ORIGINAL ARTICLE

Stroke Thrombolysis: Beating the Clock

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Abstract

Background: Recombinant tissue plasminogen activator (rtPA) has revolutionized the management of acute ischemic stroke. Shorter door-to-imaging and door-to-needle (DTN) times are crucial for improving the outcomes in thrombolysed patients. Our observational study evaluated the door-to-imaging time (DIT) and DTN times for all thrombolysed patients.

Materials and methods: The study was a cross-sectional observational study over a period of 18 months at a tertiary care teaching hospital and included 252 acute ischemic stroke patients of which 52 underwent thrombolysis with rtPA. The time intervals between arrival to neuroimaging and initiation of thrombolysis were noted.

Result: Of the total patients thrombolysed, only 10 patients underwent neuroimaging [non-contrast computed tomography (NCCT) head with MRI brain screen] within 30 minutes of their arrival in the hospital, 38 patients within 30–60 minutes and 2 each within the 61–90 and 91–120 minute time frames. The DTN time was 30–60 minutes for 3 patients, while 31 patients were thrombolysed within 61–90 minutes, 7 patients within 91–120 minutes, while 5 each took 121–150 and 151–180 minutes for the same. One patient had a DTN between 181 and 210 minutes.

Conclusion: Most patients included in the study underwent neuroimaging within 60 minutes and subsequent thrombolysis within 60–90 minutes of their arrival in the hospital. But the time frames did not meet the recommended ideal intervals, and further streamlining of stroke management is needed even at tertiary care centers in India.

Keywords: Acute ischemic stroke, Alteplase, Door-to-imaging, Door-to-needle time, Stroke, Thrombolysis.

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Highlights

Stroke thrombolysis in Indian setups is yet to meet the desired global standards set for the DIT and DTN times. Despite advances in stroke thrombolysis protocol, enhanced efforts are imperative to achieve the ideal time intervals.

Introduction

Ischemic stroke occurs as a result of an interruption in the cerebral blood flow causing extensive damage to cellular homeostasis. The main treatment objective for such patients is to reinstate the blood flow with the minimal possible delay.[1] The use of rtPA has been revolutionary in the management of acute ischemic stroke patients. Major stroke studies including the National Institute of Neurological Disorders and Stroke (NINDS) rtPA stroke study and European Cooperative Acute Stroke Study (ECASS) showed better outcomes with earlier intervention in acute stroke patients.[2,3] As per the American Heart Association and American Stroke Association (AHA/ASA) guidelines,[4] an eligible patient must receive rtPA within a window period of up to 4.5 hours from the onset of symptoms. The DTN is the time taken for a patient from their arrival to the initiation of thrombolysis. In order to provide thrombolysis to stroke patients within the ideal window period, a faster DTN time is imperative. As per the ASA guidelines,[5] the primary goal set in the Phase I of the Target:Stroke initiative[6] was for hospitals to achieve a DTN time of less than 60 minutes in at least 50% of the thrombolysed stroke patients. It was also stipulated to ideally achieve a non-contrast head computed tomography (CT) scan within 20 minutes of arrival in at least 50% of patients. With the implementation of dedicated stroke codes in institutes, there has been an attempt to reduce the DTN time for acute ischemic stroke patients to achieve the set targets. Comparative studies analyzing a pre- vs post-stroke code DTN time have shown a positive change.[7,8]

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Materials and Methods

The study was a cross-sectional observational study undertaken over a period of 18 months at a tertiary care teaching hospital and included all the acute ischemic stroke patients who presented to the hospital. Patients below 16 years of age and patients with hemorrhagic stroke were excluded. The study was approved by the Institutional Ethics Committee. After taking an informed consent, data collection was started. The onset of symptoms, arrival at the hospital time, neuroimaging time, and time at the initiation of thrombolysis were noted and respective time intervals calculated

Table 1: Arrival to imaging time

Arrival to imaging time (minutes)	*Number of patients*	*Percentage (%)*
Under 30	10	19.23
30–60	38	73.07
61–90	2	3.85
91–120	2	3.85

Table 2: Imaging-to-needle time

Imaging-to-needle time (minutes)	*Number of patients*	*Percentage (%)*
Under 30	8	15.38
30–60	33	63.46
61–90	5	9.62
91–120	2	3.85
121–150	3	5.77
151–180	1	1.92

for all those undergoing thrombolysis. All statistical analysis was done using SPSS software Version 25.0.

Result

A total of 252 acute ischemic stroke patients reported to the institute of which 52 were thrombolysed. A total of 138 of the 252 patients reached a primary care center, including our institute, within the thrombolysis window period, but, owing to various factors, were not thrombolysed. Thirty-six of those thrombolysed were men and sixteen were women. The mean age of patients was 60.36 ± 15.41 years.

The onset to hospital arrival time was under 60 minutes for 61 patients, 61–120 minutes for 45 patients and 121–180 minutes for 18 patients. Of those thrombolysed, 29 reached the hospital within 60 minutes of the symptom onset, 20 within 61–120 minutes, and 3 patients took more than 120 minutes for arrival (Table 1).

Among those lysed, 10 patients underwent neuroimaging (NCCT head with MRI brain screen) within 30 minutes of their arrival to the hospital, 38 patients within 30–60 minutes and 2 each within the 61–90 and 91–120 minute time frames (Table 2).

The DTN time was 30–60 minutes for 3 patients, while a majority of 31 of the 52 patients were thrombolysed within 61–90 minutes of their arrival to the hospital. Seven patients received thrombolytic agent within 91–120 minutes while five each took 121–150 and 151–180 minutes for the same. One patient had a DTN of 181–210 minutes (Fig. 1).

The time taken for a patient to receive thrombolytic agent since neuroimaging was under 30 minutes for 8 patients. Thirty-three patients took 30–60 minutes while 5 took 61–90 minutes for the same. Six patients had an imaging-to-needle time of over 90 minutes.

The overall onset of symptoms to thrombolysis time is shown in Figure 2. About 3.8% patients were thrombolysed within the 60–90 minute time frame since the onset of symptoms. Seven patients (13.4%) received therapy within 91–120 minutes, thirteen patients (25%) within 121–150 minutes while eleven each (21.5%) within the 151–180 and 181–210 minute time intervals.

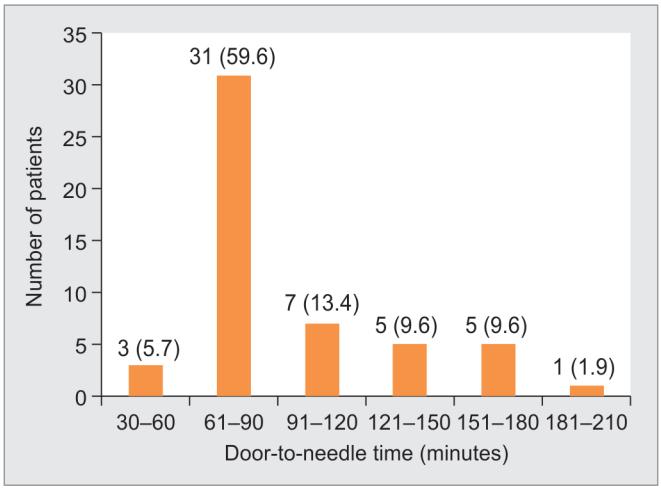

Fig. 1: DTN for thrombolysed patients

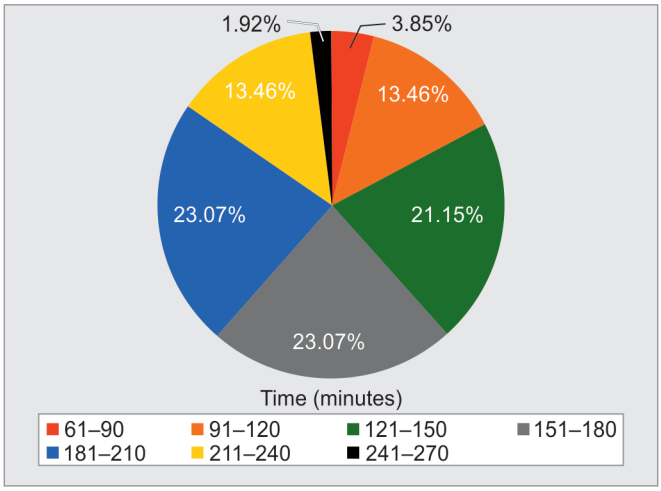

Fig. 2: Onset of symptoms to thrombolysis time

Discussion

After arriving at the emergency, patients with suspected stroke were subjected to neuroimaging for establishing a definite diagnosis. A total of 138 of the total 252 patients (54.76%) underwent neuroimaging within 30–60 minutes while 92.3% ($n = 48$) of those eventually thrombolysed had the imaging done in the same time frame. No patient could be started on thrombolytic therapy within 30 minutes of their arrival; however, 65.39% ($n = 34$) of the eligible patients received rtPA within 90 minutes. Only three patients, however, could be lysed within the stipulated 60-minute time of their arrival to the hospital, thereby failing to meet the ideal ASA standard. Although faster mobilization of patients post-imaging to critical care unit and a dedicated stroke protocol could make it possible for 78.84% ($n = 41$) of patients to be lysed within 60 minutes of undergoing neuroimaging. Apart from the 52 patients thrombolysed, 2 patients did not receive thrombolytic therapy owing to delay in consent from relatives despite them being in the window period at the time of presentation. A delay in neuroimaging within the hospital prevented further three patients from being lysed.

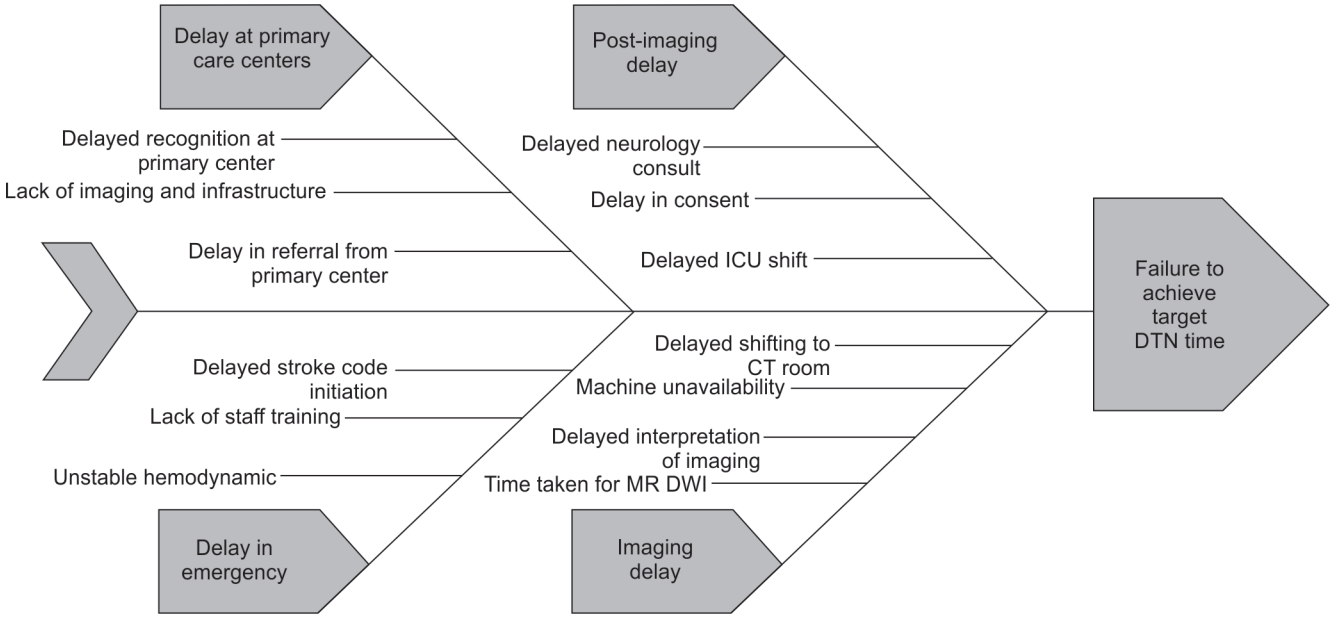

Fig. 3: Reasons for failure to achieve the target DTN time

Shorter DTN times have been found to be associated with lower all-cause mortality and lower all-cause readmission and an overall better clinical outcome.[9,10] With the significant improvement in DTN time observed with the implementation of phases I and II of the Target:Stroke initiative, the third phase was initiated globally in 2019. The phase III of Target:Stroke aims to achieve a DTN time of <60 minutes in 85% or more of the stroke patients thrombolysed.[11,12] Albeit missing the ideal DTN and imaging time frames in our study, a dedicated intra-hospital emergency medical systems and an institutional stroke protocol could still enable thrombolysis of a majority of eligible patients within satisfactory time limits. Learning collaborative, improved training of medical and paramedical staff with dedicated protocol for action can further decrease the DTN time and provide early revascularization opportunities. Various studies across the globe have compared the DTN time pre- and post-intervention implementation, showing a consistent reduction in the DTN with the use of such streamlining measures.[13,14] Resident training and education initiatives in academic medical centers and novel ideas such as use of mobile applications to improve coordination and teleconference delivered interventions have also shown efficacy in cutting down the DTN time.[15,16] A study by Noone et al. in a Southern Indian institute also showed statistically significant improvement in DTN time reduction with the use of mobile application, reaching the Target:Stroke phase III primary goal with 89% patients thrombolysed within 60 minutes.[17] Hospital training and multi-disciplinary coordination can help achieve a sustainable reduction in the DTN time as has been concluded in other Indian population based studies.[18] A Norwegian stroke study showed reduction of DTN time to 13 minutes after implementation of revised stroke protocols.[19]

In our study, the intra-hospital delay was still more than ideal for a tertiary care center and points to requirement of better streamlining of operations. It may be inferred that centers catering to rural populations may have a significantly higher delay due to poor infrastructure as has been noted in other Indian population base studies.[20,21] This delay may further contribute to a prolonged DTN time at the tertiary center. This is evident in Figure 3 fish bone diagram, which also highlights the intra-hospital factors that led to a failure to achieve the ideal DTN time. Despite an established stroke protocol in the institution, a lack of staff training and lapses in early protocol activation played a role in delaying thrombolysis. This can be overcome with extensive training programs for all health-care staff for early recognition and prompt management skills. Increasing the manpower to improve the patient transfer between emergency and radiology departments may prove valuable.

The institution in the study involved an MRI brain screening along with a non-contrast CT head for the neuroimaging as part of the hospital stroke protocol. The inclusion of an MRI study may have contributed to an added delay in the treatment initiation, and therefore the actual need for an imaging beyond NCCT needs to be looked into. The exclusion of an MR study may reduce the imaging time and, therefore, the DTN further to within the time frames as per the guidelines. A delay in acquisition and interpretation of imaging was also found to be a reason for delayed thrombolysis, among others, in a study by Mowla et al.,[22] and the same was observed as one of the causes for delay in our study. Possible corrective measures include moving stroke patients directly to the computed tomography on arrival, with adequate training of the radiology department staff and delivering thrombolytic on the CT table or in the imaging area as have been shown effective in other studies.[23] Post-imaging delay in getting a specialist neurologist opinion may be circumvented by framing an institutional policy regarding decision to initiate thrombolysis by available specialists from the critical care team. A lag in an ICU bed availability can be overcome by establishing adequate facility within the emergency department itself.

Conclusion

Most patients included in the study underwent neuroimaging within 60 minutes and subsequent thrombolysis within 60–90 minutes of their arrival to the hospital, particularly because of an

established stroke protocol and dedicated imaging facility available at all hours and a systematic coordination between the emergency medicine and critical care teams. The time frames are, however, still beyond the recommended ideal intervals, and further streamlining of stroke management is needed even at tertiary care centers to reach the phase I goals of Target:Stroke.

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