

Hurdles in stroke thrombolysis: Experience from 100 consecutive ischemic stroke patients

Sagar Badachi, Thomas Mathew, Arvind Prabhu, Raghunandan Nadig, Gosala R. K. Sarma

Department of Neurology, St. John's Medical College Hospital, Bengaluru, Karnataka, India

Abstract

Background: Acute management of ischemic stroke involves thrombolysis within 4.5 h. For a successful outcome, early recognition of stroke, transportation to the hospital emergency department immediately after stroke, timely imaging, proper diagnosis, and thrombolysis within 4.5 h is of paramount importance. **Aim:** To analyze the obstacles for thrombolysis in acute stroke patients. **Materials and Methods:** The study was conducted in a tertiary care center in South India. A total of hundred consecutive patients of acute ischemic stroke who were not thrombolysed, but otherwise fulfilled the criteria for thrombolysis were evaluated prospectively for various factors that prevented thrombolysis. The constraints to thrombolysis were categorized into: i) Failure of patient to recognize stroke symptoms, ii) patient's awareness of thrombolysis as a treatment modality for stroke, iii) failure of patient's relative to recognize stroke, iv) failure of primary care physician to recognize stroke, v) transport delays, vi) lack of neuroimaging and thrombolysis facility, and vii) nonaffordability. **Results:** The biggest hurdle for early hospital presentation is failure of patients to recognize stroke (73%), followed by lack of neuroimaging facility (58%), nonaffordability (56%), failure of patient's relative to recognize stroke (38%), failure of the primary care physician to recognize stroke (21%), and transport problems (13%). Awareness of thrombolysis as a treatment modality for stroke was seen only in 2%. **Conclusion:** Considering the urgency of therapeutic measures in acute stroke, there is necessity and room for improvement to overcome various hurdles that prevent thrombolysis.

Key Words

Hurdles, hurdles in acute stroke management, ischemic stroke, stroke thrombolysis

For correspondence:

Dr. Thomas Mathew, Department of Neurology, St. John's Medical College Hospital, Sarjapur Road, Bengaluru - 560 034, Karnataka, India.
E-mail: chakkuthom@hotmail.com

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Introduction

Acute management of stroke involves thrombolysis within 4.5 h. For a successful outcome, early recognition of stroke, transportation to the hospital emergency department immediately after stroke, timely imaging, proper diagnosis, and thrombolysis within 4.5 h is of paramount importance. The rate of thrombolysis all over the world is barely 1-3% due to many lapses in any of the above factors.

Stroke is one of the most common causes of death and long-term disability.^[1] The developing world carries the highest burden of stroke mortality and stroke-related disability. The stroke in developing countries has grown to epidemic proportions.

Two-thirds of global stroke occurs in low- and middle-income countries.^[2] There has been limited progress in management of patients with stroke in developing countries and data on stroke care in these countries are sparse.^[3] Guidelines are continuously developed and updated in the developed world, but their practicality for use in developing regions is unrealistic.^[4] The use of intravenous thrombolytic therapy with recombinant tissue plasminogen activator (r-tPA) has been demonstrated to improve clinical outcome in selected patients with ischemic stroke.^[5] Even with the extension of the time window from 3 h to the first 4.5 h after symptom onset; there is strong evidence of better outcome the earlier the treatment is started, as its efficacy is related to the time from symptom onset to treatment.^[6] In 2009, 3.4-5.2% of acute ischemic stroke patients in the United States received thrombolytics.^[7] In Scotland, 6% of stroke patients received thrombolysis in 2010.^[8] Stroke thrombolysis is currently used in few developing countries like Brazil, Argentina, Senegal, Iran, Pakistan, China, Thailand, and India.^[9] The number of stroke patients receiving r-tPA in the third world is extremely low. In a study from Pakistan, the rate of thrombolysis was 0.52-1.5%.^[10]

Aim

To analyze the obstacles for thrombolysis in acute stroke patients in a tertiary care setting.

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Materials and Methods

The study was conducted in a tertiary care center in South India with well-established emergency and neurological care. A total of 100 consecutive patients of acute ischemic stroke who were not thrombolysed but otherwise fulfilled the inclusion and exclusion criteria for thrombolysis^[5] were evaluated prospectively for various factors that prevented thrombolysis. Period of study was from January 2014 to June 2014. Demographic data was collected followed by detailed neurological examination and neuroimaging. A questionnaire was provided to investigate the factors that deprived the patients of thrombolysis. The constraints to thrombolysis were categorized into:

1. Failure of patients to recognize stroke symptoms,
2. Awareness of thrombolysis as a treatment modality,
3. Failure of patient's relative to recognize stroke,
4. Failure of the primary care physician to recognize stroke,
5. Transport delay,
6. Lack of neuroimaging and thrombolysis facility in the first hospital of arrival, and
7. Nonaffordability. Descriptive statistics were used where ever necessary.

Results

A total of 100 consecutive acute ischemic stroke patients were evaluated for various factors that prevented thrombolysis; 69 patients were males and 31 females. Average age of patient in this study was 59.23 ± 10.92 years (mean \pm standard deviation (SD)). Hypertension was the commonest risk factor for stroke (73%), followed by dyslipidemia (67%), diabetes mellitus (65%), smoking (31%), and atrial fibrillation (2%). According to Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, 62 patients had large artery stroke, 35 patients had lacunar stroke, two patients had cardioembolic stroke, and one patient had stroke due to patent foramen ovale. Seventy-two patients had anterior circulation strokes and 28 had posterior circulation strokes. During the period of study, only four patients were thrombolysed with intravenous (IV) tPA (4%).

Time to reach the nearby hospital

Thirty patients arrived at the nearest primary healthcare hospital within 3 h, three patients arrived between 3 and 4.5 h, 15 patients reached between 4.5 and 6 h, 34 patients reached nearest primary healthcare hospital between 6 and 24 h, 16 patients reached between 24 and 72 h, and two patients reached beyond 72 h. Mean time to reach nearest primary healthcare hospital was 18.02 ± 26.98 h (mean \pm SD).

Time to reach the tertiary care hospital

Seven patients arrived within 6 h after stroke onset at a tertiary care hospital where thrombolysis facility was available, 52 patients reached between 6 and 24 h, 15 patients reached between 24 and 48 h, 13 patients reached between 48 and 72 h, and 13 patients reached beyond 72 h. Median time to reach tertiary care hospital was 40.87 ± 45.17 h (mean \pm SD).

Distance to hospital with stroke care facility

Sixty-one patients had to travel 50 km or less to reach tertiary care center, 20 patients had to travel 50-100 km. Eleven, six, and

two patients had to navigate 100-150, 150-200, and more than 200 km, respectively to reach tertiary care hospital. Average distance to reach tertiary care center was 60.83 ± 66.96 km (mean \pm SD).

Patient's recognition of stroke symptoms

Seventy-three patients had neglected initial stroke symptoms which included 51 males and 22 females. 73.9% of males (51/69) and 70.9% (22/31) females in this study had neglected initial stroke symptoms. Initial stroke symptoms were right or left hemiparesis in 51 patients, slurring of speech in 20 patients, and giddiness in 29 patients. Symptoms were neglected by 74.51% patients with right or left hemiparesis, 68.9% patients with giddiness, and 75% patients with slurring of speech.

Other hurdles

In 38 patients, initial stroke symptoms went unrecognized by accompanying relative. Awareness of thrombolysis as a treatment modality was present in only two patients. Primary care physician failed to recognize stroke in 21 patients, 13 patients had difficulty arranging for transportation, and 58 primary healthcare hospitals did not have facility for neuroimaging. Annual income was less than Rs. 50,000 in 13 patients, Rs. 50,000-1,00,000 in 30 patients, Rs. 100,000-150,000 in 16 patients, Rs. 150,000-2,00,000 in four patients, and more than Rs. 2,00,000 in 37 patients. Average income per annum was Rs $190,900 \pm 200,822$ (mean \pm SD, range Rs. 10,000-60,000). When questioned, 56 patients would have refused thrombolysis citing financial constraint even if they had arrived within 3 h. Various hurdles for thrombolysis are shown in Table 1.

Discussion

The results of our study suggest that prehospital delay in patients with acute stroke was considerable and that there are long intervals between the onset of symptoms and the initiation of seeking medical help. One of the most important prehospital barriers of thrombolysis therapy in the developing world is nonrecognition of stroke warning signs by patients at risk, families, the general public, and even health workers in some places.^[11]

Failure of patients to recognize stroke

Seventy-three percent patients had neglected initial stroke symptoms in this study, by and large standing out as single most important factor for prehospital delay. There is poor recognition of stroke symptoms in developing countries.^[12] The people at the highest risk have the lowest knowledge regarding vascular disease including limitations to ascertain

Table 1: Hurdles in thrombolysis

Hurdles	Percentage (n = 100)
Failure of patients to recognize stroke	73
Awareness of thrombolysis as treatment modality	2
Failure of patient's relative to recognize stroke	38
Failure of the primary care physician to recognize stroke	21
Transport delay	13
Lack of neuroimaging facility in the first hospital of arrival	58
Nonaffordability	56

mild and transient symptoms as stroke.^[13] Several factors are related to decision delay, including failure to recognize stroke symptoms, not regarding symptoms as serious because of a lack of knowledge, a wait-and-see attitude, a hope that symptoms will resolve, and hesitation to contact emergency services.^[14] The lack of awareness regarding stroke symptoms is believed to influence prehospital delay in stroke. Less is known about the proportion of the delay accounted for by the hesitation to seek medical assistance as a response to the symptoms.^[15] Most stroke patients attending a university hospital in India were not aware of the importance of the time window in stroke management. Only one in 25 patients attending a stroke clinic and 27% of patients presenting to the stroke services in a tertiary care hospital in India were aware that they had suffered a stroke.^[16] In the study conducted by Faiz *et al.*, decision delay accounted for 62.3% of prehospital delay.^[17] In study by Chang *et al.*, decision delay accounted for 45% of the prehospital delay.^[18]

Failure of patient's relative to recognize stroke

In 38 patients, initial stroke symptoms went unrecognized by accompanying attender. This is a significant factor contributing to prehospital delay. General public needs to be enlightened about stroke symptoms so that they act in a timely manner. This is especially true for attenders of elderly stroke patients where the patients may not have acuity as well as energy to respond appropriately after stroke.

Failure of the primary care physician to recognize stroke

Primary care physician failed to recognize stroke in 21 patients. Primary care physician may not be able to recognize subtle symptoms and signs of stroke. Most common mistake done is attributing symptoms to raised blood pressure which is a normal compensatory response of body to stroke. Primary care physician without knowledge of this compensatory response may accentuate the ongoing damage by further reducing blood pressure. Training programs is needed for primary care physicians so that they will be capable enough to recognize stroke early.

Transport problem

Thirteen patients had difficulty arranging for transportation. A dedicated ambulance service for stroke patients may circumvent this hurdle as evident from study by Mosley *et al.*^[19] There is hardly any ambulance service, especially rural areas, in most of the developing countries.^[9] Government and panchayats should act in concert to provide emergency ambulance services round the clock to mitigate prehospital delay due to transport problem. Ambulance drivers should be primed about the location of nearest thrombolysis center, thereby helping patients to get maximum benefit of thrombolysis. Because of the above mentioned factors, median time to reach tertiary care hospital in our study was 40.87 ± 45.17 h (mean ± SD). In a study from the United Kingdom and Ireland, median time between symptom onset and arrival to the hospital was 123 min for those calling the emergency medical services, compared with 432 min for patients who first saw their general practitioner.^[20] In a study from Iran, 980/1,144 (85.6%) patients were initially excluded from the study because of late arrival.^[21] In a study from Lebanon, only nine out of 87 patients received IV r-TPA and delayed presentation was the main barrier to thrombolysis.^[22]

Lack of neuroimaging and thrombolysis facility in the first hospital of arrival

Fifty-eight primary healthcare hospitals did not have facility for neuroimaging in the current study. Infrastructure is a significant barrier against thrombolysis in developing world. A general overview shows that the quality and quantity of stroke care is largely patchy in low- and medium-developed countries with areas of excellence intermixed with areas of severe need depending upon location and socioeconomic status.^[16] In China, 40% of 1,500 neurology departments have the infrastructure to facilitate thrombolysis therapy for a population of 1.3 billion.^[23] In the African continent, the situation of stroke care is much worse; only northern African countries and South Africa have an appropriate number of CT and some MRI scanners.^[24] It is unfortunate to note that many tertiary care hospitals in India are not geared up to provide thrombolysis facility.

Nonaffordability

In our study, 56 patients would have refused thrombolysis citing financial constraint. In India, thrombolysis facility is mainly available in private setups and cost of r-tPA is substantial. One of the main reasons of low utilization of thrombolytic therapy in developing countries is financial constraints because r-tPA in developing countries has high cost.^[9] Government and NGOs should play an active role to make r-tPA available at a subsidized rate. A study from south India reported that 30% of stroke patients reached the hospital within 3 h post-event and 16% were eligible for thrombolysis therapy, but all of these eligible patients belonged to a lower socioeconomic group and could not afford the therapy due to its high cost.^[25] Among 23 stroke patients admitted in a private hospital in northwest India who were eligible to intravenous thrombolysis, only five actually received the drug and the remaining patients were unable to afford the high cost of treatment.^[25]

Knowledge regarding stroke among the public seems to be poor in the current study. There should be more focus on the "time is brain" paradigm to accentuate acute stroke as a condition of medical emergency in a similar manner as acute coronary syndrome (ACS). Prehospital delay is longer for stroke than for ACS.^[26] Even though there is a pathophysiological overlap between the two conditions; one of the main reasons is that pain is a symptom in the majority of patients with ACS, whereas pain is rarely associated with stroke. Equally important is the difference in symptom distribution. Patients with stroke will potentially have significant deficits, such as aphasia, reduced consciousness, or cognitive impairment; preventing them from seeking help and thereby increasing the decision delay and the prehospital delay. Public education campaigns to increase awareness of stroke symptoms such as the face arm speech time (FAST)^[27] campaign, have been initiated in several countries. Such campaigns are much needed in the developing countries. The limitation of the current study is that it is a single-center study with only 100 patients of stroke. In a country like India with almost 1 billion people belonging to diverse sociocultural, educational, and economic strata; multicenter studies involving larger number of stroke patients should be done for finding the various hurdles for stroke thrombolysis and to confirm whether our findings hold true in a larger group of stroke patients.

Conclusion

The biggest hurdles for early hospital presentation of acute stroke patients are failure of patients to recognize stroke, lack of neuroimaging facility, nonaffordability, failure of patient's relative to recognize stroke, failure of the primary care physician to recognize stroke, and transport problem.

The need of the hour is educational efforts focusing the public, the training of emergency physicians, and improving the infrastructure in district hospitals. Neuroimaging facilities should be improved and should be made affordable. Transport delays may be avoided by using dedicated ambulance services. r-TPA should be made available at subsidized rates to circumvent financial barrier of stroke thrombolysis. Finally, a national stroke prevention program with special emphasis on thrombolysis should be started.

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