarding the “Face Arm Speech” symptoms will lead to better acute management and consequently less morbidity and mortality to our stroke patients.

The effectiveness of the application of thrombolysis therapy versus the best medical treatment in patients with ischemic stroke has been documented previously. The benefit of IVT has led to the broadened of its off-label use in the population, which was earlier considered prohibited (Tsvigoulis G *et al.*, 2021), such as recent prior stroke (Koutroulou I *et al.*, 2021), minor stroke (Khatri P *et al.*, 2012), recent intake of DOACs (Meinel TR *et al.*, 2023) extended timeframe (IST-3, 2013) or cancer (Huang S *et al.*, 2020). Khatri *et al.*, (Khatri P *et al.*, 2012) performed a 90-day neurological follow-up data analysis of mild stroke patients without thrombolytic therapy and found that 29% of them, a significant proportion, developed a disability. Similarly, Haeblerlin (Haeblerlin MI *et al.*, 2020) performed an analysis of the 3-month functional outcomes of 108 patients who received iv-tPA and compared them with 262 patients who received the best available medical treatment. The findings showed that those who received thrombolytic therapy had experienced full remission. In the study of González (González RG *et al.*, 2013), treatment with IV-tPA resulted in significantly better outcomes in severely symptomatic stroke patients with major anterior circulation infarcts, with a good outcome rate of 35% (NIHSS>10), compared to patients who did not receive thrombolytic therapy. The recent cohort study of Meinel (Meinel TR *et al.*, 2023) included 64 centers in Europe, Asia, Australia, and New Zealand and a total of 33,207 patients with ischemic stroke, found that administration of intravenous thrombolysis reduced the risk of intracranial bleeding among 832 patients receiving immediate oral anticoagulation. IST-3 Collaborative Group's (Sang-Won Park *et al.*, 2022) 18-month follow-up study found that patients who received thrombolysis with rtPA were functionally better.

LIMITATIONS

Unfortunately, our department had no documentation of the precise door-to-needle time. Moreover, detailed follow-up data are missing while all the patients were referred to the Vascular Neurological outpatient clinic of our hospital. Finally, all the above cases were hospitalized before the development of the thrombectomy facilities in our hospital that now exist.

CONCLUSION

In the present retrospective analysis of clinical data, thrombolysis therapy appeared to be effective, with a limited rate of adverse events, and the clinical course of most patients had a good outcome. The improved NIHSS demonstrates the effectiveness of rtPA, which has been supported in past research. The need for the formation of interdisciplinary medical teams in the ER department to treat fast and efficient stroke patients is a fact. Complete documentation of the Department's performance regarding stroke management can lead to its constant practice improvement.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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