

Emergency medical services use and its association with acute ischaemic stroke evaluation and treatment in Singapore

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ABSTRACT

Background Emergency medical services (EMS) is a critical link in the chain of stroke survival. We aimed to assess EMS use for stroke in Singapore, identify characteristics associated with EMS use and the association of EMS use with stroke evaluation and treatment.

Methods The Singapore Stroke Registry combines nationwide EMS and public hospital data for stroke cases in Singapore. Multivariate regressions with the generalised estimating equations were performed to examine the association between EMS use and timely stroke evaluation and treatment.

Results Of 3555 acute ischaemic patients with symptom onset within 24 hours admitted to all five public hospitals between 2015 and 2016, 68% arrived via EMS. Patients who used EMS were older, were less likely to be female, had higher stroke severity by National Institute of Health Stroke Scale and had a higher prevalence of atrial fibrillation or peripheral arterial disease. Patients transported by EMS were more likely to receive rapid evaluation (door-to-imaging time ≤ 25 min 34.3% vs 11.1%, OR=2.74 (95% CI 1.40 to 5.38)) and were more likely to receive intravenous tissue plasminogen activator (tPA, 22.8% vs 4.6%, OR=4.61 (95% CI 3.52 to 6.03)). Among patients treated with tPA, patients who arrived via EMS were more likely to receive timely treatment than self-transported patients (door-to-needle time ≤ 60 min 52.6% vs 29.4%, OR=2.58 (95% CI 1.35 to 4.92)).

Conclusions EMS use is associated with timely stroke evaluation and treatment in Singapore. Seamless EMS-Hospital stroke pathways and targeted public campaigns to advocate for appropriate EMS use have the potential to improve acute stroke care.

studies have demonstrated that the use of emergency medical services (EMS) is associated with rapid evaluation and treatment of stroke.^{6–9,11} However, most of these studies were conducted in western countries such as the USA. Less is known about EMS use among stroke patients in Asian-Pacific countries such as Singapore where the cultures, healthcare and EMS systems are different from western countries.^{12–13} A previous nationwide study in Singapore showed that nearly half of the patients with ST-segment elevation myocardial infarction came to the hospital using private transportation modes.¹⁴ Regional studies also found that EMS is underutilised for only 50% stroke patients in Singapore arrived at hospitals via EMS,^{5,8} despite it being a universal service which is free for emergency calls. Identifying factors associated with EMS use will provide critical information needed to inform the design of tailored interventions to increase public stroke awareness and promote actions that will lead to early hospital arrival and treatment.

Using national data, we aimed to identify characteristics associated with EMS use in stroke patients and examine the association of EMS use with timely stroke evaluation and treatment. We hypothesise that EMS use is associated with timely in-hospital stroke care in Singapore.

INTRODUCTION

Stroke is the fourth leading cause of morbidity and mortality in Singapore.^{1–2} Despite numerous clinical trials demonstrating the effectiveness of thrombolytic therapy for improving outcomes in acute ischaemic stroke,^{3–4} utilisation of tissue plasminogen activator (tPA) has been lower in Singapore than in western countries such as the USA, suggesting further room for improvement.^{5,6} Even among those treated, only half received thrombolytic therapy within 60 min.^{7,8} Several

METHODS

Setting and data sources

Singapore is an urban city-state and island country that has the world's third highest population density.^{15–16} Unlike the EMS systems in western countries such as the USA where the structure of EMS varies by state, EMS in Singapore is a single-tier, fire department-based system.^{17–18} Run by the Singapore Civil Defence Force (SCDF), this national EMS system responds to any medical emergencies on the island and is



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free to all callers.¹⁷ Specifically, the EMS is activated by a centralised 995 dispatching system and the ambulances are manned by three crew members including an intermediate level emergency medical technician (EMT), a basic level EMT and a driver.¹⁷ Ambulance crews are trained to perform prehospital stroke assessment using the Cincinnati Prehospital Stroke Scale (CPSS)¹⁹ and transport suspected stroke patients to designated public hospitals that are approved to deliver acute stroke care.¹⁷

For this retrospective study, we extracted anonymised data related to EMS use among stroke patients from the Singapore Stroke Registry, a national stroke registry that was developed to collect and analyse epidemiological and clinical data on all stroke cases among Singapore residents aged 15 years and above who were admitted to all the public hospitals in Singapore.²⁰ The registry consists of several data sources: medical claims (ie, MediClaims) from the Ministry of Health, hospital inpatient discharge summary from all public healthcare institutions and data from the Death Registry. Stroke cases were identified based on International Classification of Diseases-Ninth and Tenth Revision clinical modification. The National Registry Disease Office (NRDO) collected and extracted relevant information on patient demographic characteristics, medical history, inpatient evaluation, treatment, events, discharge disposition and mortality. The institutional review board and NRDO approved all study procedures.

Study population

Using Singapore Stroke Registry data, we included all acute ischaemic stroke patients aged 18 or older who arrived to one of the five public hospitals between 1 January 2015 and 31 December 2016 (n=11952). We excluded patients with no documented time of symptom onset (n=5484), in-hospital strokes (n=597), transferred from another hospital (n=360), onset-to-door time greater than 24 hours (n=743) or those with missing information on mode of transportation to the hospital (n=1204). The final cohort consisted of 3555 patients. Among these patients, 600 of them received tPA treatment.

Variable of interest and process of care measures

We defined EMS use as patients who arrived at the hospital by SCDF ambulance; whereas we considered those who arrived via other transportation modes (eg, taxi, subway or private cars) as self-transported patients. Process of care measures included door-to-imaging time (continuous, % of door-to-imaging time ≤ 25 min), door-to-needle time (continuous, % of door-to-needle time ≤ 60 min) and treatment rate of intravenous tPA in all eligible ischaemic stroke patients. We also assessed the proportion of patients who arrived within 2 hours after symptom onset and were treated within 3 hours (arrival by 2 hours and treated by 3 hours) and arrival by 3.5 hours and treated by 4.5 hours.

Statistical analyses

We first described the demographic and clinical characteristics by mode of transportation to the hospital in all eligible patients and in a subgroup of patients who arrived within 3.5 hours of symptom onset. We used median and interquartile range (IQR) for continuous variables and used frequencies and percentages for categorical variables. We applied χ^2 and Wilcoxon rank-sum tests as appropriate to compare the differences in characteristics between patients who arrived via EMS and those who self-transported. Next, we identified the demographic and clinical characteristics associated with EMS use in all patients and in patients with onset to arrival within 3.5 hours (potentially eligible for the 4.5 hours treatment window) by using logistic regression models with the generalised estimating equations (GEE) that accounted for within-hospital clustering. We applied stepwise-selection methods to identify the key factors significantly associated (p value < 0.05) with EMS use. We further applied a set of linear and logistic regression models with the GEE to examine how EMS use was associated with process of care measures including door-to-imaging time, tPA treatment rate and door-to-needle time. These analyses accounted for a variety of patient demographic and clinical characteristics, including age, sex, ethnicity (Chinese, Malay, Indian or others), medical history (transient ischaemic attack (TIA), stroke, hypertension, diabetes mellitus, ischaemic heart disease, atrial fibrillation, valvular heart disease, peripheral arterial disease, hyperlipidaemia and smoking status), National Institute of Health Stroke Scale (NIHSS, 0–4, 5–15, 16+, unknown) and office-hour presentation (stroke patients presenting to the emergency department between 7:00 am and 6:00 pm on any weekdays). In the final multivariate models, we examined a series of indices including variance inflation factors, tolerance and condition values and identified no possible multicollinearity and overidentification. All statistical tests were two-tailed and considered statistically significant at p < 0.05. All statistical analyses were performed using SAS V.9.3 software.

RESULTS

Baseline characteristics and factors associated with EMS use

Table 1 displays the characteristics of our study population. Overall, the median age of patients was 69 (IQR: 60–79) and 41.7% were female. A total of 2417 acute ischaemic patients were transferred to the hospital by EMS, accounting for 68% of the entire cohort. Compared with self-transported patients, patients who arrived via EMS were older, more likely to be female, had a history of hypertension, ischaemic heart disease, or atrial fibrillation, and had more severe stroke by NIHSS (median NIHSS 8 vs 3). Similar characteristics were found in the subgroup of those who arrived within 3.5 hours of symptom onset (59.7% of the study population, table 2). After risk adjustment, older age (per 5 year increase, OR=1.06 (95% CI 1.04 to 1.09)), female sex (OR=0.87

Table 1 Characteristics of all patients arrived within 24 hours by emergency medical services use

Patient characteristics	Overall (n=3555) N (%)	EMS (n=2417) N (%)	No EMS (n=1138) N (%)	P value
Age, median (IQR)	69 (60–79)	71 (61–81)	66 (57–76)	<0.001
Female	1484 (41.7)	1043 (43.2)	441 (38.8)	0.01
Ethnicity				
Chinese	2680 (75.4)	1811 (74.9)	869 (76.4)	0.08
Malay	576 (16.2)	408 (16.9)	168 (14.8)	
Indian	233 (6.6)	161 (6.7)	72 (6.3)	
Others	66 (1.9)	37 (1.5)	29 (2.5)	
Medical history				
TIA	168 (4.7)	114 (4.7)	54 (4.7)	0.97
Stroke	849 (23.9)	589 (24.4)	260 (22.8)	0.32
Hypertension	2934 (82.5)	2020 (83.6)	914 (80.3)	0.02
Diabetes mellitus	1484 (41.7)	1015 (42.0)	469 (41.2)	0.66
Ischaemic heart disease	826 (23.2)	625 (25.9)	201 (17.7)	<0.001
Atrial fibrillation	687 (19.3)	562 (23.3)	125 (11.0)	<0.001
Valvular heart disease	98 (2.8)	72 (3.0)	26 (2.3)	0.24
Peripheral arterial disease	107 (3.0)	79 (3.3)	28 (2.5)	0.19
Hyperlipidaemia	3217 (90.5)	2174 (89.9)	1043 (91.7)	0.11
Smoking status*				
Never	2106 (60.1)	1450 (61.1)	656 (58.0)	0.13
Former smoker	502 (14.3)	340 (14.3)	162 (14.3)	
Current smoker	897 (25.6)	584 (24.6)	313 (27.7)	
Office-hour arrival†	1638 (46.0)	1098 (45.4)	540 (47.5)	0.23
Baseline NIHSS*				
Median (IQR)	5 (2–13)	8 (3–16)	3 (1–6)	<0.001
0–4	1296 (36.5)	661 (27.3)	635 (55.8)	<0.001
5–15	1082 (30.4)	792 (32.8)	290 (25.5)	
16+	559 (15.7)	519 (21.5)	40 (3.5)	
Unknown	618 (17.4)	445 (18.4)	173 (15.2)	

*50 missing values in smoking status, 618 missing values in NIHSS.

†Office-hour arrival: weekdays 7 am to 6 pm.

EMS, emergency medical services; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack.

(95% CI 0.79 to 0.97)), medical history of atrial fibrillation (OR=1.71 (95% CI 1.37 to 2.14)) or peripheral arterial disease (OR=1.29 (95% CI 1.02 to 1.64)), and more severe stroke (NIHSS 5–15 vs 0–4; OR=2.39 (95% CI 1.89 to 3.02); NIHSS 16+ vs 0–4; OR=9.53 (95% CI 3.35 to 27.13); NIHSS unknown vs 0–4; OR=1.69 (95% CI 1.23 to 2.33)) were associated with a greater likelihood of EMS use (table 3). A similar set of results were found among patients who arrived within 3.5 hours of symptom onset, with the exception of female sex (table 3).

Association between EMS use and stroke evaluation and treatment

Overall, 17.0% of stroke patients received tPA treatment. We observed differences in the timing of evaluation, the proportion of patients treated with tPA, and timing of tPA treatment between patients arriving by EMS and

self-transported individuals (table 4). After adjusting for demographic and clinical characteristics, EMS use was associated with shorter door-to-imaging time (adjusted mean difference, –74 min (95% CI –92 to –56)), and more patients with door-to-imaging time within 25 min (34.3% vs 11.1%, OR=2.74 (95% CI 1.40 to 5.38)). In addition, among those who arrived within 2 hours of symptom onset, patients transported by EMS were more likely to receive tPA within 3 hours (33.1% vs 13.9%, OR=2.25 (95% CI 1.92 to 2.62)). Similar findings for EMS use on tPA treatment rate were observed in patients with symptom onset within 3 hours and treated within 4.5 hours (31.8% vs 11.7%, OR=2.55 (95% CI 2.10 to 3.10)). Furthermore, among tPA-treated patients, those transported by EMS had significantly shorter door-to-needle time (adjusted mean difference, –11 min (95% CI

Table 2 Characteristics of all patients arrived within 3.5 hours by emergency medical services use

Patient characteristics	Overall (n=2123)	EMS (n=1696)	No EMS (n=427)	P value
	N (%)	N (%)	N (%)	
Age, median (IQR)	71 (60–81)	72 (61–81)	66 (57–77)	<0.001
Female	942 (44.4)	771 (45.5)	171 (40.0)	0.04
Ethnicity				
Chinese	1623 (76.4)	1288 (75.9)	335 (78.5)	0.40
Malay	318 (15.0)	262 (15.4)	56 (13.1)	
Indian	149 (7.0)	122 (7.2)	27 (6.3)	
Others	33 (1.6)	24 (1.4)	9 (2.1)	
Medical history				
TIA	102 (4.8)	80 (4.7)	22 (5.2)	0.71
Stroke	551 (26.0)	437 (25.8)	114 (26.7)	0.70
Hypertension	1765 (83.1)	1429 (84.3)	336 (78.7)	0.006
Diabetes mellitus	834 (39.3)	669 (39.4)	165 (38.6)	0.76
Ischaemic heart disease	547 (25.8)	458 (27.0)	89 (20.8)	0.009
Atrial fibrillation	526 (24.8)	463 (27.3)	63 (14.8)	<0.001
Valvular heart disease	75 (3.5)	64 (3.8)	11 (2.6)	0.23
Peripheral arterial disease	61 (2.9)	53 (3.1)	8 (1.9)	0.17
Hyperlipidaemia	1903 (89.6)	1518 (89.5)	385 (90.2)	0.69
Smoking status*				
Never	1295 (62.1)	1046 (63.1)	249 (58.5)	0.20
Former smoker	319 (15.3)	245 (14.8)	74 (17.4)	
Current smoker	471 (22.6)	368 (22.2)	103 (24.2)	
Office-hour arrival†	981 (46.2)	769 (45.3)	212 (49.6)	0.09
Baseline NIHSS*				
Median (IQR)	7 (3–16)	9 (4–17)	2.5 (1–6)	<0.001
0–4	679 (32.0)	432 (25.5)	247 (57.8)	<0.001
5–15	643 (30.3)	551 (32.5)	92 (21.5)	
16+	450 (21.2)	425 (25.1)	25 (5.9)	
Unknown	351 (16.5)	288 (17)	63 (14.8)	

*41 missing values in smoking status, 351 missing values in NIHSS.

†Office-hour arrival: weekdays 7 am to 6 pm.

EMS, emergency medical services; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack.

–19 to –3), [figure 1](#)) and were also more likely to receive timely treatment (door-to-needle time ≤ 60 min) than self-transported patients (52.6% vs 29.4%, OR=2.58 (95% CI 1.35 to 4.92)).

DISCUSSION

To the best of our knowledge, our study is among the first to investigate the use of EMS in a national provided system and its association with stroke evaluation and treatment in Asia-Pacific countries. Using data from the Singapore Stroke Registry that integrated several data sources, we found that still nearly one-third of acute ischaemic stroke patients were not transported to the hospital via EMS. Patients transported by EMS were more likely to receive more rapid evaluation and treatment than self-transported patients.

In our study, although the proportion of individuals transported by EMS is higher than in previous studies,^{5 8} still one-third of our stroke patients arrived to the hospital via private vehicles or taxis. A 2014 population-based study in Singapore reports that more than half of the participants could not recognise any of the FAST symptoms (facial droop, arm weakness and speech difficulty), and over 40% did not know the correct number for EMS, despite the availability of 995 universal access number for Fire and EMS.²¹ In addition, results from our multivariate analyses also suggest that age was the only significant demographic factor that was associated with EMS use among patients who arrived within 24 hours of symptom onset and among those who arrived within 3.5 hours. Therefore, it is likely that the EMS use is largely driven by recognition of stroke symptoms. The share of

Table 3 Factors associated with EMS use for patients arrived within 24 hours and patients arrived within 3.5 hours

Variables	Arrival by 24 hours (n=3555), OR (95% CI)	P value	Arrival by 3.5 hours (n=2123), OR (95% CI)	P value
Age (per 5 year increase)	1.06 (1.04–1.09)	<0.001	1.05 (1.02–1.08)	<0.001
Female	0.87 (0.79–0.97)	0.01	–	–
Atrial fibrillation	1.71 (1.37–2.14)	<0.001	1.56 (1.33–1.82)	<0.001
Peripheral arterial disease	1.29 (1.02–1.64)	0.03	1.58 (1.16–2.16)	0.004
Baseline NIHSS (ref: 0–4)				
5–15	2.39 (1.89–3.02)	<0.001	3.09 (2.86–3.34)	<0.001
16+	9.53 (3.35–27.13)	<0.001	7.53 (4.64–12.19)	<0.001
Unknown	1.69 (1.23–2.33)	0.001	1.85 (1.45–2.27)	<0.001

P values are based on logistic regressions with the generalised estimating equations, and logistic regressions with the generalised estimating equations after stepwise selection for adjusted OR.

EMS, emergency medical services; NIHSS, National Institutes of Health Stroke Scale.

stroke patients who failed to use EMS remains a concern, suggesting missed opportunities to increase public awareness of stroke signs and symptoms and the importance of EMS use when recognising symptoms suggestive of stroke. In Singapore, there have been national-level stroke awareness campaigns in Singapore annually from October 2016, emphasising stroke symptoms recognition and use of ambulance service as a call to action.²² Future research is planned to evaluate the impact of national campaigns on stroke symptom recognition, sensitivity and specificity of stroke identification, temporal trends in EMS use among stroke patients and timely tPA treatment rate.

Similar to prior studies conducted in other countries,^{6 11 23 24} we found that stroke patients with more comorbidities and more severe stroke were more likely

to utilise EMS. These findings are also comparable to the results from a recent study in Singapore that more severe onset symptoms was associated with higher likelihood of EMS use among patients experiencing myocardial infarction.²⁵ However, in line with prior research,^{6 23} our results suggest that having a previous history of stroke or TIA did not impact a patient's likelihood of using EMS in a subsequent stroke event. Stroke patients are at a greater risk for another attack and the recurrent event is often more severe and debilitating.^{26–28} Therefore, preventing and promptly treating subsequent stroke events is critical for improving the functional and health outcomes in stroke patients. Although the current guide for stroke survivors in Singapore included information on immediate actions for a second stroke, the implementation and effectiveness of this aspect of stroke education in clinical practice

Table 4 Timeliness of acute stroke evaluation and treatment by EMS use

	EMS	No EMS	Unadjusted OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Overall (n=3555)						
Door to imaging time in min, mean (SD)	91 (254)	165 (272)	–74 (–92 to –56)†	<0.001	–58 (–74 to –42)‡	<0.001
Door to imaging time ≤25 min	829/2417 (34.3%)	126/1137 (11.1%)	4.19 (3.42 to 5.13)	<0.001	2.74 (1.40 to 5.38)	0.003
tPA treatment rate	552/2417 (22.8%)	52/1138 (4.6%)	6.18 (4.61 to 8.29)	<0.001	4.61 (3.52 to 6.03)	<0.001
tPA arrival by 2 hours and treatment by 3 hours	444/1343 (33.1%)	34/244 (13.9%)	3.05 (2.09 to 4.46)	<0.001	2.25 (1.92 to 2.62)	<0.001
tPA arrival by 3.5 hours and treatment by 4.5 hours	539/1696 (31.8%)	50/427 (11.7%)	3.51 (2.57 to 4.80)	<0.001	2.55 (2.10 to 3.10)	<0.001
Among patients received tPA (n=600)						
Door to imaging time in min, mean (SD)	26 (16)	35 (16)	–9 (–13 to –4)†	<0.001	–8 (–13 to –4)‡	<0.001
Door to imaging time ≤25 min	282/549 (51.4%)	15/51 (29.4%)	2.53 (1.36 to 4.74)	0.003	2.51 (1.38 to 4.58)	0.002
DTN in min, mean (SD)	66 (28)	77 (27)	–11 (–19 to –3)†	0.008	–11 (–19 to –3)‡	0.006
DTN ≤60 min	289/549 (52.6%)	15/51 (29.4%)	2.67 (1.43 to 4.98)	0.002	2.58 (1.35 to 4.92)	0.004
DTN ≤45 min	127/549 (23.1%)	2/51 (3.9%)	7.37 (1.77 to 30.7)	0.006	8.03 (1.63 to 39.5)	0.01

P values are based on logistics regression models with the generalised estimating equations for adjusted OR, and linear regression models with the generalised estimating equations for adjusted mean differences.

*Adjusted for age, sex, ethnic group, previous stroke/TIA, history of hypertension, diabetes mellitus, ischaemic heart disease, atrial fibrillation/flutter, valvular heart disease, peripheral arterial disease, hyperlipidaemia, smoker, Office-hour arrival and National Institutes of Health Stroke Scale (NIHSS).

†Unadjusted mean differences.

‡Adjusted mean differences.

DTN, door to needle; EMS, emergency medical services; TIA, transient ischaemic attack; tPA, tissue plasminogen activator.

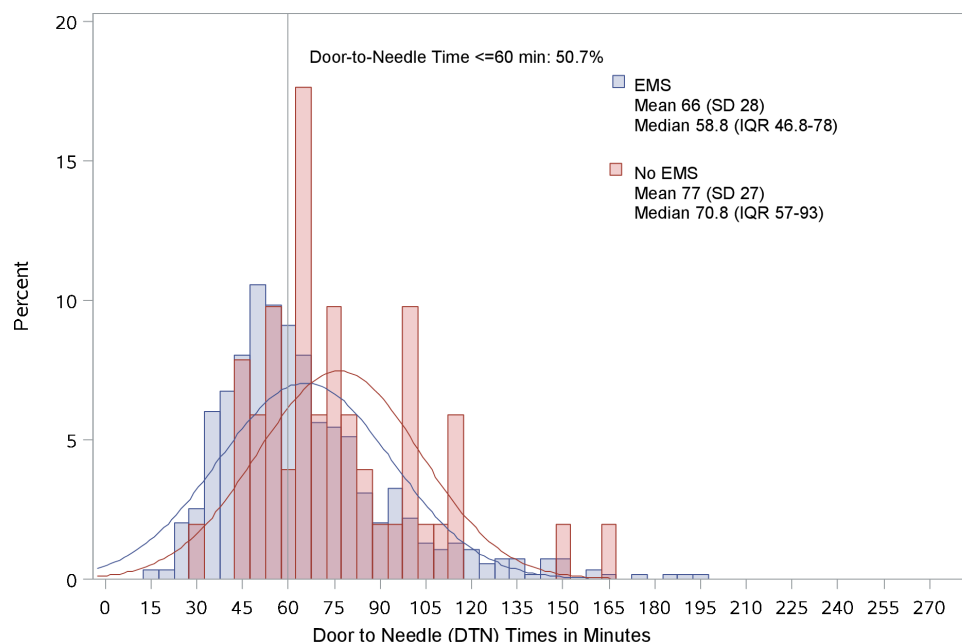


Figure 1 Distribution of door-to-needle (DTN) among patients receiving intravenous tissue-type plasminogen activator. EMS, emergency medical services.

may not be sufficient. More enhanced education may be needed for stroke patients before discharge to improve their understanding of the emergency nature of this disease.

Consistent with prior literature from western countries,^{6 9–11} our study suggests that EMS use was associated with rapid evaluation and treatment for acute ischaemic stroke in a large urban setting where tertiary care and stroke units are more available, and professional EMS services are easily accessible and coordinated with hospitals. Patients transported by EMS were more likely to receive tPA and were also more likely to receive the treatment faster. On average, among those who received tPA treatment, EMS-transported patients had an 11-min reduction in door-to-needle time. Prior research suggests that every minute reduction in the tPA administration can save nearly 2 million neurons, which translates into approximately 2 more days in healthy life.^{29 30} Therefore, this significant improvement in evaluation and treatment of acute ischaemic stroke has considerable clinical impacts on patient outcomes. Furthermore, increasing evidence has demonstrated the benefits of early endovascular thrombectomy for patients with ischaemic stroke due to intracranial large-vessel occlusions (LVO).^{31 32} Therefore, EMS use can potentially gain considerable treatment time for patients with LVO stroke. The current EMS system in Singapore implemented a stroke protocol that primarily focused on using CPSS to identify stroke patients who present early and might benefit from thrombolysis.¹⁷ Given that thrombectomy has become a critical component of stroke care, future research is needed to identify and implement strategies that increase the EMS capacity to recognise suspected LVO stroke cases in prehospital settings.

Limitations

We acknowledge several limitations of this study. First, the study was based on observational data, therefore, causality cannot be assessed. Furthermore, due to lack of information on stroke patients' socioeconomic status, we were unable to assess how other factors such as education, income, place of residence and health literacy impact EMS use.^{33 34} Similarly, we lack information on the reason why some patients used EMS, whereas others did not. It is possible that patients who did not use EMS were due to failure in stroke symptom recognition. We also acknowledge that stroke patients with missing information on mode of transportation were excluded in the analyses, which may introduce potential bias to the study findings. We conducted exploratory analyses by coding these patients with missing information on transportation mode as self-transferred patients. The results were essentially the same as we presented in this study. Relatedly, due to data limitation, we were unable to differentiate patients who were transported by private ambulance from those transported by SCDF ambulance. Nevertheless, as we noted above, most stroke cases are transported by the national EMS system. Finally, the Singapore Stroke Registry only captured stroke patients who were Singapore citizens or permanent residents. Therefore, the study findings may not be generalisable to stroke patients who were foreigners.

Conclusion

In this study, more than one-third of acute ischaemic stroke patients in Singapore failed to activate EMS. Patients transported by EMS had significantly faster evaluation and a greater likelihood of receiving tPA treatment than those self-transported. Targeted public campaigns

to advocate for stroke symptom recognition and appropriate EMS use are needed to enhance a seamless EMS-hospital stroke pathway.

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