

## ORIGINAL RESEARCH



# Prolonged boarding in emergency department with neurologist coverage does not worsen the outcomes for patients with acute ischemic stroke

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## Abstract

Shortage of hospital beds is a common phenomenon and some acute ischemic stroke patients have to be cared for in emergency department with their staffs. However, boarding acute stroke patients in emergency department for hospital ward beds has been associated with worse outcomes. Whether an additional coverage of neurologist for them would benefit was not elucidated. All acute ischemic stroke patients admitted to our hospital between January 2016 and December 2018 were retrospectively analyzed. Patients were classified according to the various emergency department length of stay. A binary Logistic regression was used to explore the relationship of coverage of neurologist for acute ischemic stroke patients admitted but boarded in emergency department to their hospital outcomes by adjusting for age, patient gender, comorbidities, triage urgency, initial National Institute of Health Stroke Scale (NIHSS) score, whether underwent thrombolysis, admitted to Intensive care unit (ICU) and complications. A total of 1150 acute ischemic stroke patients were evaluated. 24.1% of them were admitted within 4 hours, 10.3% within 4–8 hours while 65.6% patients boarded in emergency department more than 8 hours although they were admitted, due to the shortage ward beds. However, with the neurologist coverage, their prolonged waiting hours in emergency department was not associated with poor patients' outcomes including Modified Rankin Scale (mRS)  $\geq 4$  at discharge, long hospital length of stay and high hospital cost. In summary, with additional neurologist coverage for acute ischemic stroke patients who were admitted but boarded in emergency department, prolonged waiting hours in emergency department was not associated with worse patients' outcomes including mRS  $\geq 4$  at discharge, long hospital length of stay and high hospital cost.

## Keywords

Acute ischemic stroke; Emergency department; Neurocritical care; Survival

## 1. Introduction

Acute stroke is a time-dependent emergency situation, requiring multidisciplinary and timely care that is typically delivered in designated areas such as stroke units [1]. However, boarding admitted acute ischemic stroke patients in the emergency department due to limited hospital bed availability is a worldwide problem. Given the limited space, understaffing, underperformance of emergency physicians for stroke and overcrowding of emergency department, compromised care delivery to these patients is inevitable. Consequently, this practice has been demonstrated with increased serious complications and compromised patients' outcomes [2, 3]. A delay of more than 5 hours for critically sick stroke patients before admission to neurocritical care is independently associated with poor patient outcomes [4]. Theoretically, extending the neurologist's care to patients who boarded in emergency department is a potential

solution with intuitive appeal. Thus, therapeutic interventions that are traditionally initiated after admission could be implemented earlier while the patient awaiting a bed in the emergency department [5]. We hypothesized that extended this neurologist coverage to the emergency department-boarded acute ischemic stroke patients would reverse the confirmed increased risk and comprised outcomes. To answer above-mentioned question, the association between the emergency department length of stay and outcomes for all patients with acute ischemic stroke in a tertiary Chinese hospital over a 3-year period was examined.

## 2. Methods

### 2.1 Study design and setting

This is a cross-section study included all patients with acute ischemic stroke presented to our hospital, a 1200-bed tertiary

teaching hospital (Qingchun Campus) in Hangzhou, China, from 01 January 2016 to 31 December 2018. The SRRSH was co-established with the Loma Linda University, California, USA, in 1994 [6], and the hospital and subsequently its stroke center had been accredited by the Joint Commission International.

After initial triaged by a senior emergency nurse, the patient was first assessed by the emergency department physician and thereafter specific specialists would be consulted if necessary. To early recognize the patients with potential acute stroke and early initiate aggressive interventions such as intravenous thrombolysis or intravascular therapy, the on-duty emergency department physician and neurologist would be informed simultaneously whenever this kind patient was triaged. Thereafter, the on-duty neurologist would carefully evaluate the patient with the help of CT (Computed Tomography) findings and physical examination. Since the frequently shortage of inpatient bed for stroke patients needing hospitalization, some critically ill stroke patients may have to board in emergency department. Under that circumstance, the emergency physicians were obligated to care for both the boarded patients and continuously urgent visitors. In order to guarantee the care quality of boarded stroke patients, routine coverage of ward rounds by neurologists for them were proposed, especially given our previous study has demonstrated that boarded admitted patients in emergency department for inpatient beds was associated with increased of serious complications [6]. The neurologists would see these patients once or twice daily at least during their stay in emergency department waiting for ward beds. Generally, they routine check patients' signs and symptoms, suggest the emergency physicians to increase fluid intake, or to order another CT scan should the patient's situation is deteriorating. Of note, the emergency physicians are responsible for the care for boarded patients for most time of the day.

## 2.2 Data sources and processing

All the admitted patients with the diagnosis of acute ischemic stroke during the study period were enrolled. We excluded those patients secondary to acute aortic dissection with involvement of carotid artery, post cardiopulmonary resuscitation, or patients with acute ischemic stroke but onset-to-door time more than 36 hours. For each patient, the following data elements were extracted: (1) arrival time and way, (2) age and gender, (3) risk factors, (4) triage category, (5) initial signs and symptoms, (6) hours from last known well, (7) initial National Institute of Health stroke scale (NIHSS), (8) when the patient underwent a CT scan and possible stroke aetiology, and Oxford Community Stroke Project (OCSP) stroke classification, (9) time the neurologist first evaluated the stroke patient, (10) initial treatment and whether the patient received rt-PA (Recombinant Human Tissue Plasminogen Activator for Injection) thrombolysis and the administration time, (11) disposition location, (12) date and time of transfer to inpatient ward, (13) date and time the patient had another head CT scan, and complete the initial investigation of echocardiogram and vascular imaging, (14) whether the patient had a secondary intracranial bleeding, underwent a decompression surgery, with a hospital

acquired pneumonia or deep vein thrombosis, (15) all-cause hospital mortality, NIHSS and modified Rankin scale (mRS) at discharge, (16) hospital cost and hospital length of stay.

## 2.3 Definitions and hospital outcomes

As practice, 08:00–17:00 was defined as office hours. NIHSS was routine included in the initial and discharge evaluation of neurologists. NIHSS is a scale tool to help to objectively quantify the impairment caused by a stroke, ranging from 0 to possible maximal score 42. We categorized stroke severity according to the NIHSS into groups as NIHSS <5 (mild), NIHSS 5–14 (moderate) or NIHSS >14 (severe) [7]. As for some patients with missing NIHSS data, we used the previously reported retrospectively chart review method to estimate the NIHSS [7]. The mRS is a 7-point scale ranging from no symptoms (score 0) to death (score 6). A score of 2 or less indicates functional independence. Neurological outcomes at discharge for some patients were estimated from the charts and scaled according to mRS. OCSP stroke classification was determined on the clinical assessment and CT findings. As to the outcomes, the secondary intracranial hemorrhage was defined as new-onset neurologic deterioration and evidence of intracranial hemorrhage on imaging follow-ups. Hospital acquired pneumonia was defined as any pneumonia happened to a patient at least 48–72 hours after being admitted, whereas the diagnosis of deep vein thrombosis was based on the clinical assessments and ultrasound findings. Emergency department length of stay (ED LOS) was calculated as the difference between the time of registration and time of the patient departure from the emergency department. Hospital cost was calculated as all the fees charged during patients' stay in emergency department and wards.

The primary outcome was mRS  $\geq 4$  at hospital discharge, indicative of death or severe disability. Secondary outcomes included hospital length of stay, complications and hospital cost.

## 2.4 Primary data analysis

Descriptive data were reported as either mean  $\pm$  SD, median (interquartile range) or number and percentage. The Kolmogorov-Smirnov test was used to determine normality. Comparisons between groups were made using chi-square analysis for categorical variables. Continuous variables were compared using Independent Sample *t* test for normally distributed data and Mann-Whitney U test for non-normally distributed data. Then emergency department length of stay was categorized into  $\leq 4$ , 4–8 and  $\geq 8$  hours. To examine whether prolonged boarding in emergency department for acute ischemic stroke patients was associated with worse outcomes, the median values of the hospital cost and hospital length of stay were used as cutoffs to dichotomize the data into categorical variables for regression analysis.

To identify potential correlation between neurologist coverage and hospital outcomes, binary logistic regression analysis was performed using hospital outcomes (high hospital cost (yes/no), long hospital length of stay (yes/no), and mRS at hospital discharge  $\geq 4$  (yes/no)) as the dependent variable and neurologist coverage, patient demographics, arrival hours,

clinical condition, stroke aetiology, whether received t-PA thrombolysis as the independent variables. Odds ratios and their 95% confidence intervals (95% CIs) were calculated. Statistical analysis was performed, using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Significance was defined as a  $p$  value  $< 0.05$ .

### 3. Results

The study cohort comprised of 1150 acute ischemic stroke patients. After triage and primary management in emergency department, 277 patients were admitted within 4 hours, 119 within 4–8 hours, while 754 (65.6%) patients boarded in emergency department more than 8 hours although they were admitted due to the shortage ward beds. Although the triage urgency categories 1 and 2 percent were similar between groups, patients with emergency department length of stay  $\geq 8$  hours were less to arrive with ambulance ( $p < 0.001$ ), less possible with motor deficit ( $p = 0.004$ ) or cognitive impairment ( $p < 0.001$ ), and with a higher incidence of visiting within night shift ( $p < 0.001$ ) (Table 1). As for the onset-to-door time, those boarded longer in the emergency department were significantly longer than those admitted immediately (median 19 vs. 12 hours,  $p = 0.005$ , Table 1). Generally, those admitted quickly were with a higher percent of initial NIHSS  $> 14$  (10.8% vs. 4.2% vs. 4.0%,  $p < 0.001$ ) (Table 1). There was significant difference between the three groups as to the Stroke aetiology ( $p = 0.002$ ) and OSCP stroke classification (Oxford Community Stroke Project) ( $p < 0.001$ ) (Table 1).

With respect to the care process, the door-to-CT time was comparable between groups (36.0 vs. 42.0 vs. 35.1 min for three groups respectively) and was no correlation with the emergency department length of stay. There were more significant patients in the ED LOS  $\leq 4$  hours' group received t-PA thrombolysis (14.8% vs. 10.1% vs. 2.1%,  $p < 0.001$ ) (Table 2). Simultaneously, a significant higher percent patient in the ED LOS  $\leq 4$  hours' group received vascular imaging within 24 hours (33.6% vs. 26.9% vs. 15.4%,  $p < 0.001$ ) and were admitted to ICU (35.7% vs. 27.7% vs. 6.4%,  $p < 0.001$ ) (Table 2).

ED LOS, emergency department length of stay; ICU, intensive care unit; rt-PA, Recombinant Human Tissue Plasminogen Activator for Injection; CT, computed tomography; MRI, magnetic resonance imaging.

With respect to the outcomes of stroke patients with various emergency department length of stay, there were significant higher percent patient in the ED LOS  $\leq 4$  hours' group underwent early neurological deterioration (16.6% vs. 11.8% vs. 6.1%,  $p < 0.001$ ), secondary intracranial hemorrhage ( $p = 0.005$ ) and decompression surgery (10.5% vs. 5.9% vs. 2.1%,  $p < 0.001$ ) (Table 3). The median hospital cost and hospital length of stay were \$1624.5 and 9.0 days respectively. The median hospital cost was significantly higher in ED LOS  $\leq 4$  hours' group than those in ED LOS 4–8 hours' group and ED LOS  $\geq 8$  hours' group (median \$2091.2 vs. \$1651.5 vs. \$1518.6 respectively,  $p < 0.001$ ) (Table 3). Median hospital length of stay for patients in ED LOS  $\leq 4$  hours' group was also significantly longer than other two groups (median 10.0 vs. 9.0 vs. 8.0 days,  $p < 0.001$ ) (Table 3). Meanwhile, the mRS  $\geq 4$

percent and all-cause mortality were significant higher in the ED LOS  $\leq 4$  hours' group (both  $p < 0.001$ ) (Table 3).

Then, the hospital cost and hospital length of stay were dichotomized into long ( $\geq$ median) and short hospital length of stay, and high ( $\geq$ median) and low hospital cost respectively. The association between prolonged emergency department length of stay for patients with acute ischemic stroke and hospital outcomes were further assessed by regression analysis with adjustment for age, comorbidities, triage urgency, initial NIHSS score, whether underwent thrombolysis, admitted to ICU and complications (Table 4). Acute ischemic stroke patients admitted but boarded in emergency department, prolonged waiting hours in emergency department was not associated with mRS  $\geq 4$  at discharge, long hospital length of stay and high hospital cost when covered with neurologist (Table 4).

### 4. Discussion

This study demonstrated that after triage and primary management in emergency department, 24.1% patients with acute ischemic stroke were admitted within 4 hours, 10.3% within 4–8 hours while 65.6% patients boarded in emergency department more than 8 hours although they were admitted due to the shortage ward beds. With the neurologist coverage, however, their prolonged waiting hours in emergency department was not associated with patients' outcomes including mRS  $\geq 4$  at discharge, long hospital length of stay and high hospital cost.

Stroke is the fourth leading cause of mortality and is the leading cause of disability in the United States, affecting nearly 800,000 people annually. Timely identification and treatment may improve patient outcomes given that the stroke is a time-sensitive disease. Every minute in delay of treatment for acute ischemic stroke would lead to estimated 1.9 million neurons lost [1]. Consequently, mobile ambulance stroke units with staff and CT may enable more rapid treatment with tissue plasminogen activator compared to standard emergency medical services (72 min vs. 108 min) improved utility-weighted disability outcomes at 90 days [8]. Because of the busy nature of practice in emergency department, where patients with varying degrees of severity and different diagnosis are being simultaneously treated, the physicians and nurses may not be able to provide the close constant attention to sick patients. The major advantage of early admission to the stroke unit is to ensure that an especially trained multidisciplinary team focuses on protocols that reduce the risk of complications [9]. Stroke patients who have to board in emergency department for a ward or ICU bed may be at risk of further neurological deterioration and complications that can lead to significant mortality and morbidity [10]. Rincon and his colleague proven that critically ill stroke patients with an ED LOS  $\geq 5$  hours had a 4-fold increase in the odds of poor outcome compared with those with an ED LOS  $< 5$  hours, and this effect was independent of age, sex, admission diagnosis, and stroke severity [4].

Fortunately, these risks can be anticipated and minimized in most cases although such care is complex and necessitates a multidisciplinary and timely approach that may be lacking in the emergency department setting. Stroke units have been proven to decrease mortality and improve outcomes. A direct "potential thrombolysis" pathway with direct admission to

**TABLE 1. Characteristics of study population.**

Variables	Overall (n = 1150)	ED LOS ≤4 h (n = 277)	ED LOS 4–8 h (n = 119)	ED LOS ≥8 h (n = 754)	<i>P</i>
Male gender (n, %)	719 (62.5%)	173 (62.5%)	73 (61.3%)	473 (62.7%)	0.995
Age, yr	67.9 ± 12.8	67.9 ± 13.1	68.67 ± 11.7	67.71 ± 12.8	0.753
Risk factors (n)					
Coronary heart disease	104	22	8	74	0.442
Hypertension	828	200	87	541	0.842
Diabetes mellitus	319	60	33	226	0.030
Chronic lung disease	41	10	3	28	0.823
Carotid artery stenosis	79	18	5	56	0.437
Atrial fibrillation	195	66	21	108	0.002
Smoking history	360	93	34	233	0.694
Renal insufficiency	50	12	4	34	0.865
Previous stroke or TIA	203	45	21	137	0.770
Arrival with ambulance (%)	20.2	27.8	25.2	16.6	<0.001
Triage urgency (% category 1 and 2)*	62.9	67.9	64.7	60.7	0.100
Arrival time (n)					
Day shift (08:00–17:00)	693	195	92	406	<0.001
Night shift (17:01–07:59)	457	82	27	348	
Signs and symptoms (n)					
Headache	34	8	4	22	0.955
Motor deficit	787	203	91	493	0.004
Speech disorder	551	142	60	349	0.276
Sensory impairment	352	80	21	251	0.003
Visual disturbances	60	9	1	50	0.008
Gait disturbances	152	32	18	102	0.546
Seizures	11	3	3	5	0.141
Cognitive impairment	130	54	11	65	<0.001
Onset-to-door time, (IQR), h	14.0 (5.0–24.0)	12.0 (3.5–24.0)	12.0 (4.0–24.0)	19.0 (5.0–30.0)	0.005
Initial NIHSS, (IQR)	2.0 (1.0–6.0)	3.0 (2.0–7.0)	2.0 (1.0–7.0)	1.0 (1.0–4.0)	
NIHSS 5–14	261	70	36	155	<0.001
NIHSS >14	65	30	5	30	
Stroke aetiology (n)					
Cardioembolic	172	62	20	90	0.002
Atherosclerotic	927	201	93	633	
Lacunar	19	6	2	11	
Mixed	21	6	0	15	
OCSP stroke classification (n)					
TACI	106	48	19	39	<0.001
PACI	784	169	75	540	
POCI	235	54	19	162	
LACI	25	7	2	16	

*IQR*, Inter quartile range; *ED LOS*, emergency department length of stay; *TIA*, transient ischemic attack; *NIHSS*, National Institute of Health stroke scale; *OCSP*, Oxford Community Stroke Project; *TACI*, total anterior circulation infarct; *PACI*, partial anterior circulation infarct; *POCI*, posterior circulation infarct; *LACI*, lacunar infarct; \*Triage category on the Emergency Severity Index, a 5-level triage system, where 1 represents the sickest or most urgent cases and the 5 for the least urgent.

**TABLE 2. Comparison of care processes between stroke patients with various emergency department length of stay.**

Variables	Overall (n = 1150)	ED LOS ≤4 h (n = 277)	ED LOS 4–8 h (n = 119)	ED LOS ≥8 h (n = 754)	<i>P</i>
Door-to-CT time, (IQR), min	36.0 (21.0–61.8)	36.0 (20.0–58.0)	42.0 (27.0–72.0)	35.1 (20.0–64.2)	0.04
Initial platelet antiaggregants therapy (n)					
Aspirin	783	209	100	470	<0.001
Combined aspirin and clopidogrel	234	41	18	175	
Received rt-PA thrombolysis (n)	69	41	12	16	<0.001
Door-to-needle time, (IQR), min	36.6 (12.0–78.0)	43.2 (21.6–69.0)	22.2 (11.4–68.4)	27.9 (14.1–143.1)	0.878
Admitted to ICU from emergency department (%)	15.7	35.7	27.7	6.4	<0.001
Vascular imaging within 24 h (%)	21.0	33.6	26.9	15.4	<0.001
Echocardiography within 24 h (%)	58.3	65.7	55.5	56.0	0.017
Serum creatinine on admission (μmol/L)	78.5 ± 40.4	75.5 ± 24.9	79.0 ± 43.4	79.5 ± 44.2	0.372
Numbers of CT/MRI follow-ups within 72 h (n)	1.1 ± 0.8	1.1 ± 0.9	1.2 ± 0.8	1.1 ± 0.8	0.105

ED LOS, emergency department length of stay; ICU, intensive care unit; rt-PA, Recombinant Human Tissue Plasminogen Activator for Injection; CT, computed tomography; MRI, magnetic resonance imaging.

**TABLE 3. Comparison of outcomes between stroke patients with various emergency department length of stay.**

Variables	Overall (n = 1150)	ED LOS ≤4 h (n = 277)	ED LOS 4–8 h (n = 119)	ED LOS ≥8 h (n = 754)	<i>P</i>
Early neurological deterioration	106	46	14	46	<0.001
Underwent decompression surgery	52	29	7	16	<0.001
Secondary intracranial hemorrhage	54	23	4	27	0.005
Hospital acquired pneumonia	154	63	20	71	<0.001
Venous thrombosis embolism*	27	10	4	13	0.154
Gastroenteral/urinary tract bleeding	44	11	8	25	0.197
Hospital cost (\$)	1624.5 (1207.0–2583.0)	2091.2 (1386.2–4031.1)	1651.5 (1237.9–2736.1)	1518.6 (1156.7–2196.4)	<0.001
Hospital length of stay (d)	9.0 (7.0–13.0)	10.0 (7.0–15.0)	9.0 (7.0–14.0)	8.0 (7.0–12.0)	<0.001
All-cause hospital mortality (n, %)	49 (4.3%)	27 (9.7%)	8 (6.7%)	14 (1.9%)	<0.001
mRS at discharge (n, %)					
mRS ≥4 at discharge	266 (23.1%)	89 (32.1%)	36 (30.3%)	141 (18.7%)	<0.001

ED LOS, emergency department length of stay; mRS, modified Rankin Scale; \*includes Deep vein thrombosis and pulmonary embolism.



**TABLE 4. Association between hospital outcomes and prolonged emergency department length of stay for stroke patients<sup>†</sup>.**

Outcomes	ED length of stay before admission (h)	OR (95% CI)	p
mRS ≥4	≤4 h	Reference	-
	4–8 h	0.88 (0.52–1.49)	0.639
	≥8 h	1.52 (0.78–2.97)	0.220
Long hospital length of stay	≤4 h	Reference	-
	4–8 h	1.19 (0.85–1.67)	0.323
	≥8 h	1.08 (0.67–1.72)	0.761
High hospital cost	≤4 h	Reference	-
	4–8 h	1.68 (1.17–2.40)	0.005
	≥8 h	0.95 (0.57–1.57)	0.830

<sup>†</sup>Regression model adjusted for age, patient gender, comorbidities, triage urgency, initial NIHSS score, whether underwent thrombolysis, admitted to ICU and complications. ED, emergency department; OR, Odds Ratio; mRS, modified Rankin Scale; CI, confidence interval.

a neurological stroke unit for patients with ischemic stroke, can result in earlier admission, reaching the recommended care delay, and a large proportion of patients receiving rt-PA therapy [11]. Moreover, specialized units may benefit from economies of scale to improve efficiency and optimize the allocation of emergency department and hospital resources. In a Brazil hospital, a “vascular unit” located within hospital’s emergency department and functions as a “crowding-proof” area to allow better quality of care for acute vascular emergencies and was implemented to reduce wait times and consolidate the personnel and resources needed for similar types of emergencies [12, 13]. Additional solutions for this problem would be the implementation of advanced ICU monitoring in the ED by increasing the availability of ICU beds within the ED, deployment of critical care trained ED staff, improvement or facilitation of the ICU physician presence in the ED, and improvement of patient flow within each hospital system [6]. We can speculate a creation of “new perception and culture of stroke care”. The major benefits of a comprehensive acute stroke care are the monitoring of cardiovascular parameters, adherence to treatment protocols, training of the staff, presence of a dedicated stroke specialist, and early integration of neuro-rehabilitation programs [14]. This “stroke-focused” approach offers better stroke management by continuity of the primary team, a multidisciplinary neuro-rehabilitation program, and comprehensive medical, nursing protocols, and treatment algorithms [14]. In our study, with the neurologist coverage, their prolonged waiting hours in emergency department was not associated with poor patients’ outcomes including mRS ≥4 at discharge, long hospital length of stay and high hospital

cost. This is because boarding stroke patients still receive care provided by related disciplines as a mobile service in our institution, which could have eliminated some of the effect of prolonged emergency department boarding. Saukkonen *et al.* [15] found that ED LOS did not impact outcome in critically ill patients who admitted but boarded in emergency department when invasive hemodynamic monitoring, access to high intensity nursing, and rapid transfer to the ICU were available in emergency department. Therefore, admitted patients should be promptly distributed to inpatient care providers in the event of emergency department crowding, even if these patients are physically located in an emergency department. The delivery of care for acute ischemic stroke should be patient-centered rather than based on their physical locations. Therefore, therapeutic interventions that are traditionally initiated during the ward phase of an admission could be implemented while the patient remains in the emergency department awaiting a bed [6].

Our study has several limitations. First, our study demonstrated the findings by retrospective chart review in a single institution and a particular country, which may raise concerns about the generalization of the study. However, previous studies have demonstrated an association between prolonged ED LOS and worse outcomes in unclassified patients and stroke patients. Of note, common needs among these patients are for both time-sensitive intervention and continuous monitoring, as with those patients in our study [16]. Therefore, we believe our findings can be generalized to other hospital structures. Secondly, we only evaluated the outcomes including mRS ≥4, high hospital cost and long hospital length of stay rather than the effect on the thrombolysis or intravascular interventions because inherent drawbacks of the retrospective study. Lastly, we did not evaluate the staffing of emergency department and targeted wards in the study. Staffing levels are thought to another important factors affect the patients’ outcomes as which assessed in our study.

## 5. Conclusions

In summary, approximate two thirds of the acute ischemic stroke patients boarded in emergency department more than 8 hours due to the shortage stroke ward beds although they were admitted. Nevertheless, after coverage with neurologist for the ED-boarded stroke patients, their prolonged waiting hours in emergency department was not associated with poor outcomes including mRS ≥4 at discharge, long hospital length of stay and high hospital cost.

## AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

## AUTHOR CONTRIBUTIONS

XH and BWY—designed the research study. QFY, HJY and BWY—performed the research. XH, DSP and BWY—analyzed the data. XH and BWY—wrote the manuscript. All

authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the institutional review board of Sir Run Run Shaw Hospital (SRRSH) (20200423-37) with waived from the need for a consent form given it was a retrospective study and all the information were de-identified.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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