Original Article

Factors Associated with Hospital Arrival Time in Acute Stroke

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Background: Acute stroke management is a time-dependent process, and early intervention is associated with more favorable outcomes. Given the time sensitivity of stroke management, the high morbidity and mortality rate, and the high cost of long-term post-stroke care, more information is needed about the factors that influence hospital arrival time after acute stroke in Thailand.

Objective: To investigate the factors that significantly influence hospital arrival time after acute stroke.

Materials and Methods: A retrospective chart review of acute stroke patients treated at the Division of Neurology, Department of Medicine, Siriraj Hospital, Bangkok, Thailand between 2007 and 2010 was conducted. Patients were allocated to either early (4.5 hours or less) or delayed (more than 4.5 hours) hospital arrival group. Demographic data, comorbidities, stroke severity using the NIHSS, current medications, mode of transportation to the hospital, referral status, and final diagnosis were collected.

Results: Of 1,045 patients, mean age was 65.4±13.8 years, 46.0% were female, and the median NIHSS score was 6. Regarding arrival time, 40.2%, 51.6%, and 59.14% of patients arrived at the hospital within 3, 4.5, and 6 hours, respectively. Only 6.6% arrived by ambulance. Multivariate logistic regression analysis revealed previous ischemic stroke/transient ischemic attack (p=0.022), diagnosis of severe stroke (NIHSS score >15) (p=0.001), seizure as an initial symptom (p=0.023), and diagnosis of hemorrhagic stroke (p=0.004) to be associated with early hospital arrival. Awakening or unknown-onset stroke (p<0.001) and referral from other centers (p<0.001) were factors associated with late arrival.

Conclusion: The factors that significantly influenced hospital arrival time after acute stroke in Thai population are the very low rate of EMS used and the delay in the referral of patients from other hospitals. Further study to investigate strategies to improve stroke awareness and referral protocols are warranted.

Keywords: Stroke, Cerebrovascular disease, Early hospital arrival time

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Acute stroke management is a time-dependent process. Thrombolytic therapy with intravenous recombinant tissue plasminogen activator (rt-PA) in acute ischemic stroke was proven effective if administered within 4.5 hours of stroke onset[1-7]. However, previous studies revealed that only small numbers of patients with acute ischemic stroke received intravenous rt-PA, even in developed countries like the United States[1-3,8-12]. In Thailand, only 3.8% to 5.5% of ischemic stroke patients received intravenous rt-PA[13,14]. Delayed hospital arrival after acute stroke is one of the main reasons patients are excluded from receiving rt-PA[7]. That same study found delayed hospital arrival after acute stroke to be significantly associated with lower probability of achieving a favorable outcome. A prior hospital-based study reported that only 18.7% of acute stroke patients arrived at the emergency department within 3 hours after onset of symptoms[13]. Other studies showed that 34.6% to 49.6% of patients arrived at the hospital within 4.5 hours after stroke onset[15,16]. Early hospital arrival is an essential component of successful stroke treatment.

The factors associated with hospital arrival time after the attack of acute stroke have been studied in different countries and clinical trials. The few

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studies conducted in Thailand evaluated a small study population[15,16]. Given the time sensitivity of stroke management, the high related morbidity and mortality, and the high cost of long-term post-stroke care, more information is needed about the factors that influence hospital arrival time after acute stroke in Thailand. Accordingly, the aim of the present study was to investigate the factors that significantly influence hospital arrival time after acute stroke in Thai population.

Materials and Methods

Patients and study design

The present retrospective study included acute stroke patients treated at the Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand between the June 2007 and September 2010. Siriraj Hospital is Thailand's largest national tertiary referral center. Patients' data were collected from the Siriraj Stroke Registry. The protocol for the present study was approved by the Siriraj Institutional Review Board (SIRB) (COA No.169/2555-EC2).

Patients aged 18 years and older who arrived at Siriraj Hospital within 24 hours after onset of stroke symptoms were eligible for inclusion. Diagnosis of stroke was confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) brain imaging. Patients with stroke mimic, in-hospital stroke, or lack of initial signs and/or symptoms of acute stroke were excluded. The demographic data, comorbidities, family history of stroke, history of cerebrovascular/cardiovascular disease, current medications, mode of transportation to the hospital, and referral status were collected. During the study period, intravenous thrombolysis treatment in acute stroke was available only at large academic medical centers in Thailand. Clinical characteristics of stroke, including initial signs and symptoms, time of onset, and hospital arrival time were determined. If symptoms occurred during sleep, the time of onset was considered to be the time the patient was last seen normally. These patients were categorized as having awakening or unknown-onset stroke. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS)[17,18]. The authors classified the severity of stroke into the following three categories, 0 to 4 for mild, 5 to 15 for moderate, and more than 15 for severe.

Patients were allocated to either the early (4.5 hours or less) or delayed (more than 4.5 hours) hospital arrival group based on the reported finding that post-stroke intravenous thrombolysis therapy is most effective if given within 4.5 hours after onset of stroke symptoms[1-7].

Statistical analysis

Demographic data were summarized using descriptive statistics. Categorical variables were presented as frequency and percentage. Continuous variables were reported as mean ± standard deviation (SD) for normally distributed data, and median and interquartile range for non-normally distributed data. Kolmogorov-Smirnov test was employed to test for normal distribution of data between groups. Comparisons of categorical variables between patients with and without adverse outcomes were performed using Chi-square test or Fisher's exact test. Continuous variables were compared using Student's t-test or Mann-Whiney U test. Factors affecting hospital arrival time were evaluated using univariate and multivariate analysis. Factors with a p-value of less than 0.2 in univariate analysis were entered into multivariate analysis using binary logistic regression model (backward stepwise method). For all tests performed, a two-tailed p-value of less than 0.05 was considered statistically significant. PASW Statistics version 20.0 (SPSS Inc., Chicago, IL, USA) was used to perform all statistical analyses.

Results

Of the 2,584 stroke patients identified in the Siriraj Stroke Registry during the study period, 1,539 (60.40%) were excluded for the following reasons, aged less than 18 years (0.04%), stroke mimickers (0.89%), in-hospital stroke patients (5.07%), lack of initial signs and/or symptoms of acute stroke (1.35%), lack of hospital arrival time information (13.24%), and duration from stroke onset to hospital arrival greater than 24 hours (38.97%). The remaining 1,045 patients were enrolled. The mean age was 65.4±13.8 years, 481 (46.0%) were female, and the median NIHSS score was 6 (IQR 3 to 13). Regarding type of stroke, 758 (72.50%) had acute ischemic stroke, 77 (7.40%) had transient ischemic stroke, 197 (18.90%) had acute hemorrhagic stroke (intracerebral hemorrhage or subarachnoid hemorrhage), and 13 (1.20%) had unknown type of cerebrovascular disease.

Regarding time of arrival at the hospital, 420 patients (40.19%) arrived within 3 hours after onset of symptoms, 119 (11.39%) arrived between 3 hours and 4.5 hours, 79 (7.56%) arrived between 4.5 hours and 6 hours, and 427 (40.86%) arrived later than 6 hours after symptoms onset (Figure 1). Hospital arrival time ranged from 0 to 23.75 hours. The mean±SD and

Table 1. Characteristics of the study population at baseline

Characteristics	Total (n = 1,045) n (%)	Early (≤4.5 hours) (n = 539) n (%)	Late (>4.5 hours) (n = 506) n (%)	p-value
Age (years), Mean ± standard deviation	65.40±13.80	64.89±13.96	65.94±13.63	0.216
Demographic data				
Female gender	481/1,045 (46.0)	255/539 (47.3)	226/506 (44.7)	0.391
Thai ethnicity	1,024/1,045 (98.0)	531/539 (98.5)	493/506 (97.4)	0.212
Income ≥30,000 baht/month*	143/331 (43.2)	67/164 (40.9)	76/167 (45.5)	0.393
Single marital status	117/1,043 (11.2)	70/537 (13.0)	47/506 (9.3)	0.055
Living alone	177/922 (19.2)	92/468 (19.7)	85/454 (18.7)	0.718
High school education or higher	160/465 (34.4)	84/246 (34.1)	76/219 (34.7)	0.900
Universal coverage health scheme (Thailand)	338/1,045 (32.3)	184/539 (34.1)	154/506 (30.4)	0.201
Risk factors				
Diabetes mellitus	246/1,040 (23.7)	126/536 (23.5)	120/504 (23.8)	0.909
Hyperlipidemia	343/1,041 (32.9)	173/538 (32.2)	170/503 (33.8)	0.573
Hypertension	693/1,042 (66.5)	360/537 (67.0)	333/505 (65.9)	0.707
Family history of stroke (first-degree relatives)	15/663 (2.3)	4/329 (1.2)	11/334 (3.3)	0.072
Previous ischemic stroke/transient ischemic attack	204/1,039 (19.6)	118/537 (22.0)	86/502 (17.1)	0.050
Previous intracerebral hemorrhage	35/1,043 (3.4)	21/539 (3.9)	14/504 (2.8)	0.316
Atrial fibrillation or flutter	145/1,042 (13.9)	81/539 (15.0)	64/503 (12.7)	0.283
Smoking	341/1,030 (33.1)	165/529 (31.2)	176/501 (35.1)	0.179
Alcohol drinking	214/665 (32.2)	108/334 (32.3)	106/331 (32.0)	0.932
Medications				
Antiplatelet/Anticoagulant	204/626 (32.6)	110/316 (34.8)	94/310 (30.3)	0.231
Lipid-lowering agent	192/622 (30.9)	102/313 (32.6)	90/309 (29.1)	0.350
Antihypertensive	288/629 (45.8)	140/316 (44.3)	148/313 (47.3)	0.453

* Approximately 1,000 USD/month

A p-value <0.05 indicates statistical significance

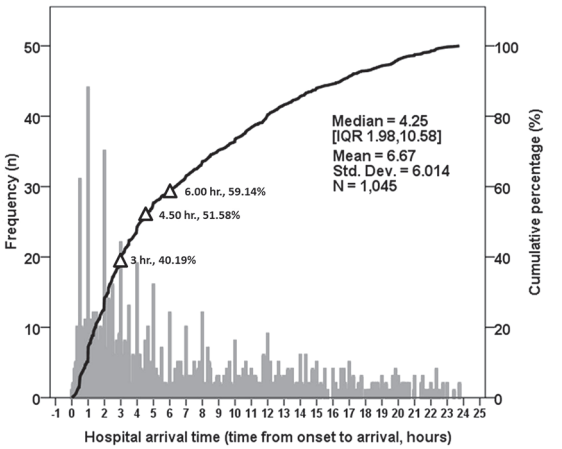

Figure 1. Distribution of time from stroke onset to hospital arrival by hour.

median (IQR) hospital arrival time was 6.67±6.014 hours and 4.25 hours (IQR 1.98 to 10.58), respectively.

Baseline patient characteristics, including vascular risk factors and medications used between the early and delayed groups, are shown in Table 1. The results of univariate analysis are presented in Table 2. Neither vascular risk factors nor history of previous stroke was found to be significantly different between the early and the delayed arrival groups. For initial symptoms at stroke onset, seizure was found to be significantly associated with early hospital arrival, and weakness was correlated with late hospital arrival. Impaired consciousness demonstrated a trend toward association with early arrival, but the relationship failed to achieve statistical significance. Multivariate logistic regression analysis is shown in

Table 2. Univariate analysis for factors significantly associated with early or late hospital arrival

Patient features	Total (n = 1,045) n (%)	Early (≤4.5 hours) (n = 539) n (%)	Late (>4.5 hours) (n = 506) n (%)	p-value
Hospital arrival time (hours), Median (IQR)	4.25 (1.98 to 10.58)	2.00 (1.00 to 3.00)	10.75 (7.24 to 15.00)	<0.001
Arrived to the hospital by ambulance/paramedics	68/1,038 (6.6)	31/538 (5.8)	37/500 (7.4)	0.287
Referred from other hospitals/private clinics	112/1,045 (10.7)	38/539 (7.1)	74/506 (14.6)	<0.001
NIHSS, Median (IQR)	6 (3 to 13)	7 (3 to 14)	6 (3 to 11)	0.245
NIHSS >15 (severe)	183/1,045 (17.5)	116/539 (21.5)	67/506 (13.2)	<0.001
Awakening stroke	428/1,045 (41.0)	161/539 (29.9)	267/506 (52.8)	<0.001
Initial symptoms				
Alteration of consciousness	106/691 (15.3)	61/344 (17.7)	45/347 (13.0)	0.082
Seizure	48/691 (6.9)	36/344 (10.5)	12/347 (3.5)	<0.001
Weakness	540/691 (78.1)	257/344 (74.7)	283/347 (81.6)	0.029
Sensory impairment	111/691 (16.1)	47/344 (13.7)	64/347 (18.4)	0.087
Speech difficulty	361/691 (52.2)	173/344 (50.3)	188/347 (54.2)	0.306
Dysphagia	31/691 (4.5)	16/344 (4.7)	15/347 (4.3)	0.835
Vertigo	60/691 (8.7)	24/344 (7.0)	36/347 (10.4)	0.113
Gait difficulty	291/691 (42.1)	139/344 (40.4)	152/347 (43.8)	0.366
Monocular blindness	3/691 (0.4)	2/344 (0.6)	1/347 (0.3)	0.558
Double vision	15/691 (2.2)	4/344 (1.2)	11/347 (3.2)	0.070
New onset headache	93/691 (13.5)	49/344 (14.2)	44/347 (12.7)	0.547
Final diagnosis				
Ischemic stroke or TIA	835/1,045 (79.9)	406/539 (75.3)	429/506 (84.8)	<0.001
Hemorrhagic stroke	197/1,045 (18.9)	127/539 (23.6)	70/506 (13.8)	<0.001
Undetermined CVD	13/1,045 (1.2)	6/539 (1.1)	7/506 (1.4)	0.694

IQR=interquartile range; NIHSS=National Institutes of Health Stroke Scale; TIA=transient ischemic attack; CVD=cerebrovascular disease

A p-value <0.05 indicates statistical significance

Table 3. Multivariate logistic regression analysis for factors that significantly influence early hospital arrival

Factors	Unstandardized coefficients		Wald	df	p-value	Exp (B)	95.0% CI for B	
	B	Standard error					Lower bound	Upper bound
Constant	0.294	0.125	5.527	1	0.019	1.342		
Previous ischemic stroke/TIA	0.522	0.227	5.276	1	0.022	1.685	1.080	2.631
NIHSS >15 (severe)	0.818	0.247	10.986	1	0.001	2.266	1.397	3.675
Seizure at onset	0.867	0.382	5.148	1	0.023	2.380	1.125	5.035
Diagnosis of hemorrhagic stroke	0.661	0.226	8.508	1	0.004	1.936	1.242	3.018
Referred from other hospitals/private clinics	1.048	0.279	14.161	1	<0.001	0.351	0.203	0.605
Awakening stroke or unknown onset stroke	1.524	0.184	68.279	1	<0.001	0.218	0.152	0.313

Df=degrees of freedom; CI=confidence interval; TIA=transient ischemic attack; NIHSS=National Institutes of Health Stroke Scale

A p-value <0.05 indicates statistical significance

Table 3. Factors significantly associated with early hospital arrival included previous ischemic stroke/ transient ischemic attack (OR 0.522; 95% CI 1.080 to 2.631; p=0.022), severe stroke (NIHSS >15) (OR 0.818; 95% CI 1.397 to 3.675; p=0.001), seizure as an initial symptom (OR 0.867; 95% CI 1.125 to 5.035; p=0.023), and diagnosis of hemorrhagic stroke (OR 0.661; 95% CI 1.242 to 3.018; p=0.004). Factors associated with late hospital arrival were awakening or unknown-onset stroke (OR 1.524; 95% CI 0.152 to 0.313; p<0.001) and referral from other hospitals or clinics (OR 1.048; 95% CI 0.203 to 0.605; p<0.001).

Discussion

The authors have shown that 40.2% (420/1045), 51.6% (539/1045), and 59.1% (618/1045) of acute stroke patients who seek medical attention within 24 hours arrived within 3, 4.5, and 6 hours, respectively. The authors also found that severe stroke (NIHSS >15), seizure at onset, and hemorrhagic stroke were significantly associated with early hospital arrival, while awakening stroke, stroke of undetermined onset, and referral from other hospitals were associated with late arrival.

The present study results are in line with the previous studies conducted in Thailand[16] that reported that 38.2% (83/217) and 49.5% (89/181) of patients presented within 4.5 hours. Results from other countries varied from 17.5% to 46% and from 37% to 75% for 3 and 6-hour hospital arrival, respectively[19-28]. Previous studies reported median arrival times varied from 2.51 to 15 hours[26-33]. Studies conducted in Western populations suggest that Westerners tend to arrive earlier than Asians. This difference may be explained by a higher rate of ambulance transport of stroke patients as well as better stroke awareness knowledge in Western populations[31,34,35].

Many studies have shown that the use of emergency medical services (EMS) is associated with early hospital arrival[15,22-24,26-28,31-33,36-38]. However, the authors' result did not show any significant relationship between early hospital arrival and the use of EMS. This result was similar to that reported in another study in Thailand[16]. Possible explanations included traffic problems in big cities, and the low rate of the EMS usage (6.6%). Several studies[28,31,36] demonstrated that referral of stroke patients from other centers significantly associated with longer arrival time. This finding reflects the need to study the referral process to improve the arrival time.

Many studies[15,24-27,31,33,37,39] reported severe stroke (defined by either NIHSS or Glasgow Coma Score) to be associated with shorter hospital arrival, which is similar to the present finding. Sudden onset symptoms were reported to be associated with early arrival at the hospital[16,27]. Consistent with previous reports[28,31,36,40], the authors found that hemorrhagic stroke significantly influenced earlier hospital arrival. In addition, the median NIHSS score were higher in hemorrhagic stroke than in ischemic stroke [11 (IQR 6 to 17) versus 6 (3 to 12), respectively, p<0.001] (data not shown). Awakening stroke or nocturnal/ unclear-onset stroke was reported to be correlated with delayed arrival[29,32,33,36,41,42], which corresponded with the findings of the present study.

Concerning the presenting symptoms of stroke, impaired consciousness was described as an early arrival factor in several previous reports[25-28,32,36]. In the present study, although patients with this symptom tended to arrive at the hospital earlier than those without, awareness of this symptom did not significantly influence early hospital arrival. However, seizure was shown to be strongly associated with early hospital arrival. No other stroke symptoms were correlated with the arrival time in the present study, which raised concerns about stroke awareness and symptoms detection among Thai people.

Although stroke risk factors including diabetes mellitus, hypertension, hyperlipidemia, atrial fibrillation, smoking, and family history of stroke were reported to be associated with hospital arrival time in several studies[23,28,32,33,37], these factors did not exert any significant influence in the present study. In contrast, patients with prior ischemic stroke or TIA were likely to arrive at the hospital earlier than those without. This finding was statistically significant in multivariate analysis, which is similar to earlier studies[20,25].

The present study had some limitations. Firstly, the data were collected from a single tertiary care center located in Bangkok, Thailand, as such, the findings may not represent the whole country. Secondly, with the retrospective design, some information might have been missing or incomplete. Moreover, the authors were not able to evaluate stroke awareness among the study cohort, and this could be an important factor that influences hospital arrival time. The fact that neither stroke risk factors nor stroke symptoms demonstrated significant influence on hospital arrival time may suggest poor stroke awareness and knowledge among the Thais.

Despite limitations, the present study is the largest study in Thailand that aimed to investigate factors associated with hospital arrival time. The results of the

present study highlight the urgent need to develop a strategy to improve inter-hospital transfer process. In addition, a different model of acute stroke care, i.e., the use of tele-consultation or mobile stroke unit should be considered to reduce door to needle time in tPA eligible stroke patients. Social activities to improve stroke knowledge and awareness among Thai people are also required.

Conclusion

Severe stroke with an initial NIHSS of more than 15, seizure as a presenting symptom, and hemorrhagic stroke are significantly associated with early hospital arrival. Awakening stroke as well as stroke of undetermined onset and referral from other hospitals are associated with delayed arrival. Strategies to improve stroke awareness and referral protocols together with the use of tele-medicine and mobile stroke unit should be considered.

What is already known on this topic?

Severe stroke, stroke with sudden onset symptom, and the use of EMS were previously reported in studies conducted in Thailand as significant factors associated with early hospital arrival.

What this study adds?

Hemorrhagic stroke and stroke presenting with seizure were associated with early hospital arrival, while awakening or unknown onset stroke and referral from other hospitals were reported to be correlated with delayed arrival. This information is crucial and can be used for strategic design to shorten the pre-hospital care for acute stroke patients.

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Authors' contributions

All authors contributed to the drafting and revising of this manuscript.

Conflicts of interest

The authors declare no conflict of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in the present report.

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