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ORIGINAL ARTICLES

Barriers to thrombolysis in acute ischemic stroke: Experience from a Level 1 hospital in South Australia

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Abstract

Objective: We studied the mean pre- and in-hospital delay of patients presenting with symptoms suggestive of acute stroke to assess the major barriers to thrombolysis. *Methods:* The study was a retrospective audit of all patients presenting to Emergency Department (ED) of Lyell McEwin Health Services, Adelaide, Australia with symptoms suggestive of acute cerebral ischemia in the year 2008. We assessed from ambulance and medical records the time of onset of symptoms, delay in presentation to ED, and in-hospital delay for evaluation and imaging. Results: Of 216 patients (Male=123, Female=93) with mean age 70.2 years, 103 (47.7%) presented within 3 hours of onset of symptoms. 42.85% of acute strokes presented within 1 hour 30 minutes. Only Australasian Triage Scale Level 1 and 2 had a positive association with completion of evaluation within 1 hour of arrival to ED. Patients with motor symptoms had less pre-hospital delay as compared with those presenting with other neurological symptoms. Arrival by ambulance or direct presentation to ED had no significant impact on pre-hospital delay.
Conclusions: More number of patients are presenting to emergency services within 3 hours of onset of symptoms suggestive of acute stroke. However present triage system at ED often is inadequate in capturing all the strokes who are potential candidates for thrombolysis.

INTRODUCTION

Despite the world wide approval of thrombolytic therapy for acute ischemic stroke[1,2], only a small percentage of patients receive the benefit. Audits of recombinant tissue Plasminogen Activator (rtPA) use in Australia currently indicate that only 0.9% of all ischemic stroke patients receive thrombolysis.[3] Patient delay in presentation seems to be the single most important factor leading to under utilization of this potentially tissue salvaging treatment across most of the reported studies.

National Stroke Foundation in Australia has issued guidelines for acute as well as long term management of stroke in 2007.[4] However, how far guidelines could be translated to clinical practice needs to be evaluated, especially in tertiary care centers without a dedicated stroke team. So we conducted an audit of all patients presenting to the Emergency Department (ED) of our hospital with symptoms suggestive of stroke or transient ischaemic attack (TIA) to assess the mean pre-hospital and in hospital delay and predictors for the same. The aim of the audit was to look into barriers in delivering thrombolytic therapy in a peripheral tertiary care centre and identify the patient subgroup who will be potential candidates for reperfusion strategies.

METHODS

The study was a retrospective audit of all patients who presented with acute neurological symptoms suggestive of TIA/stroke in ED of Lyell McEwin Health services (LMHS) in the year 2008. The hospital is a Level 1 hospital situated in the Northern suburb of Elizabeth in Adelaide, South Australia with nearly 50,000 patients utilizing ED services in 2008. The hospital has facility for thrombolytic therapy which remains underutilized. The list of patients who presented with a diagnosis of ischemic stroke and TIA to ED were obtained from medical records database

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using ICD-10 (International Coding for Diseases) codes for ischemic stroke and TIA. Stroke was defined as focal (or at times global) neurological impairment of sudden onset, lasting for ≥24 hours (or leading to death) and of presumed vascular origin.[5] TIA was defined as a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia without acute infarction.[6] Prior approval was obtained from Institutional Ethics Committee for conducting the audit. The data on demographics, mode of presentation, symptomatology, triage level, time delay in being evaluated by ED and medical team and adherence to treatment protocol was collected from medical records using a structured proforma. All the patients on arrival were triaged into Level 1 to 5 as per Australasian Triage Scale (ATS) guidelines[7], with Level 1 indicating life threatening emergencies which need immediate action on arrival. Level 2, 3, 4 and 5 patients should be evaluated by ED physician within 10, 30, 60 and 120 minutes of arrival. For all the patients being evaluated in ED, treating physician had to complete an ED assessment sheet as per hospital protocol, where time of arrival, time of initial evaluation by ED physician and Physician from Medical team were mandatorily recorded. The time of onset of symptoms was verified from ambulance records. In cases where the time of onset of symptoms was not clear from the ambulance records, including wake up strokes, the time patient was last seen as normal was taken as the time of onset. Details of antiplatelets and anticoagulant use and discharge diagnosis were also collected. Final diagnosis was grouped as TIAs, ischemic strokes and others. Outcome from ED was measured as discharge, admission to ward, ICU (Intensive Care Unit) / HDU (High Dependency Unit), expiry and referral to higher centers (with specialized stroke care services) for thrombolysis / other reasons. The data was analyzed using SPSS version 17 software (SPSS Inc,Illinois,Chicago). The variables were expressed in frequencies and percentages. The relationships between variables were calculated using Fisher's exact test and chi-square test. P values less than 0.05 were taken as statistically significant.

RESULTS

There were a total of 216 patients who attended the ED of LMHS with a presumed diagnosis of TIA / stroke in the year 2008 (Male: 123, female: 93). Mean age of the patients was 70.2 years (Male: 69.2, Female 71.5). Age distribution is shown in Figure 1 and baseline characteristics of the patient population in Table 1.

Factors associated with pre-hospital delay are given in Table 2. Mean pre-hospital delay in patients with ischemic stroke was 4.25 hours and TIA was 5.15 hours. Mean in-hospital delay for evaluation in ED was 1.30 hours (ischemic stroke=65 minutes and TIA=110 minutes). According to triage level, mean in-hospital delay was triage Level 1=no delay, triage Level 2=7

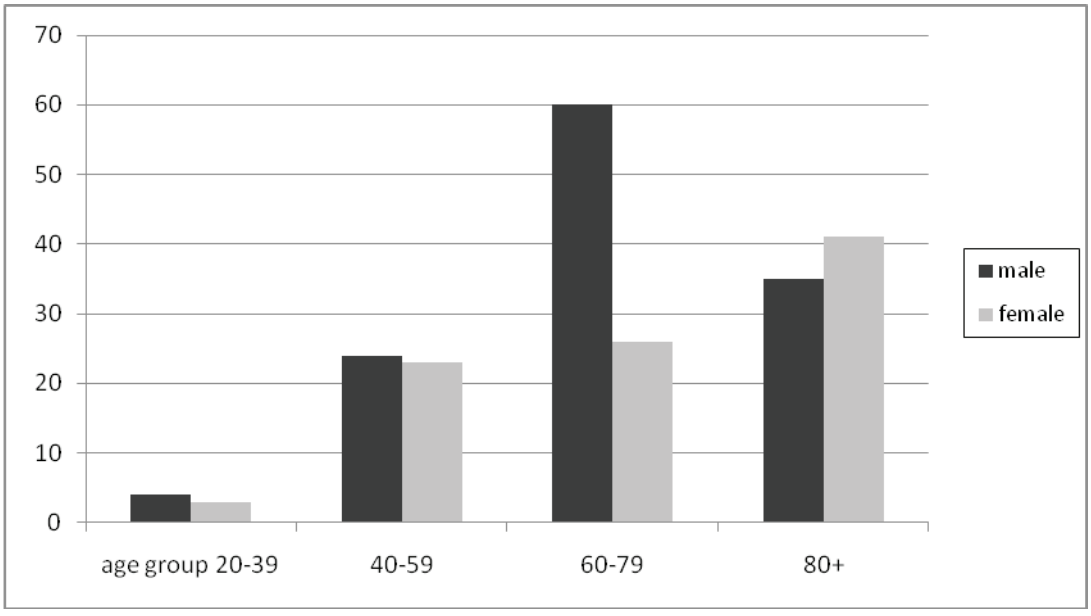

Figure 1. Age distribution of the stroke patients

Table 1: Baseline data of the stroke patients

	Frequency N=216	Percent
Prior TIA	22	10.2
Prior stroke	27	12.5
First presentation to ED	175	81
Mode of presentation		
Weakness	73	33.8
Multiple neurological symptoms	46	21.3
Collapse	28	13
Duration at first encounter		
<1 hr 30 min	60	27.8
1.31-3.00 hr	43	19.9
Triage at ED		
Level 1	6	2.8
Level 2	49	22.7
Level 3	135	62.5
Mode of arrival		
Ambulance	131	60.6
Self	85	39.4
Diagnosis at arrival		
Ischemic stroke	130	60.2
TIA	80	37
ICH	6	2.8
Mode of imaging		
CT	177	81.9
MRI	5	2.3
None	34	15.7
ED Imaging diagnosis		
Infarct	45	20.8
Bleed	3	1.4
Normal	133	61.6
Others	1	0.5
Prior anticoagulation	21	9.7
Prior antiplatelet	69	31.9

TIA: transient ischaemic attack, ED: Emergency Department, ICH: intracerebral hemorrhage

minutes, triage Level 3=1.05 hours and triage Level 4=2.30 hours. Mean door to image time for strokes and TIA were 55 minutes and 100 minutes respectively.

Close to half of the patients (103/216=47.7%) presented within 3 hours of onset of symptoms to ED. Only 6 and 49 patients (2.8 and 22.7%) were given appropriate triage Levels of 1 and 2

Table 2: Univariate analysis of factors associated with pre-hospital delay

	P value
Referral pattern, GP or direct	0.99
Age	0.77
Gender	0.732
Arrival by ambulance	0.06
Motor versus non motor symptoms at onset	0.009
Final diagnosis, TIA or stroke	0.151

GP: general practice, TIA: transient ischaemic attack

at ED, which could have facilitated thrombolysis, if eligible. 135 of patients were triaged at Level 3 (62.5%). Univariate analysis showed that younger age group (<60 years) presented more often with motor weakness while older age group presented with multiple neurological symptoms or altered sensorium (p=0.009). Older patients with acute neurological symptoms were more likely to get admitted in ward (p value 0.016) and also had increased rate of readmissions with same or different symptoms (p=0.018). Gender had association with only diagnosis at discharge from ED, with more females being diagnosed with TIA (p=0.003).

Multivariate analysis showed a statistically significant association between mode of arrival and age with >60 age groups using more ambulance service as against younger patients. However there was no influence of age or gender in pre-hospital delay or ED outcome. Strokes compared to TIAs were more likely to be imaged (p<0.001). More TIAs were likely to be discharged from ED (p<0.001) and have repeat presentations within one year (p=0.01).

Patients whose evaluation was completed within one hour of arrival were analyzed for predictors of early workup which is shown in Table 3. 20.6% (26/126) of TIAs and 42.9% (33/77) of strokes presented within 1hour 30 minutes of onset of ictus and 15.1% (19/126) of TIAs and 31.2% (24/77) of strokes presented between 1hour 30 minutes and 3 hours of onset. However only 2 patients received thrombolytic therapy and another 2 were referred to a specialized stroke care center for the same. The duration at first encounter had no association with triage level or time seen by ED or final diagnosis. Patient outcomes are given in Table 4. Among 216 patients with diagnosis of presumed stroke / TIA at arrival, 11 patients had a different diagnosis at discharge (vasovagal syncope=5, post ictal Todd's paresis=3, metabolic encephalopathy=3).

Table 3: Univariate analysis of factors associated with evaluation within one hour of arrival to Emergency Department

	P value
Mode of arrival, ambulance versus direct	0.07
Age <60 versus 60+	0.11
Gender	0.2
Motor versus non motor symptoms	0.08
ATS level 1 and 2 versus 3 and above	0.001
Final diagnosis, stroke versus TIA	0.06

ATS: Australasian Triage Scale, TIA: transient ischaemic attack

Table 4: Outcome of the stroke patients

	Frequency	Percent
Anticoagulation	35	16.2
Antiplatelets	146	67.6
Aspirin+dipyridamole	15	6.9
Clopidogrel	39	18.1
Aspirin	104	48.1
ED outcome		
Ward	152	70.4
ICU/HDU	2	0.9
Discharge	45	20.8
Expired	6	7.9
Final diagnosis		
TIA	126	58.4
Ischemic stroke	77	35.6
Atherosclerotic	44	
Cardioembolic	20	
Lacunar	7	
Others-specific	2	
Undetermined	4	0.9
ICH	2	5.1
Others	11	
Repeat presentations		
TIA	9	
Ischemic stroke	3	
Non neurological causes	60	

ED: Emergency Department, ICU: Intensive Care Unit, HDU: High Dependency Unit

DISCUSSION

IV rtPA is the only worldwide approved medical therapy for treatment of acute ischemic stroke, which has been associated with improved neurological outcomes.[8] However, timely identification of acute stroke symptoms and early presentation to ED are the most important factors determining the extend of utilization of thrombolytic therapy. Most of the population studies have shown that <5 % of eligible patients receive the benefit of thrombolysis. Mean delay from onset of stroke to arrival at hospital ranged between 2-6 hours across different studies.[9] Median delay in patients with TIA was longer in most of the studies, with 20% presenting after 24 hours.[10] An earlier South Australian study[11] on pre-hospital delay and factors showed that mean delay in patient arrival was 6 hours (12 min to 2 days) with 35% of patients presenting within 3 hours of symptom onset. The figures are showing a changing trend recently. MMWR 2007[12] showed that 48% of patients with symptoms suggestive of acute stroke presented to emergency medical services within 2 hours in USA.Our study also showed a high proportion of patients with stroke and TIA presenting within 3 hours of onset of symptoms.

Kwan *et al*[9], in their meta-analysis had identified 9 types of barriers to delivery of thrombolysis, which were grouped as pre-hospital and in-hospital barriers. The most consistently reported pre-hospital barrier was patient or family's poor recognition of acute stroke symptoms. A systematic review of delays in seeking medical attention after TIA[13] also confirmed the lack of response from patients as a major determinant of pre-hospital delay. Giles *et al*[14], found that correct identification of symptoms did not always translate to less delay. Motor symptoms were more likely

associated with less pre-hospital delay, which was also observed in our study. This could be explained by the fact that paresis is more quickly recognized by patients and relatives as an urgent medical symptom requiring immediate attention. Severe strokes were associated with early presentation in an earlier report[11], which could not be clarified in our study.

The impact of emergency medical services on pre-hospital delay and protocol based interventions to reduce them have been studied by a number of authors. Paramedic recognition of acute stroke symptoms and hospital notification was associated with shorter time from first ambulance call to first medical assessment.[15] Quain *et al*[16] found that proportion of patients receiving rtPA could be increased from 4.7% to 21.4% with protocol implementation and education, which was associated with reduction in median time from symptom onset to ED arrival from 150 to 90.5 minutes. Our study showed a trend for less pre-hospital delay in those using emergency medical services, which did not assume statistical significance. This translates to similar delay in transport, irrespective of mode (ambulance versus self) in our patient population, making early recognition of stroke more important. The influence of general practice (GP) on pre-hospital delay has also been studied[17], with more delays in those utilizing GP services initially. In our study only a very small proportion of patients consulted GP before attending ED services, which was not associated with any significant pre-hospital delay. But this result cannot be generalized as patient numbers attending GP services were small.

The concept of triage, first applied on the military battlefield has assumed a central role in the initial evaluation and classification of patients seeking emergency treatment. First developed in UK, this has been adapted and modified for use by several other countries, including Australia. The ATS[7], designed for use in hospital-based emergency services throughout Australia and New Zealand is a scale for rating clinical urgency with patients rated into Levels 1 to 5, in the descending order of priority. Since the focus of triage in emergency is to timely intervene in all life threatening situations, we hypothesized that acute stroke patients who are the ideal candidates for thrombolysis may not be receiving a priority like acute myocardial infarction in ED, especially in centres like ours without a comprehensive stroke care programme and hence will be triaged below level 2. This will produce a significant delay in the initial assessment itself ,thus missing out those who were eligible for thrombolysis at presentation.

A number of studies have looked into in-hospital delay at different levels, ranging from ED evaluation to neuroimaging. The median delay from arrival at hospital to first medical assessment varied considerably from 20 minutes[18] to 4 hours.[19] But very few studies have looked into the impact of triage levels given at ED on arrival and delay in assessment and neuroimaging. Rapid assessment of all patients presenting with symptoms suggestive of acute stroke is essential to identify potential candidates for thrombolysis and direct resources to this subgroup, to reduce door to needle time to 40-50 minutes as recommended in acute stroke treatment guidelines. In our study, majority of patients with acute stroke symptoms were triaged Level 3, which reflects the low priority given to acute neurological symptoms in peripheral hospitals without a dedicated stroke team. This probably reflects the ground reality in other peripheral centres especially in the developing world. When we analysed the subgroup of patients who had completed clinical assessment and neuroimaging within one hour of arrival, we found that only triage Level 1 and 2 had a significant association with quick workup. Some of the previous studies[20,21] have also found that triaging as high priority and interventions to reduce time to alerting stroke team might increase percentage of patients receiving thrombolysis. One Australian study[22] had found that 24-hour protocol driven approach with ascertaining all strokes presenting within 3 hours of symptom onset as triage Level 2 and completing initial assessment by Senior ED consultant within 10 minutes of arrival resulted in extending the benefit of thrombolytic therapy to 14% of patients with acute stroke and 95% of those eligible for the same.

Our study is not without its limitations. Being a retrospective study we could not assess patient and caregiver awareness about acute stroke symptoms which has a significant role in pre-hospital delay. Also ours being a Level 1 hospital, we found that ED services often were unable to strictly adhere to the ATS protocol of assessing patients in lower levels of triage like level 3 and 4 within the recommended time frame of 30 and 60 min respectively. We have not looked into severity of stroke in our study population, which also might have had an impact on pre and in hospital delay. The absence of a dedicated stroke team would have been a contributory factor to delay at the level of ED. In centres with acute stroke care teams, fast

tracking patients has enabled quick response and more utilization of thrombolytic services.

In conclusion, more patients with symptoms suggestive of acute stroke are seeking attention at emergency medical services rather than GP services. However, lower levels of triage at ED is associated with delay in identification of potential candidates of thrombolysis. Fast tracking patients with acute stroke symptoms who present within window period is an effective way to optimize use of thrombolytic services in peripheral hospitals with limited resources.

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