Factors delaying management of acute stroke: An Indian scenario

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ABSTRACT

Background and Purpose: The purpose of this study was to assess factors causing delay in treatment of acute stroke in a tertiary care institute in South India.

Methods: All clinically suspected cases of acute stroke presenting to the emergency department over a period of 1 year were prospectively followed up and data collected as per a preset pro forma. The various time intervals from stroke onset to definitive management and other pertinent data were collected. The time delays have been evaluated in the decision tree model: Chi-squared Automatic Interaction Detection. Significance was assessed at 5% level of significance ($P < 0.05$).

Results: The mean prehospital time delay for all clinically suspected stroke ($n = 361$) in our institute was 716 min and the median time 190 min. The mean total in-hospital delay was 94.17 ± 54.5 min and median time being 82 min. The onset of symptoms to first medical contact was the main interval that influenced the prehospital delay. Computed tomographic (CT) diagnosis to stroke unit admission influenced the in-hospital delay the most.

Conclusions: Lack of awareness regarding stroke leads to delayed seeking of treatment for the same. The factors that contribute to the in-hospital delay included patient admission procedure delay, lack of staff to transport the patient, and the distance between the stroke unit and CT room. Educating the community with regard to “stroke” and implementation of a better pre- and in-hospital stroke care system is a need of the hour in the country.

Key Words: Decision tree analysis, in-hospital, prehospital, stroke, thrombolysis, time delays

INTRODUCTION

Cerebrovascular accident (CVA) constitutes a serious public health problem and is one of the leading causes of morbidity and mortality among adults. This is because they not only affect the victim but also their caregiver, relatives, family, and society.[1,2] The impact of ischemic and hemorrhagic CVA in a developing country like India is still a subject of scrutiny.[3,4]

One of the most important prehospital barriers to thrombolytic therapy in the developing world is the nonrecognition of stroke warning signs by the victims, families, the general public, and even health workers in some places.[5,6] Very few studies have looked into the prehospital stroke care scenario in India.[7]

The in-hospital treatment of stroke has changed drastically with the advent of intravenous recombinant tissue plasminogen activator (IV-rtPA) in the most Western nations.[8] This study analyses the various causes of delays in the pre- and in-hospital phases of acute stroke care in a tertiary referral teaching hospital in central Kerala, South India.
METHODS

This study was conducted in the Emergency Medicine Department and Neurology-Stroke Unit of a tertiary care teaching institute in Thrissur, Kerala, India, over a period of 1 year after approval from the Institutional Ethics Committee and Institutional Research Committee.

Our case series consisted of all clinically suspected cases of acute stroke seen by the physician at the emergency department (ED). All acute ischemic stroke patients were included in the study if they were more than 18 years of age and if they or their caregiver consented to be part of the study.

Initial evaluation of a potential stroke patient was similar to that of other critically ill patients: immediate stabilization of the airway, breathing and circulation. This was followed by a quick neurological examination and brief targeted history using a selected pro forma.

All suspected stroke patients were then sent for a noncontrast computed tomographic (CT) imaging of the brain, after an initial assessment including random blood glucose, an ECG, a baseline National Institute of Health Stroke Scale (NIHSS), and Glasgow coma scale scoring as per the institutional stroke management protocol. CT was interpreted by the radiologist on call, following which the patients were shifted to the stroke unit in the department of neurology where the neurologist took the final decision regarding thrombolysis. Standard protocol for IV rtPA was followed, and patients with any contraindication were excluded from IV thrombolysis.

During the interim, the time intervals from stroke onset to definitive management and other pertinent data were collected.

Stroke to therapy time

The various temporal parameters [Figure 1] studied are listed below.

- Stroke onset time - Stroke onset time was taken as the time the person was last seen normal
- First medical contact (FMC) - The first contact made with a medical professional was taken as the FMC time. The interval between the two was recorded as “onset to FMC.” This was obtained from the patients or caregiver history or the reference letter if present. In case a person woke up with stroke, the onset time was taken as the time when he was last found normal. If the FMC was at our ED, the FMC to ED door was assigned a value of zero
- ED door time was taken as the earliest time recorded in the ED. The time taken from FMC to the ED door constituted the “FMC to ED door” time
- Detection time was defined as the time stroke was suspected clinically in the ED. The time taken was the time the ED physician signed off on the patient or ordered shift to CT. The time taken for recognition of stroke in ED was taken as “ED door to detection” time
- Diagnosis time was defined as the time the CT was interpreted. Detection of stroke to CT interpretation “detection to diagnosis” time
- Stroke unit admission time was taken as the earliest recorded time in the neurology stroke unit where IV thrombolysis was carried out. The time interval between CT interpretation and admission to stroke unit was taken as the “diagnosis to stroke unit” admission time. This time was taken from the nurses’ admission register or doctors notes

| Stroke to therapy time frames                  | Ischemic n=273 | Hemorrhagic n=63 | Others n=25 (18+7 TIA) |
|----------------------------------------------|----------------|-----------------|------------------------|
| ONSET                                        |                |                 |                        |
| ONSET TO FMC                                 |                |                 |                        |
| FMC TO ED                                    |                |                 |                        |
| DOOR TO DETECTION                            |                |                 |                        |
| DETECTION TO DIAGNOSIS                       |                |                 |                        |
| DIAGNOSIS TO STROKE UNIT                     |                |                 |                        |
| STROKE UNIT TO CONSENT                       |                |                 |                        |
| CONSENT TO DRUG                              |                |                 |                        |

Figure 1: Stroke to therapy time frames: onset - Stroke onset time; onset to first medical contact - time of onset of symptoms to first medical contact time; first medical contact to emergency department - time taken from first medical contact to the emergency department door; emergency department door to detection - time taken for detection of stroke; detection to diagnosis - detection of stroke to computed tomographic interpretation; diagnosis to stroke unit - computed tomographic interpretation to admission to neurology Intensive Care Unit/stroke unit; stroke unit to consent - Time taken to obtain consent; consent to drug - time taken for administering the drug. AIS: Acute ischemic stroke
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Consent time was taken as the time at which the consent form was signed. Time taken to obtain consent after admission to stroke unit was noted as the “stroke unit to consent” time.

Drug time was defined as the time when rtPA was started. The time taken for administering the drug after obtaining the consent was noted as the “consent to drug” time.

Total delay was taken as the sum of both in- and pre-hospital delays.

Prehospital delay was taken as the sum of onset to FMC and FMC to ED door.

In-hospital delay was the time taken from ED door to drug administration time for all ischemic stroke within window period and till stroke unit admission for all ischemic stroke.

Data collection process
The data were collected on a pro forma sheet which was added to the individual case sheets and later retrieved. The ED physician and subsequently the neurologist added details to this sheet. The data were followed up every day till the patient was discharged, dead, or till 7 days postadmission, whichever was earliest. In a circumstance where the patient was sent home before 7 days, they were telephonically followed up.

Statistical methods
Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ± standard deviation.

The time delays have been evaluated in the decision tree model: Chi-squared automatic interaction detection. Significance is assessed at 5% level of significance (P<0.05).

Statistical software
The Statistical software namely International Business Machines Statistical Package for the Social Sciences (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) were used for the analysis of the data. Microsoft Word® and Excel® have been used to enter data and generate graphs, tables, and charts.

RESULTS
Three hundred and sixty-one clinically suspected stroke cases that presented to the ED over a period of 1 year were observed, data collected, and analyzed prospectively.

Of the total clinically suspected stroke, there were 273 (76%) infarcts. Eighteen cases which were initially diagnosed as ischemic stroke later turned out to be stroke mimics (conditions with stroke-like symptoms).

Sixty-two patients that presented within the window period for IV rtPA (n = 159) were offered thrombolysis, whereas 97 were not since they were considered not eligible candidates for thrombolysis. Twenty-nine percent (46/159) patients were thrombolysed using IV rtPA. Nearly 17% (27/159) of the ones that presented within 270 min (n = 159) were out of window period by the time they reached the stroke unit. Thirty-one had a minor stroke (NIHSS <4) and 13 had rapidly improving or minor symptoms as deemed by the treating neurologist after discussing with the patient that in their judgment would not lead to substantial disability. Stroke mimics and having contraindications for thrombolysis constituted the reason for not offering thrombolysis to the rest. Of the individuals who were given the option of thrombolysis by the neurologist (n = 62), 46 got thrombolysed, whereas 11 could not afford the treatment and 5 did not consent for fear of risk of hemorrhagic complications.

Only 13% of all clinically suspected stroke patients reached the hospital on an ambulance.

Among the patient/primary caregiver who gave the history, 84% had not either heard of “stroke” or recognized any of the symptoms as that of a stroke.

Of the 46 thrombolysed cases, 32 had data regarding the place from where they were transported. The minimum distance was 7 km and maximum was 89 km (mean 31.88 ± 20.3 km).

Prehospital time delay
The mean prehospital time delay [Table 1] for all clinically suspected stroke (n = 361) in this study was 716 min.
(11 h 56 min) and the median time 190 min (3 h and 10 min).

**In-hospital delay**
The mean total in-hospital delay [Table 1] for all clinically suspected stroke \((n = 361)\) in this study was 94.17 ± 54.47 min and median time being 82 min. The median door to diagnosis time was 35 min, door to detection time 5 min, detection to diagnosis time 35 min, and diagnosis to stroke unit admission time 30 min.

Decision tree analysis of the prehospital time of all clinically suspected stroke \((n = 361)\) with onset to FMC and FMC to door as independent variables revealed that onset to FMC influenced prehospital time delay the most [Figure 3].

Decision tree analysis of the total in-hospital time for all ischemic stroke \((n = 273)\), with FMC to ED, ED door to detection, detection to diagnosis, diagnosis to stroke unit, stroke unit to consent, consent to drug, and onset of symptoms to FMC as the independent variables revealed that diagnosis to stroke unit admission was the main interval that influenced the in-hospital time delay [Figure 4].

In this study, except for the door to drug time (median time of 75 min), the door to physician, door to CT interpretation and door to stroke unit admission times were comparable to National Institute of Neurological Disorders and Stroke and American Heart Association recommendation [Table 2].

**DISCUSSION**

**Prehospital time delays**
Prehospital time delays may be influenced by geographical, demographical, educational, socioeconomic, or organizational factors.[11‑16] Prehospital time delay in our study was divided into two components - the onset of symptoms to FMC (onset to FMC) time and FMC to ED door (FMC to door) time.

The median time from symptom onset to ED arrival was 2.6 h in a large-scale prospective study done in the United States.[15] Indian literature review did not yield any large-scale multicentric studies on the prehospital time delays. However, many institution-based studies have been conducted in India.[17‑22] 34 ± 6 h was the mean time of arrival to the hospital by a stroke victim

**Table 1: Pre- and in-hospital time delay in stroke victims \((n = 361)\)**

| Group                                      | \(n\) | Pre hospital delay (in mins) | In hospital delay (in mins) | Additional data (median) (in mins) |
|--------------------------------------------|-------|------------------------------|-----------------------------|----------------------------------|
| Mean ± SD                                  | Mean ± SD | Door to detection | Detection to diagnosis | Diagnosis to stroke unit admission |
| All clinically suspected stroke            | 361    | 715.49 ± 1622.07          | 190                         | 94.17 ± 54.47 | 82          | 5           | 35          | 30               |
| All ischemic stroke                        | 273    | 847.6 ± 1805.45           | 250                         | 90.92 ± 46.79 | 82          | 5           | 35          | 30               |
| All ischemic stroke that presented within  | 233    | 280 ± 276.11              | 188                         | 83.50 ± 39.44 | 80          | 5           | 35          | 25               |
| 1440 mins (24 hrs) of onset of symptoms    |        |                             |                             |                                  |              |              |              |                  |
| All ischemic stroke that presented within  |        |                             |                             |                                  |              |              |              |                  |
| 270 mins (4 ½) hours of onset of symptoms  |        |                             |                             |                                  |              |              |              |                  |
| All ischemic stroke that underwent thrombolysis | 46     | 114.20 ± 56               | 105                         | 84.20 ± 35.13 | 75          | 5           | 30          | 15               |
| All ischemic stroke that presented after 24 h | 40     | 4152.13 ± 3025.99         | 2880                        | 134.13 ± 61.41 | 155         | 5           | 0           | 60               |
A prospective study conducted in a rural area in Kolkata, eastern part of India in 2011.[17] A prospective study conducted in North of India, in New Delhi, to assess the factors influencing the delay in admission of 110 acute stroke cases, the median time to casualty arrival was 7.66 h.[39] It should be noted that the study included strokes whose symptoms began within 72 h of presentation, whereas in our study, all first-time presentation of strokes were included. The advantage was that this would give us a picture closer to reality, but the disadvantage was that the data would be unduly skewed. The maximum delay recorded in our study was 10,140 min (7 days), which would explain the unusually large standard deviation in this study - 1622 min (=27 h).

To minimize the skew, time delays were analyzed in subgroups [Table 1].

**Onset to first medical contact**

Decision tree analysis of the prehospital time with revealed that ONSET TO FMC was the factor that affected the prehospital time delay the most. Poor recognition of early stroke symptoms and low perception of threat leads to delayed arrival of stroke victims at hospitals.[20] Although Kerala is the most literate state in the country,[23] our study done showed that 84% of population was neither aware of stroke nor recognized the symptoms as that of stroke. This lack of awareness also probably contributed to delay in seeking treatment.

**First medical contact to emergency department**

Door-prehospital care emergency medical services

A prospective study conducted to assess the factors influencing the delay in admission of 110 acute stroke cases, distance from hospital, low threat perception of symptoms of stroke, and contact with a local doctor were independent factors associated with delay in arrival, whereas urban area residence, presence of family history, and older age were associated with early arrival.[20] 34 ± 6 h was the mean time of arrival to the hospital by a stroke victim in a study conducted in a rural area in India.[17]

The causes of FMC to ED DOOR delay in our study included delay in diagnosis, delay for investigations (mostly CT), and lack of availability of transport.

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**Table 2: Median emergency department time delays in this study compared to the American Heart Association recommendation**

| The 2013 American Heart Association recommended ED time frames[8] | Median time delay in this study |
|---------------------------------------------------------------|--------------------------------|
| Door to physician                                            | ≤10 minutes                     | 5 min                         |
| Door to CT interpretation                                    | ≤45 minutes                     | 45 min                        |
| Door to drug                                                  | ≤60 minutes                     | 75 mins                       |
| Door to stroke unit admission                                 | ≤3 hours                        | 70 mins                       |

National Hospital Ambulatory Medical Care Survey showed that 53% of stroke patients in America used EMS to reach the hospital.[8] In a developing nation like India, the need for prehospital care and EMS are only being recognized.[21] There are no large-scale data on prehospital system in stroke available because there exists no integrated prehospital health-care system in the country. Small population-based studies on trauma have shown that mostly it is the lay onlooker or even more commonly - the local police that bring the victim to the hospital in India.[22] First responder often transports the victim by taxi to the nearest hospital in most of these situations.[22] The literatures tend to point out that stroke patients who arrive by ambulance, arrive early.[24] Of the patients presenting to our emergency department, 13% arrived by ambulance. The rest employed other means of private or hired vehicle to transport the victim.

Western literature does not emphasize on the distances covered by the ambulance.[20] In our scenario, it is imperative that such data are collected since a tertiary care institute like ours in Kerala caters to people coming from a geographic radius of more than a 100 km. Data from 36 individuals in the thrombolysed group (n = 46) show that they were from a mean distance of 31.9 ± 20 km radius. The farthest from our institute, from where a patient who got thrombolysed arrived was 89 km. Transportation, especially with poor road conditions, is an important issue that is seldom addressed in the management of a stroke victim in India. Poor availability of transport in rural areas and congestion in urban areas also are considered constraints or barriers to immediate hospitalization and initiation of treatment.[25]

**In-hospital delay**

CT diagnosis to stroke unit admission in this study was the most influential factor causing the in-hospital delay. It was affected by factors such as patient admission procedure delay, lack of staff to transport the patient, and distance between stroke unit and CT room.

**Economic constraints and lack of infrastructure**

Lack of access to stroke care, financial constraints, and lack of infrastructure are of concern in developing nations.[26-27]

In a study of 64 stroke victims who presented to a tertiary hospital in South India, 30% reached within 3 h of onset and 16% were eligible for thrombolysis therapy, but none of these patients could be thrombolysed since the treatment was not affordable to this population.[6]

In our study, 17.8% of the individuals who were considered thrombolytic candidates by the neurologist could not afford thrombolysis as the high cost of thrombolytic therapy makes it inaccessible to the
uninsured. Infrastructure deficiencies and lack of human resources impede stroke care delivery in India.[28] The government needs to make amends and implement insurance policies so that health-care expenses are not largely out of one’s own pocket.[29,30]

Limitations of the study
Although the authors have taken all efforts possible to get the time intervals as accurate as possible, systematic error due to inaccuracy of recall to memory was evident at certain junctures of the study. For instance, the FMC time was recorded mostly by recall. Measures such as “time” when recorded vary from person to person.

The applicability of this study is unique to the ethnogeographical population, in which it was conducted. Logistical factors such as distance between stroke unit and CT room are one of the many hurdles that may vary from center to center.

CONCLUSIONS
This study was conducted in India where, like all other developing nations of the world, is in the phase of transition from infectious diseases to lifestyle diseases. Stroke is silently growing to epidemic proportions in developing nations, and there exists an unmet need to address this issue.

Our study shows that lack of awareness regarding stroke in the community and health-care professionals alike, poor prehospital EMS, lack of a coordinated in-hospital stroke care system, and financial constraints are the factors delaying management of acute stroke victim. The chain of events favoring good functional outcome from an acute ischemic stroke begins with the recognition of stroke when it occurs. Public education is one key step in the direction to reduce the onset to FMC time. Implementation of a better pre- and in-hospital emergency medical system tailored to the needs and resources that befit regional scenario should be considered. Promoting public education and medical research in the country and implementation of national policies in the management of stroke victim is essential in reducing the time delays of managing a stroke victim.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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