Original Article

Timing of Arrival to a Tertiary Hospital after Acute Ischaemic Stroke – A Follow-up Survey 5 Years Later

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Abstract

Introduction: Intravenous tissue plasminogen activator (tPA) within 3 hours of stroke onset is a licensed proven therapy for ischaemic stroke, with recent trial data showing benefit up to 4.5 hours. We previously published in this journal data of a survey conducted in 2004 showing only 9% of ischaemic stroke patients presenting to the Singapore General Hospital (SGH) arrived within 2 hours of onset. We aimed to determine whether the problem of delayed hospital arrival persists in 2009 and to establish the impact of widening the time window for intravenous tPA to 4.5 hours. Materials and Methods: We prospectively surveyed consecutive ischaemic stroke patients admitted to the SGH from 9th March to 30th April 2009. Patients and/or relatives were interviewed with a standardised form similar to the 2004 survey. Results: Among the 146 ischaemic stroke patients surveyed (median age 67 years, 59% male, median NIHSS score 2), 6% presented to SGH within 2 hours and 15% within 3.5 hours of onset. Median time from stroke onset to hospital arrival was 1245 minutes (20.75 hours). Pre-hospital consultation was significantly associated with hospital arrival after 2 hours from onset. Main reasons cited for delay were not realising the gravity of symptoms (31%) and not recognising them as stroke (27%). Conclusion: Delayed arrival to SGH following acute ischaemic stroke remains a problem in 2009. This confirms the lack of stroke awareness in Singapore and highlights the need for public stroke education. Furthermore, these data confirm that widening the time window for intravenous tPA treatment to 4.5 hours at SGH will increase its utilisation.

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Key words: Hospital presentation, Singapore, Stroke, Timing

Introduction

Intravenous tPA is a proven treatment for acute ischaemic stroke.[1] However as it has to be given in a narrow time window from symptom onset, utilisation is limited by delayed arrival of most patients to hospital. In the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study trial published in 1995, intravenous tPA given within 3 hours of stroke symptom onset improved functional outcome at 3 months.[1] This landmark trial established the 3-hour time window for intravenous tPA for acute ischaemic stroke.[1] The European Cooperative Acute Stroke Study (ECASS) III trial published in 2008 found that the time window for improving outcome of acute ischaemic stroke with intravenous tPA can be widened, demonstrating improved 3-month functional outcome when given in the 3 to 4.5 hour window.[2] Subsequent to the ECASS III publication, the European,[3] Canadian[4] and North American[5] authorities amended their licensing of intravenous tPA for acute ischaemic stroke, widening the time window for intravenous tPA to 4.5 hours.

In Singapore, intravenous tPA was licensed for treatment of acute ischaemic stroke in the 3-hour time window in 2004. At SGH, a 1500-bed tertiary hospital, we have been treating eligible acute ischaemic stroke patients with intravenous tPA since 2006. In a published paper in this journal, we reported data on the timing of hospital arrival after acute ischaemic stroke. This was based on a survey of 100 patients admitted to SGH in 2004, prior to licensing of intravenous tPA for acute ischaemic stroke in Singapore.[6] The median time to hospital arrival was 16 hours and 5 minutes and only 9%

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presented within 2 hours from onset with an additional 3% in the 2- to 3-hour window.[6] Despite the availability of effective early treatment of stroke, there is underutilisation of thrombolysis mainly due to late arrival.[7]

We repeated a similar survey of hospital arrival timings and reasons for delayed arrival in 2009 with the aims of determining whether the problem of delayed hospital arrival following acute ischaemic stroke had improved in the last 5 years as well as to establish the feasibility of widening the time window for intravenous tPA to 4.5 hours.

Materials and Methods

We prospectively surveyed acute ischaemic stroke patients admitted from the emergency department to SGH from 9th March to 30th April 2009. The methodology was similar to the survey conducted in 2004.[6] Patients were diagnosed to have an acute ischaemic stroke by a neurologist based on clinical findings and brain imaging. There were no exclusion criteria.

Patients or their relatives were interviewed with standardised questions (Appendix 1). Data collected included time of stroke symptom onset, patient demographics, pre-hospital consultation and stroke subtype using the Oxfordshire Community Stroke Project (OCSP)[8] classification. Time of stroke onset was defined as when the stroke symptoms started or when the patient was last seen well. Time of hospital arrival was taken as the time the patient arrived at the emergency department as noted in the emergency department notes. We selected specific time windows from stroke onset to hospital arrival of 2 hours and 3.5 hours, in order to allow for clinical, laboratory and imaging assessment in view of the recommended maximum door to needle time of 60 minutes or less by the American Stroke Association.[9]

Large stroke was defined as Total Anterior Circulation Infarction (TACI) and Partial Anterior Circulation Infarction (PACI) using the OCSP classification and non-large stroke was defined as Lacunar Infarction (LACI) and Posterior Circulation Infarction (POCI). Patients and/or their relatives were asked to indicate the reason/s for delay in hospital arrival from a list of options: did not recognise symptoms of stroke, did not recognise gravity of symptoms, financial concerns, unable to seek medical care unaided, unable to communicate need for help. They could select more than 1 option and were also given the option of expressing other potential reasons for delayed arrival.

Univariate analyses were carried out using chi-square or Fisher's exact for nominal data and Wilcoxon rank sum for numerical data. This study was approved by the Singapore General Hospital ethics committee.

Results

We surveyed 150 acute ischaemic stroke patients over the 52-day period. Time of stroke onset could not be established for 4 patients because of language or cognitive impairment. Among the remaining 146 patients, the median age was 67 years (IQR, 56 to 76), 59% were male and the ethnic distribution was 78% Chinese, 13% Malay, 7% Indian and 2% of other ethnicity (Table 1). Median baseline NIHSS score was 2 (IQR 2-5) with a range of 0 to 17. Stroke subtype distribution by the OCSP classification was 3% TACI, 15% PACI, (therefore 18% with large stroke) 80% LACI and 2% POCI (Table 1). This 146-patient cohort recruited over 52 days is similar to a 3-year cohort of 3118 ischaemic stroke patients admitted to SGH in 2001, 2002 and 2003 (median age 66 years [IQR 58 to 74], 56% male, ethnic distribution of 82% Chinese, 10% Malay, 6% Indian and 2% of other ethnicity, and 17% prevalence of large stroke [TACI & PACI]).

The median time of hospital arrival from stroke onset was 1245 minutes (20 hours and 45 minutes) (IQR 367 to 3855 minutes) with 6% of patients presenting within 2 hours, 15% within 3.5 hours and 44% within 24 hours of symptom onset. Only 1 of these patients was treated with acute intravenous tPA. Only 17% of patients were transported to hospital by ambulance, with 41% coming by private vehicle, 26% by taxi, 7% by bus or mass rapid transit (MRT) trains. We found that 53% of patients sought medical consultation in an outpatient setting prior to hospital arrival. As shown in Table 2, patients who consulted a medical practitioner prior to arrival in hospital were more likely to arrive after 2 hours of symptom onset (89% vs 11%, $P = 0.080$).

With regard to reasons for delayed hospital arrival,

Table 1. Characteristics of the 146 Ischaemic Stroke Patients in the Survey

Characteristics	No. of patients (%)
Gender	
Male	86 (59)
Female	60 (41)
Race	
Chinese	114 (78)
Malay	19 (13)
Indian	10 (7)
Others	3 (2)
Marital status	
Single/Divorced/Widowed	51 (36)
Married	92 (64)
OCSP	
TACI	5 (3)
PACI	22 (15)
POCI	3 (2)
LACI	116 (80)

Table 2. Associations of Hospital Arrival Timing

	Timing of hospital arrival from onset		
	Within 2 hours	**After 2 hours**	***P***
Median age (y)	57	67	0.631
Male (%)	7 (8)	79 (92)	0.307
Female (%)	2 (3)	58 (97)	
Chinese (%)	8 (7)	106 (93)	0.606
Malay (%)	0 (0)	19 (100)	
Indian (%)	1 (10)	9 (90)	
Others (%)	0 (0)	3 (100)	
Single (%)	8 (9)	84 (91)	0.158
Married (%)	1 (2)	50 (98)	
Large stroke [TACI/PACI] (%)	1 (4)	26 (96)	1.000
Non-large stroke [POCI/LACI] (%)	8 (7)	111 (93)	
Pre-hospital consultation (%)	2 (3)	75 (97)	0.080
No pre-hospital consultation (%)	7 (11)	58 (89)	

LACI: Lacunar Infarction (LACI); PACI: Partial Anterior Circulation Infarction; POCI: Posterior Circulation Infarction (POCI); TACI: Total Anterior Circulation Infarction

31% did not realise the gravity of symptoms, 26% did not recognise their symptoms as stroke, 7% were waiting for spontaneous resolution, 3% were unable to present unaided, 3% had difficulty with communication and 1% had financial concerns. None of the patients cited fear of hospitals as a reason for delayed arrival.

Discussion

The majority of patients admitted for acute ischaemic stroke at SGH in 2009 have delayed hospital arrival. There has been no reduction in hospital arrival timings from 2004 to present in terms of median time (965 minutes in 2004 and 1245 minutes in 2009) nor increase in the proportion of patients presenting within 2 hours (9% in 2004 and 6% in 2009). Therefore eligibility for intravenous tPA remains very limited by delayed hospital arrival. This is in spite of interim licensing of intravenous tPA for treatment of acute ischaemic stroke and availability in Singapore public hospitals including SGH. The common reasons for delayed arrival in 2009 were similar to those in 2004: failure to recognise symptoms of stroke and not recognising the gravity of symptoms. Mild neurological deficit may be a factor for delayed hospital presentation and lack of use of emergency ambulance services. These data show that there is no improvement of stroke awareness in Singapore over

this 5-year period and provide evidence that current stroke public education in Singapore is inadequate. Currently, there is no concerted stroke public education programme in Singapore, with mostly ad-hoc publicity through posters and public forums particularly during the stroke awareness month in October. Based on this study's data, there are now ongoing efforts for a campaign to increase public awareness of stroke in Singapore, which should include utilisation of mass media such as television, public education via primary healthcare providers, as well as targeting individuals with stroke risk factors such as hypertension and diabetes.

Based on our findings, public stroke education should emphasise identification of stroke symptoms and awareness that stroke is an emergency with treatment that can limit the extent of damage and improve outcomes, hence the need to arrive expediently to hospital. Stroke educational programmes have been shown to reduce delay to hospital arrival after stroke and increase intravenous tPA utilisation. An education programme in North Carolina, USA, targeted at both the public and medical community resulted in a higher proportion of stroke patients presenting to hospital within 24 hours (37% in the pre-education period vs 86% in the post-education period).[10] In a controlled study conducted in East Texas, USA, a community that underwent a stroke education intervention saw an increase in intravenous tPA utilisation (2.21% to 8.65%, *P* = 0.02 among all ischaemic stroke patients; and 14% to 52%, *P* = 0.003 among patients deemed eligible for the treatment) whereas there was no change in the control community which did not receive the stroke education intervention (0.71% to 0.86%, *P* = 1.00 among all ischaemic stroke patients; and 7% to 6%, *P* = 1.00 among those eligible for the treatment).[11]

The proportion of patients presenting within 3.5 hours was more than double that in the 2.5-hour window (15% vs 6%). This indicates that widening of the time window of intravenous tPA to 4.5 hours has the potential to markedly increase its utilisation at SGH, maximising the proportion of patients who stand to benefit from this proven treatment. Based on these findings and evidence from the ECASS III trial,[2] the SGH neurology department has decided to widen the time window for intravenous tPA and now treats eligible acute ischaemic stroke patients up to 4.5 hours from stroke onset. However, patients should be treated as early as possible, in view of the known diminishing benefit-risk ratio with increasing duration from onset to treatment with intravenous tPA.[12]

There were some limitations in this study. We did not assess the eligibility for intravenous tPA based on inclusion and exclusion criteria in guidelines, other than timing from stroke onset. Furthermore, the study was limited to 1 hospital in Singapore with the potential for hospital bias. However, Singapore is geographically small and SGH accounts for a

sizeable proportion of acute hospital beds in the country.

In conclusion, delay in hospital arrival following acute stroke remains a significant problem among acute ischaemic stroke patients admitted to SGH in 2009. Our data supports the need for public stroke education and the feasibility of widening the window for intravenous tPA treatment to 4.5 hours from stroke onset.

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Appendix 1

Questionnaire for study entitled "Timing of hospital arrival to the Singapore General Hospital after acute ischaemic stroke"

Part 1: Timing & Baseline Characteristics

1. Age (years) ....

2. Gender   □ Male (1)   □ Female (2)

3. Race   □ Chinese (1)   □ Malay (2)   □ Indian (3)   □ Others (4)

4. Date/Time of Onset (9 if unknown) ....……

5. Wake up Stroke?   □ Yes (1)   □ No (2)

6. Date/Time of ED Arrival..

7. Duration from onset to ED arrival (mins) ....

8. Time of ED triage (mins) ....
   a. Duration from ED arrival to triage (mins)...

9. Time of ED Doctor Review...
   a. Duration from Triage to ED Doctor review (mins) ....

10. Time CT of brain ordered ....

11. Time CT performed...
    a. Duration from CT ordered to CT performed (mins) ....
    b. Duration from ED Doctor to CT (mins) ....
    c. Comments

12. Name of Neuro Doctor Review ....

13. Time of Neuro Doctor Review ....
    a. Duration from Triage to Neuro review ....

14. NIHSS score at presentation ....

15. Marital Status   □ Married (1)   □ Single/Divorced/Widowed (2)

16. Living   □ Living alone (1)   □ Not living Alone (2)

17. Pre-morbid mRS (Modified Rankin Scale) ....

18. ACIS   □ Definite (1)   □ Probable (2)   □ Possible (3)   □ Not (4)

19. OCSP   □ TACI (1)   □ PACI (2)   □ POCI (3)   □ LACI (4)

20. TOAST   □ Large (1)   □ CE (2)   □ Small (3)   □ Other (4)   □ Undetermined (5)

21. Diagnosis at A&E ....

22. Diagnosis at Department of NEM ....

Part II: Presentation

1. Transportation to hospital   □ Ambulance (1) □ Taxi (2)
                                                       □ Bus/MRT (3)   □ Private Vehicle (4)
                                                       □ Inpatient referral

2. Medical Consultation before presentation   □ Yes (1)   □ No (2)

3. Reasons for delayed Presentation   □ Did not recognise symptoms of stroke (1)
                                                               □ Did not realise gravity of symptoms (2)
                                                               □ Inability to present to hospital unaided (3)
                                                               □ Difficulty in communication need to go to hospital (4)
                                                               □ Waiting for Spontaneous Resolution (5)
                                                               □ Trial of self medication (6)
                                                               □ Financial concerns (7)
                                                               □ Other (8)