

# In-Hospital Emergency Treatment Delay Among Chinese Patients with Acute Ischaemic Stroke: Relation to Hospital Arrivals and Implications for Triage Pathways

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**Introduction:** Timely access to emergency treatment during in-hospital care phase is critical for managing the onset of acute ischaemic stroke (AIS), particularly in developing countries. We aimed to explore in-hospital emergency treatment delay and the relation of door-to-needle (DTN) time to ambulance arrivals vs walk-in arrivals.

**Methods:** Data were collected from 1276 Chinese AIS patients admitted to a general, tertiary-level hospital for intravenous thrombolysis. Information on patients' characteristics and time taken during in-hospital emergency treatment was retrieved from the hospital registry data and medical records. Ambulance arrival was defined as being transported by emergency ambulance services, while walk-in arrival was defined as arriving at hospital by regular vehicle. In-hospital emergency treatment delay occurred when the DTN time exceeded 60 minutes. We performed multivariable logistic regression analysis to explore the association between hospital arrivals (by ambulance vs by walk-in) and treatment delay after adjustment for age, sex, education, marital status, residence, medical insurance, number of symptoms, clinical severity and survival outcome.

**Results:** Over half (53.76%) of patients aged over 60 years. Around one-fifth (20.61%) of patients admitted to hospital through emergency ambulance services, while their counterparts arrived by regular vehicle. Overall, the median time taken from the hospital door to treatment initiation was 86.0 minutes. Patients arrived by ambulance (adjusted odds ratio [aOR] = 1.744, 95% confidence interval [CI] = 1.185–2.566,  $p = 0.005$ ), had higher socio-economic status (aOR = 1.821, 95% CI = 1.251–2.650;  $p = 0.002$ ), or paid out-of-pocket (aOR = 2.323, 95% CI = 1.764–3.060;  $p < 0.001$ ) had an increased likelihood of in-hospital emergency treatment delays.

**Conclusion:** In-hospital emergency treatment delay is common in China, and occurs throughout the entire emergency treatment journey. Having a triage pathway involving hospital arrival by ambulance seems to be more likely to experience in-hospital emergency treatment delay. Further efforts to improve triage pathways may require qualitative evidence on provider- and institutional-level factors associated with in-hospital emergency treatment delay.

**Keywords:** in-hospital emergency treatment, acute ischaemic stroke, treatment delay, hospital arrival, triage pathways

## Introduction

Ischaemic stroke is the most common type of stroke,<sup>1–4</sup> accompanied by substantial economic burden posed to families and societies.<sup>4,5</sup> Approximately 15 million people worldwide suffer from stroke annually.<sup>6,7</sup> In China, stroke has become the top cause of disability and the third leading cause of death.<sup>8,9</sup> From a clinical perspective, the therapeutic time

window after stroke onset is narrow but paramount for early treatment to ensure minimising total ischaemic time and restoring blood flow.<sup>10</sup> A robust body of evidence from the National Institute of Neurological Disorders and Stroke (NINDS), the European Cooperative Acute Stroke Study (ECASS), and the Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS) study, etc., consistently confirmed that therapeutic effects were closely related to the time interval of clinical responses.<sup>8,11–15</sup>

However, significant delays often occur during both prehospital and in-hospital care phases, which sharply increase the risks of neurological worsening, functional impairment, and severe disability.<sup>16,17</sup> At least two recent meta-analyses showed that in-hospital system interventions could bring about significant improvements in mortality, rate of symptomatic intracerebral haemorrhage, and time to reperfusion.<sup>18</sup> The prehospital stroke workflow optimisation (PSWO) consists of improved intravenous thrombolysis (IVT) triage, large-vessel occlusion (LVO) bypass, and mobile stroke unit (MSU), which could significantly improve several time metrics related to stroke treatment, including door-to-needle time for IVT, and door-to-perfusion time and call-to-perfusion time for endovascular thrombectomy.<sup>19</sup> Literature suggested that the patient's response time from symptom onset to the first call for help was related to behavioural, cognitive and contextual factors.<sup>20</sup> These factors may also include the time interval between symptom onset and hospital arrival.<sup>21</sup> Data from pooled analysis of stroke trials on rapid treatment of intravenous recombinant tissue plasminogen activator (rt-PA) showed a decreased proportion of patients with complete recovery accompanying with an increased time interval from stroke onset to treatment commencement.<sup>22</sup> This indicates that the effectiveness of treatment during the early stage of stroke onset directly determines the prognosis. Global evidence showed that ischaemic stroke patients who were given rapid thrombolytic therapy within 90 minutes after the stroke onset had an increased likelihood of favourable outcomes,<sup>14,23</sup> and suggested that treatment should be started within 60 minutes since the patient's arrival at the emergency department.<sup>8,11,15</sup> A door-to-needle (DTN) time over 60 minutes could thus indicate a delay in the emergency treatment.<sup>12</sup>

It has been widely shown that the use of emergency medical system has the potential to shorten the total length of time patients arriving at hospital from home by 15–30 minutes, thus potentially improving the number of patients eligible for intravenous thrombolysis.<sup>24</sup> Previous studies suggested that a call for emergency medical services (EMS) from either a patient or a witness could be associated with objective signs of severe stroke and subjective perception of severity.<sup>25</sup> Although in-hospital treatment is of equal importance for effective secondary prevention of adverse events, knowledge of risk factors for emergency treatment delay occurring after hospital arrival remains scanty.<sup>23</sup> In this study, we aimed to explore in-hospital emergency treatment delay and the relation of door-to-needle (DTN) time to ambulance arrivals vs walk-in arrivals to inform strategies for optimising triage pathways.

## Methods

### Study Settings and Subjects

We conducted a retrospective registry-based study with data retrieved from the hospital registry and medical records at a general, tertiary-level hospital in Guangzhou, southern China, where the healthcare infrastructure is well positioned. A total of 1276 Chinese patients admitted with acute ischaemic stroke (AIS) who fulfilled the eligibility criteria were captured in the present study. The inclusion criteria included (i) admitted to emergency department due to the onset of cerebrovascular disease symptoms (ie, one limb is weak, clumsy, heavy or numb; one side of the face is numb or the angle of mouth is crooked; aphasia, unclear enunciation or difficulty in understanding language; binocular gaze; sudden blurred vision, or double vision; vertigo, tinnitus, balance disorder; sudden headache or change in the nature of headache, with or without vomiting; or disturbance of consciousness);<sup>9</sup> (ii) presented with a clinical diagnosis of AIS; and (iii) received intravenous thrombolysis with or without endovascular thrombectomy. The diagnosis was made on the basis of clinical symptoms and cerebrovascular imaging examinations performed by clinical neurologists, including computed tomography (CT) scan or magnetic resonance imaging (MRI) scan. Patients with haemorrhagic stroke or transient ischaemic attack were excluded.

## Data Collection and Variables

In-hospital emergency treatment referred to immediate treatment with intravenous thrombolysis for AIS patients upon arrival at the emergency department in the hospital. The key checkpoints for patients treated upon arrival were determined with international reference to the goals for time frames in stroke management in the emergency department.<sup>11,15</sup> The starting time and ending time points of each key procedure of stroke chain since hospital arrival were captured with regard to vital signs monitoring, medical history collection, physical examination, cardiac monitoring, electrocardiogram (ECG) examination, blood samples taken for laboratory tests, neurological evaluation, initiation of brain imaging (eg, CT scan or MRI scan), obtaining imaging report with interpretation, and administration of appropriate treatments.

In our study, the patient's clinical data were retrieved directly from the hospital registry data. Study variables included the length of time during in-hospital emergency treatment, number of symptoms,<sup>9</sup> the severity of condition, and survival outcomes (death vs survival). Survival was further classified as (a) recovered well with mild neurological disorders and capable of living normally; (b) moderately disabled but could still take care of themselves; (c) severely ill, disabled, or unable to take care of themselves despite having clear consciousness; and (d) being unaware and/or unresponsive.<sup>14</sup> Information on demographic and socio-economic status (SES) was retrieved from medical record documented by the attending clinical staff.

## Variables and Measurements

In-hospital emergency treatment delay occurred when the DTN time exceeded 60 minutes.<sup>26–29</sup> A critical or urgent level of clinical severity was defined in cases with the presence of severe intracranial hypertension, gastrointestinal bleeding, epilepsy, abnormal blood glucose, or fever, while a mild or non-urgent case was defined in the absence of any of the above clinical symptoms or conditions.<sup>9</sup> We reclassified SES using a bivariate approach, and low SES was defined as having a monthly household income per head below the average level of study participants overall. Patients were classified into death or survival groups according to whether death occurred during treatment or hospitalisation. Ambulance arrival was defined as being transported by emergency ambulance services, while walk-in arrival was defined as arriving at hospital by regular vehicle such as cars, taxis, or public buses.

## Statistical Analysis

The SPSS software (version 23.0) was used for data analysis. The between-group differences were examined by the chi-square test, or two-sample *t*-test, where appropriate. Categorical data was presented by percentage, while continuous data was presented either by median with quartile or by means with standard deviation (SD). The Wilcoxon rank sum test was used to compare the time taken during in-hospital emergency treatment with the time goals for optimising stroke patient care according to the NINDS.<sup>15</sup> Multivariable logistic regression analysis was performed to explore factors associated with in-hospital emergency treatment delay. The association between hospital arrivals (by ambulance vs by walk-in) and treatment delay was adjusted for age, sex, education level, marital status, place of residence, medical insurance, number of symptoms, clinical severity and survival outcome that were included in the full model. A *p* value of less than 0.05 was considered statistically significant.

## Results

### Characteristics of Study Subjects

Of 1276 patients admitted with a diagnosis of AIS, the majority of patients aged 60 years or older. Around one-fifth (263/1276 [20.61%]) of patients arrived at hospital by emergency ambulance services, while their counterparts arrived by regular vehicle. In-hospital treatment delay occurred in 81.75% of ambulance arrivals and 70.78% of walk-in arrivals, respectively. There were no significant differences in sex ( $p = 0.246$ ), marital status ( $p = 0.135$ ), number of symptoms ( $p = 0.940$ ), and survival outcome ( $p = 0.128$ ) between the two groups. Out-of-pocket payment was most common for ambulance arrivals (79.47%), while slightly over half (55.05%) of walk-in patients had medical insurance coverage. Besides, walk-in arrivals had higher SES (89.93% vs 50.57%,  $p < 0.001$ ) and had more cases of mild or non-urgent clinical severity (39.11% vs 46.39%;  $p = 0.032$ ) compared to those who arrived by ambulance (Table 1).

**Table 1** Characteristics of All Subjects in the Study

| Characteristics                                | Ambulance Arrivals (n = 263) | Walk-In Arrivals (n = 1013) | Total (N = 1276)  | $\chi^2$ | P value |
|--|------------------------------|-----------------------------|-------------------|----------|---------|
| Sex, n (%)                                     |                              |                             |                   | 1.345    | 0.246   |
| Male   | 161 (61.22)                  | 580 (57.30)                 | 741 (58.09)       |          |         |
| Female   | 102 (38.78)                  | 433 (42.70)                 | 535 (41.91)       |          |         |
| Age (years), n (%)                             |                              |                             |                   | 7.843    | 0.049   |
| 20–39  | 6 (2.28)                     | 15 (1.46)                   | 21 (1.63)         |          |         |
| 40–59  | 71 (27.00)                   | 201 (19.84)                 | 272 (21.30)       |          |         |
| 60–79  | 133 (50.57)                  | 553 (54.57)                 | 686 (53.76)       |          |         |
| 80 and above                                   | 53 (20.15)                   | 244 (24.12)                 | 297 (23.31)       |          |         |
| Mean $\pm$ SD (Mean age, years)                | 67.02 $\pm$ 13.52            | 69.14 $\pm$ 12.67           | 68.70 $\pm$ 12.87 |          |         |
| Education, n (%)                               |                              |                             |                   | 34.062   | < 0.001 |
| Illiteracy                                     | 55 (20.91)                   | 350 (34.53)                 | 405 (31.76)       |          |         |
| Primary school                                 | 108 (41.06)                  | 267 (26.36)                 | 375 (29.36)       |          |         |
| Junior secondary school                        | 55 (20.91)                   | 178 (17.61)                 | 233 (18.28)       |          |         |
| Senior secondary school                        | 22 (8.37)                    | 140 (13.81)                 | 162 (12.70)       |          |         |
| College and above                              | 23 (8.75)                    | 78 (7.68)                   | 101 (7.90)        |          |         |
| Marital status, n (%)                          |                              |                             |                   | 4.007    | 0.135   |
| Single   | 5 (1.90)                     | 21 (2.04)                   | 26 (2.01)         |          |         |
| Married  | 245 (93.16)                  | 967 (95.43)                 | 1212 (94.97)      |          |         |
| Divorced or others                             | 13 (4.94)                    | 26 (2.53)                   | 39 (3.02)         |          |         |
| Residence, n (%)                               |                              |                             |                   | 217.445  | < 0.001 |
| Lower SES                                      | 130 (49.43)                  | 102 (10.07)                 | 230 (18.18)       |          |         |
| Higher SES                                     | 133 (50.57)                  | 911 (89.93)                 | 1046 (81.82)      |          |         |
| Medical insurance, n (%)                       |                              |                             |                   | 101.305  | < 0.001 |
| PEMI   | 7 (2.66)                     | 49 (4.86)                   | 56 (4.39)         |          |         |
| MIE  | 41 (15.59)                   | 422 (41.63)                 | 463 (36.28)       |          |         |
| MIR  | 1 (0.38)                     | 25 (2.43)                   | 26 (2.04)         |          |         |
| RCMI   | 3 (1.14)                     | 50 (4.96)                   | 53 (4.15)         |          |         |
| CHI  | 2 (0.76)                     | 12 (1.17)                   | 14 (1.10)         |          |         |
| Out-of-pocket payment                          | 209 (79.47)                  | 455 (44.95)                 | 664 (52.04)       |          |         |
| Number of symptoms, n (%)                      |                              |                             |                   | 0.123    | 0.940   |
| 1  | 134 (50.95)                  | 517 (51.07)                 | 651 (51.04)       |          |         |
| 2  | 81 (30.80)                   | 319 (31.52)                 | 400 (31.37)       |          |         |
| 3 and above                                    | 48 (18.25)                   | 176 (17.41)                 | 224 (17.58)       |          |         |
| Clinical severity, n (%)                       |                              |                             |                   | 4.609    | 0.032   |
| Critical or urgent                             | 122 (46.39)                  | 396 (39.11)                 | 518 (40.59)       |          |         |
| Non-urgent                                     | 141 (53.61)                  | 617 (60.89)                 | 758 (59.41)       |          |         |
| In-hospital emergency treatment started, n (%) |                              |                             |                   | 12.758   | < 0.001 |
| $\leq$ 1 hour                                  | 48 (18.25)                   | 296 (29.22)                 | 344 (26.96)       |          |         |
| > 1 hour                                       | 215 (81.75)                  | 717 (70.78)                 | 932 (73.04)       |          |         |
| Survival outcome, n (%)                        |                              |                             |                   | 2.316    | 0.128   |
| Death  | 4 (1.52)                     | 6 (0.58)                    | 10 (0.77)         |          |         |
| Survival                                       | 259 (98.48)                  | 1007 (99.42)                | 1266 (99.23)      |          |         |

**Abbreviations:** SD, standard deviation; SES, socio-economic status; PEMI, public expense medical insurance; MIE, medical insurance for employees; MIR, medical insurance for residents; RCMI, rural cooperative medical insurance; CHI, commercial health insurance.

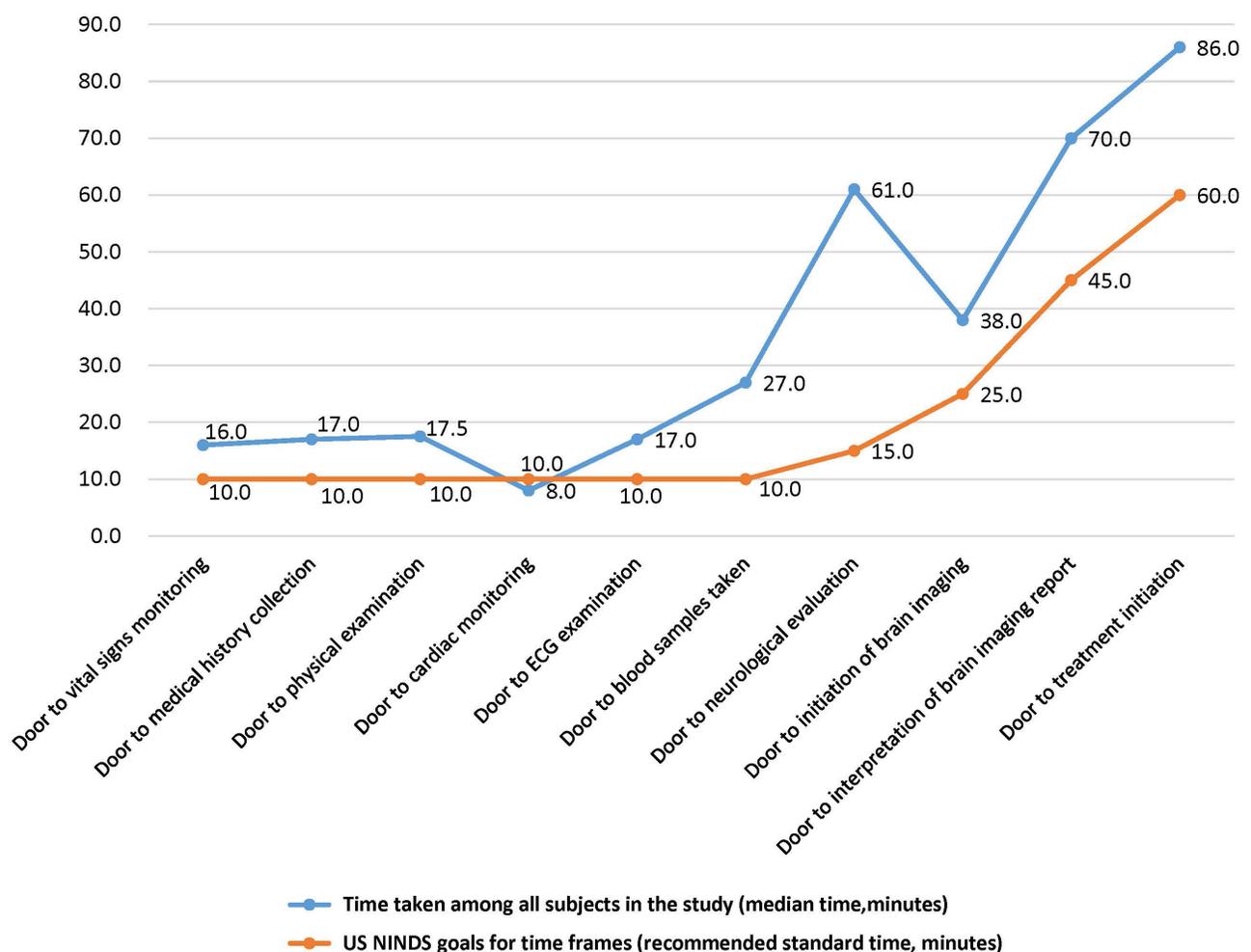
## Length of Time for In-Hospital Emergency Treatment Among Stroke Patients

Overall, the length of time from the hospital door to initiation of treatment among patients in our study was significantly greater than that recommended in the NINDS goals for time frames (86.0 vs 60.0 minutes;  $p < 0.001$ ). In our study, the time taken for all in-hospital emergency treatment procedures, except for that from the door to cardiac monitoring, were

significantly longer than the NINDS standard time ( $p < 0.001$ ). In particular, there was a sharp rise in the length of time for neurological evaluation compared to the NINDS standard course of treatment procedures (Figure 1). Prior to treatment initiation, the longest time interval was documented from the door to interpretation of brain imaging report (70.0 minutes; median), followed by the intervals from the door to neurological evaluation (61.0 minutes; median) and from the door to initiation of brain imaging (38.0 minutes; median) (Table 2). Compared to walk-in arrivals, patients arrived by ambulance tended to spend less time on procedures with regard to intermediate checkpoints including cardiac monitoring, ECG examination, blood samples taken, neurological evaluation, initiation of brain imaging, and interpretation of brain imaging report. However, the length of time from the door to treatment initiation was greater for ambulance arrivals than their counterparts (87.0 minutes vs 85.0 minutes;  $p = 0.018$ ) (Table 3).

## Factors Associated with the Occurrence of In-Hospital Emergency Treatment Delay

Multivariable logistic regression analysis showed that having a triage pathway that involved hospital arrival by an ambulance seemed to have an increased likelihood of in-hospital emergency treatment delay (adjusted odds ratio [aOR] = 1.744, 95% confidence interval [CI]=1.185–2.566,  $p = 0.005$ ). Besides, patients who had a higher SES (aOR = 1.821, 95% CI = 1.251–2.650;  $p = 0.002$ ) or paid out-of-pocket (aOR = 2.323, 95% CI = 1.764–3.060;  $p < 0.001$ ) were also more likely to experience in-hospital emergency treatment delay (Table 4).



**Figure 1** In-hospital emergency treatment procedures of stroke patients based on the time taken on in-hospital emergency treatment compared with the NINDS standard time.

**Table 2** Time Taken on In-Hospital Emergency Treatment Procedures Among Stroke Patients in the Study Compared with the NINDS Standard Time

| Procedures                                     | Time Taken Among All Subjects in the Study, Minutes | US NINDS Goals for Time Frames, Minutes | Z Score |
|--|---|---|---------|
| Door to vital signs monitoring                 | 16.0 (7.0–29.5)                                     | ≤10.0                                   | 9.314*  |
| Door to medical history collection             | 17.0 (7.0–30.0)                                     | ≤10.0                                   | 9.974*  |
| Door to physical examination                   | 17.5 (7.0–32.0)                                     | ≤10.0                                   | 10.428* |
| Door to cardiac monitoring                     | 8.0 (4.0–21.0)                                      | ≤10.0                                   | 7.569*  |
| Door to ECG examination                        | 17.0 (7.0–66.0)                                     | ≤10.0                                   | 14.594* |
| Door to blood samples taken                    | 27.0 (8.0–75.0)                                     | ≤10.0                                   | 21.074* |
| Door to neurological evaluation                | 61.0 (31.0–104.0)                                   | ≤15.0                                   | 25.079* |
| Door to initiation of brain imaging            | 38.0 (19.0–135.0)                                   | ≤25.0                                   | 17.987* |
| Door to interpretation of brain imaging report | 70.0 (36.0–207.0)                                   | ≤45.0                                   | 19.529* |
| Door to treatment initiation                   | 86.0 (59.0–134.0)                                   | ≤60.0                                   | 20.427* |

**Notes:** Data were presented as median (25th –75th percentile). \*P values <0.001 for all Z score tests.  
**Abbreviations:** ECG, electrocardiogram; NINDS, National Institute of Neurological Disorders and Stroke.

**Table 3** Time Taken on In-Hospital Emergency Treatment Procedures Between Ambulance Arrivals and Walk-in Arrivals Among Patients Admitted with Acute Ischaemic Stroke in the Study

| Procedures                                     | Ambulance Arrivals, Minutes | Walk-In Arrivals, Minutes | P value |
|--|-----------------------------|---------------------------|---------|
| Door to vital signs monitoring                 | 17.0 (8.0–30.5)             | 16.0 (7.0–29.75)          | 0.077   |
| Door to medical history collection             | 16.5 (9.25–28.25)           | 17.0 (7.0–30.0)           | 0.130   |
| Door to physical examination                   | 16.0 (6.0–30.5)             | 19.0 (7.0–32.0)           | 0.187   |
| Door to cardiac monitoring                     | 7.0 (4.0–24.0)              | 10.0 (6.0–21.0)           | 0.391   |
| Door to ECG examination                        | 8.0 (4.0–37.25)             | 21.0 (8.0–76.0)           | 0.033   |
| Door to blood samples taken                    | 17.0 (6.0–52.0)             | 30.0 (10.0–82.0)          | 0.001   |
| Door to neurological evaluation                | 51.5 (31.0–87.0)            | 66.5 (31.0–112.0)         | 0.004   |
| Door to initiation of brain imaging            | 22.0 (13.0–57.0)            | 46.0 (21.25–157.75)       | < 0.001 |
| Door to interpretation of brain imaging report | 39.0 (30.25–114.5)          | 56.0 (28.0–191.0)         | < 0.001 |
| Door to treatment initiation                   | 87.0 (67.0–131.0)           | 85.0 (53.0–134.0)         | 0.018   |

**Note:** Data were presented as median (25th –75th percentile).  
**Abbreviation:** ECG, electrocardiogram.

**Table 4** Factors Associated with In-Hospital Emergency Treatment Delay

| Variables          | aOR   | 95% CI      | P value |
|--------------------|-------|-------------|---------|
| <b>Sex</b>         |       |             |         |
| Male               | Ref   |             |         |
| Female             | 1.083 | 0.831–1.412 | 0.554   |
| <b>Age (years)</b> |       |             |         |
| 20–39              | Ref   |             |         |
| 40–59              | 1.396 | 0.504–3.863 | 0.521   |
| 60–79              | 1.472 | 0.539–4.018 | 0.451   |
| 80 and above       | 1.757 | 0.623–4.954 | 0.286   |

(Continued)

**Table 4** (Continued).

| Variables                          | aOR   | 95% CI      | P value |
|------------------------------------|-------|-------------|---------|
| <b>Education</b>                   |       |             |         |
| Illiteracy                         | Ref   |             |         |
| Primary school                     | 1.222 | 0.869–1.718 | 0.249   |
| Junior secondary school            | 1.138 | 0.774–1.672 | 0.511   |
| Senior secondary school            | 0.904 | 0.592–1.381 | 0.641   |
| College and above                  | 0.877 | 0.530–1.452 | 0.611   |
| <b>Marital status</b>              |       |             |         |
| Single                             | Ref   |             |         |
| Married                            | 1.536 | 0.665–3.548 | 0.315   |
| Divorced or others                 | 1.761 | 0.548–5.658 | 0.342   |
| <b>Residence</b>                   |       |             |         |
| Lower SES                          | Ref   |             |         |
| Higher SES                         | 1.821 | 1.251–2.650 | 0.002   |
| <b>Medical insurance</b>           |       |             |         |
| With social medical insurance      | Ref   |             |         |
| Out-of-pocket payment              | 2.323 | 1.764–3.060 | <0.001  |
| <b>Number of symptoms</b>          |       |             |         |
| 1                                  | Ref   |             |         |
| 2                                  | 1.174 | 0.878–1.570 | 0.280   |
| 3 and above                        | 1.141 | 0.787–1.654 | 0.487   |
| <b>Clinical severity</b>           |       |             |         |
| Critical or urgent                 | Ref   |             |         |
| Non-urgent                         | 1.023 | 0.788–1.328 | 0.865   |
| <b>Hospital admission pathways</b> |       |             |         |
| Walk-in arrivals                   | Ref   |             |         |
| Ambulance arrivals                 | 1.744 | 1.185–2.566 | 0.005   |

**Abbreviations:** aOR, adjusted odds ratio; CI, confidence interval; SES, socio-economic status.

## Discussion

### Main Findings

Around one-fifth of patients arrived at hospital by emergency ambulance services in our study. The median time taken from the hospital door to treatment initiation was significantly greater than that recommended in the NINDS goals for time frames. Except for the time from door to cardiac monitoring, the time taken for all other in-hospital emergency treatment flow (ie, door-to-neurological evaluation, door-to-initiation of brain imaging, door-to-interpretation of brain imaging report, and door-to-treatment initiation) in our study were significantly longer than the NINDS standard time. Having a triage pathway involving hospital arrival by an ambulance seemed to have an increased likelihood of in-hospital emergency treatment delay. Besides, patients who had a higher SES or paid out-of-pocket were also more likely to experience in-hospital emergency treatment delay.

### Relationship with Other Studies

Time window is an important determinant of treatment outcome in the management of AIS on a global scale. According to the American Heart Association (AHA), the American Stroke Association (ASA),<sup>26</sup> and the NINDS,<sup>15</sup> a delay during in-hospital emergency treatment was considered when the DTN time exceeds 60 minutes.<sup>9,26,30</sup> In our study, nearly three in four (73.35%) Chinese AIS patients had in-hospital treatment delay. This was greater than that (49%) reported from the US and that (38%) reported in Europe.<sup>30</sup> However, our results were similar to that (79%) documented in another Chinese study.<sup>31</sup> The median of DTN time (86.0 minutes) reported in our study was comparable to studies conducted in

Shandong, Eastern China (91.45 minutes),<sup>31</sup> Ningxia, Western China (180 minutes),<sup>32</sup> and Beijing, Northern China (107.4 minutes),<sup>33,34</sup> and also in India (82 minutes).<sup>35</sup>

Compared to the NINDS reference goals, a significantly longer DTN time was observed in most checkpoints in the present study setting. This was particularly distinct in the time from the hospital door to neurological evaluation (51.5 minutes for ambulance arrivals and 66.5 minutes for walk-in arrivals vs 15.0 minutes for the NINDS goals). The differences in the length of DTN time observed between our study and the NINDS standards may be explained by the absence of a standardised model for the stroke unit setting to improve treatment and rehabilitation.<sup>36</sup> Although multi-disciplinary professionals from the neuro-interventional therapy group, rehabilitation department and neurosurgery are involved, they are not closely integrated into a cohesive team. The absence of a separate venue area exclusive to stroke care in our study setting is also similar to that in most other hospitals in China. Moreover, not all procedures were performed by neuroscientists who were specialised in acute stroke care, which may cause delays in the rapid evaluation and diagnosis of stroke. This might explain a greater time from the hospital door to interpretation of brain imaging report compared to the NINDS recommendations. Similar findings were reported in Egypt, where the investigators found that limited availability of services during night shifts and the lack of well-trained medical team may serve as barriers to optimal performance in emergency treatment.<sup>37</sup> Poor communication may also lead to an increased possibility of in-hospital emergency treatment delay, eg, the sharp rise in the time intervals from the hospital door to neurological evaluation. It is common that the CT image was not sent directly from the imaging department to the physician for online preview but was sent in hard copies together with other examination results in the full report. This may take a much longer time for interpretation of brain imaging report on non-urgent cases. Similarly, studies from Switzerland and India indicated that poor recognition of stroke symptoms and longer distance between the stroke unit and CT room could cause a delay in the emergency treatment.<sup>35,38</sup>

Overseas studies showed that the use of emergency medical system such as ambulance, helicopter, or with the assistance of telemedicine could help reduce pre-hospital delay,<sup>27</sup> and that a transportation by ambulance could significantly shorten the admission delay for AIS patients in comparison with the patient's own means.<sup>38</sup> Patients who receive immediate evaluation and neurological assessment could achieve early stabilisation thereafter.<sup>26,39</sup> Previous literature suggests an association between the use of ambulance services and shorter prehospital times (ie, from the ambulance call to hospital arrival) and in-hospital times (ie, from hospital arrival to first medical assessment).<sup>28,40–42</sup> We did not observe a favourable impact of ambulance practice on acute stroke care in the present study. We speculate that the ambulance vehicle setting may have played a role of mobile stroke unit. This means that the ambulance vehicle was not solely used for transportation purpose per se but also enabled patients an opportunity to get examined and stabilised on the way to the hospital. Besides, given the availability of clinical resources per patient, physicians tend to pay their attention to those who need more urgent care. Hence, patients admitted by ambulance might not be given the highest priority during the in-hospital treatment than those walk-in arrivals whose clinical conditions were less likely to get pre-examined and pre-stabilised prior to hospital arrival.

Apart from the transportation, a rich body of literature also suggests possible factors that may have important impact on in-hospital acute stroke pathway.<sup>43</sup> This included the presence of complex hospitalisation procedures, limited clinical infrastructure, physicians' insufficient knowledge, and lack of first aid awareness.<sup>44–47</sup> An absence of primary care gatekeeping and coordinated computerised system may pose additional challenge in timely access to patients' routine health record, thus leading to treatment delays.<sup>44</sup> It is noteworthy that the SES could also exert an influence on the effectiveness of transportation.<sup>10</sup> We found that higher SES and the absence of social medical insurance were independently associated with increased likelihood of in-hospital emergency treatment delays. It is possible that a hospital located in higher SES localities might have higher patient volume, which could result in less clinical resources per patient and suboptimal clinical efficiency. Moreover, patients with higher SES may have gained more health consciousness and disease-related knowledge such that they tended to realise the importance of early management of AIS and recognise the early symptoms. The speculation may also be applicable to those without medical insurance, who might be more aware of their health symptoms to avoid potentially increased expenses on a deteriorated condition.

Alongside the efforts in shortening in-hospital treatment delay for stroke by procedure-specific improvement, the awareness of AIS symptoms should also be strengthened among patients and their families. This engagement of patients'

family members in shared-decision making based on the CT scan results may greatly help facilitate the emergency treatment process. Recent evidence suggests that community-based educational interventions for early stroke recognition, coupled with efforts to establish comprehensive stroke centres, improve emergency services, and establish telestroke facilities, could make a difference in how patients access acute stroke services, thereby preventing delayed hospital presentation and contributing to improved management of AIS.<sup>48,49</sup>

## Strengths and Weaknesses of the Study

The demographic distributions of our study subjects were consistent with that in other studies conducted in China elsewhere.<sup>13,39</sup> Compared to international studies, we provided a hospital registry-based profile of in-hospital emergency treatment delay among Chinese AIS patients from a relatively large sample size, following a standard method that is comparable to international recommendations. We also explored the impact of ambulance arrivals and walk-in arrivals on in-hospital emergency treatment delay which was determined using reliable data retrieved from hospital registry record. The study setting had well-positioned medical personnel, facilities, and equipment, which could improve the comparability of our findings with international evidence. There are also several limitations of this study. First, the selection bias may exist due to the inherent nature of a single-centre study with a relatively low proportion of patients admitted by ambulance. Second, our analysis using retrospective data may not account for other baseline confounding variables that were not originally captured. For example, the National Institute of Health Stroke Scale (NIHSS) and the Modified Rankin Scale (MRS) were not available in the existing registry record system, and thus the grade of clinical severity adjusted for in our analysis may not be directly comparable to others.<sup>50</sup> Third, provider- and institutional-level factors such as medical staff capacity, specialist training, and clinical facilities may play a role but were not measured. However, our study setting was a university-affiliated teaching hospital where healthcare resources were strongly supported by both the university and the local government. The clinical procedures were regularly accredited by health authorities following the national standard. Therefore, the additional impact of provider- and institutional-level factors on the association between patient-level factors and in-hospital emergency treatment delay may be considered minimal. Last but not least, patients with other types of stroke such as haemorrhagic stroke or transient ischaemic attack were not included in our study as we focused on the most common type of stroke. Future efforts to evaluate the effects of a modified stroke management algorithm and triage pathways are warranted in AIS patients in areas of different SES strata.

## Implications for Research and Practice

An optimisation in the emergency treatment triage pathways would require a streamlined and standardised workflow that takes into account both the NINDS recommendations and the local context with regard to the widened disparities in SES and clinical resource availability. This may start with the realignment of the procedure for the initiation of brain imaging. Suspected stroke patients, upon arrival at the hospital door, should be immediately assigned to a stroke team for direct transport for brain imaging prior to patient registration and payment. Routine procedures on physical examination, cardiac monitoring, and blood samples taken can be probably arranged after the brain imaging. This may be helpful in shortening the delayed triage caused by the between-department transportation within the hospital. The CT scan results could inform the type of stroke and clinical severity that helps physicians' decision of treatment regime. Medical staff at the brain imaging department should also get prepared in advance to shorten the time spent performing report interpretation. A realigned triage pathway shall require reallocation of physician resources and shift works within and across different departments within the hospital. The involvement of a stand-by neurologist in the emergency department may also reduce the time spent waiting for transportation to the intervention centre. Previous studies showed that an experienced stroke centre can shorten the time intervals associated with brain imaging by continuously improving clinical pathways and may be more likely to save the ischaemic brain from infarction (ie, "time is brain").<sup>51</sup> Evidence also suggests that the first attending physician's diagnosis and emergency treatment of stroke is key to the success of early treatment.<sup>35,52</sup> Experiences from Egypt suggested that a centre-wide comprehensive action plan on enhancing the availability of medications and appropriate training could avoid inappropriate treatment decisions, missed window while performing brain imaging, and unavailability of intermediate care bed.<sup>53</sup> Improvements in triage pathways that take into account the poor recognition of and response to symptoms of AIS among the public and frontline medical staff

could help in achieving effective communications and significant reduction of DTN time with more favourable patient outcomes.<sup>54–56</sup>

## Conclusion

In-hospital emergency treatment delay is common in China, and occurs throughout the entire emergency treatment journey. The median time taken from the hospital door to treatment initiation in our study setting was significantly greater than the NINDS recommended goals for time frames. Having a triage pathway involving hospital arrival by ambulance seems to be more likely to experience in-hospital emergency treatment delay. Besides, patients who had a higher SES or paid out-of-pocket were also more likely to experience in-hospital emergency treatment delay. Our results may signal an urgent need to take action on standardising the stroke unit care and enhancing the coordination and cooperation within and across various departments involved in the in-hospital emergency treatment for AIS. Further efforts to improve triage pathways may require qualitative evidence on provider- and institutional-level factors associated with in-hospital emergency treatment delay.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Statement of Ethics

Data anonymisation was performed by removing all patient identifiers from the dataset prior to data analysis. All research activities were conducted with integrity and were in line with the generally accepted ethical principles. The anonymous use of data for research purpose was approved by the ethics committee of The First Affiliated Hospital of Guangzhou Medical University.

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## Disclosure

The authors have no conflicts of interest to declare in this work.

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## References

1. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. 2018;392(10159):1789–1858.
2. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American heart association. *Circulation*. 2018;137(12):e67–e492.
3. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;119(3):480–486.
4. Roth GA, Mensah GA, Johnson CO, et al.; GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol*. 2020;76(25):2982–3021.
5. Oviagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. *Stroke*. 2013;44(8):2361–2375.
6. Ding Q, Liu S, Yao Y, Liu H, Cai T, Han L. Global, regional, and national burden of ischemic stroke, 1990–2019. *Neurology*. 2022;98(3):e279–e290.

7. Iso H. Cardiovascular disease, a major global burden: epidemiology of stroke and ischemic heart disease in Japan. *Glob Health Med.* 2021;3(6):358–364.
8. Long FQCY, Su QJ. Visiting time of acute ischemic stroke patients and its influencing factors [In Chinese]. *J Kunming Med Univ.* 2013;34(4):94–97.
9. Chinese Stroke Association. *Guidelines and Consensus on Diagnosis and Treatment of Cerebrovascular Diseases in China (2016 Edition)*. Beijing, China: People's Medical Publishing House; 2016.
10. European Stroke Organisation Executive C, Committee ESOW. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis.* 2008;25(5):457–507.
11. Willeit J, Geley T, Schoch J, et al. Thrombolysis and clinical outcome in patients with stroke after implementation of the Tyrol Stroke Pathway: a retrospective observational study. *Lancet Neurol.* 2015;14(1):48–56.
12. Evenson KR, Foraker RE, Morris DL, Rosamond WD. A comprehensive review of prehospital and in-hospital delay times in acute stroke care. *Int J Stroke.* 2009;4(3):187–199.
13. Jiang B, Wang WZ, Chen H, et al. Incidence and trends of stroke and its subtypes in China: results from three large cities. *Stroke.* 2006;37(1):63–68.
14. Yang H. *Study on Stroke in-Hospital Emergency Treatment Based on the "Time Window" [In Chinese]*. Huazhong University of Science & Technology; 2015.
15. Marler JR, Jones PW, Emr M Setting new directions for stroke care. Proceedings of a National Symposium on Rapid Identification and Treatment of Acute Stroke; 1997.
16. Kwan J, Hand P, Sandercock P. A systematic review of barriers to delivery of thrombolysis for acute stroke. *Age Ageing.* 2004;33(2):116–121.
17. Evenson KR, Rosamond WD, Morris DL. Prehospital and in-hospital delays in acute stroke care. *Neuroepidemiology.* 2001;20(2):65–76.
18. Baskar PS, Chowdhury SZ, Bhaskar SMM. In-hospital systems interventions in acute stroke reperfusion therapy: a meta-analysis. *Acta Neurol Scand.* 2021;144(4):418–432.
19. Chowdhury SZ, Baskar PS, Bhaskar S. Effect of prehospital workflow optimization on treatment delays and clinical outcomes in acute ischemic stroke: a systematic review and meta-analysis. *Acad Emerg Med.* 2021;28(7):781–801.
20. Soto-Cámara R, González-Santos J, González-Berna J, Trejo-Gabriel-Galán JM. Factors associated with a rapid call for assistance for patients with ischemic stroke. *Emergencias.* 2020;32(1):33–39.
21. Soto-Cámara R, González-Santos J, González-Berna J, Martín-Santidrián A, Cubo E, Trejo-Gabriel-Galán JM. Factors associated with shortening of prehospital delay among patients with acute ischemic stroke. *J Clin Med.* 2019;8(10):1712.
22. Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet.* 2004;363(9411):768–774.
23. Zhang J, Wang XH, Yang HJ, et al. Social determinants of pre-hospital delays after onset of stroke [In Chinese]. *Chin J Health Manag.* 2014;8(1):40–43.
24. Santana Baskar P, Cordato D, Wardman D, Bhaskar S. In-hospital acute stroke workflow in acute stroke - Systems-based approaches. *Acta Neurol Scand.* 2021;143(2):111–120.
25. Soto-Cámara R, Trejo-Gabriel-Galán JM, González-Berna J, González-Santos J, Cubo E. Factors associated with the activation of emergency medical services in patients with acute stroke: a prospective study. *Emergencias.* 2019;31(2):86–90.
26. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2018;49(3):e46–e110.
27. Hu YT, Yang N, Wei XE, et al. Clinic value of reducing in-hospital delay in patients with acute ischemic stroke after intravenous thrombolysis [In Chinese]. *Stroke Nerv Dis.* 2014;5:280–282.
28. Kleindorfer DO, Lindsell CJ, Broderick JP, et al. Community socioeconomic status and prehospital times in acute stroke and transient ischemic attack: do poorer patients have longer delays from 911 call to the emergency department? *Stroke.* 2006;37(6):1508–1513.
29. Lacy CR, Suh DC, Bueno M, Kostis JB. Delay in presentation and evaluation for acute stroke: stroke time registry for outcomes knowledge and epidemiology (S.T.R.O.K.E.). *Stroke.* 2001;32(1):63–69.
30. Mikulik R, Kadlecova P, Czlonkowska A, et al. Factors influencing in-hospital delay in treatment with intravenous thrombolysis. *Stroke.* 2012;43(6):1578–1583.
31. Wang XL. *Yantai City Hospital of Traditional Chinese Medicine Diagnosis and Treatment of Acute Ischemic Stroke Delay Related Factors Analysis [In Chinese]*. DaLian Medical University; 2013.
32. Wang ZH, Xie LQ, Zhao CM, Liu Q. Pre-hospital and in-hospital delay after acute ischemic stroke among 231 patients [In Chinese]. *Chin Gen Pract.* 2012;15(8B):2605–2608.
33. Li JH, Chen L, Chen Z. Analysis of the factors affecting the onset-to-door time of acute ischemic stroke in a primary hospital [In Chinese]. *Chin J Neuroimmunol Neurol.* 2014;21(5):364–367.
34. Li K, Gong T, Liu F, Sheng AZ, Chen HB. Intravenous thrombolysis for acute ischemic stroke: analysis of 22 cases [In Chinese]. *Chin J Gen Pract.* 2012;11(8):607–609.
35. Abraham SV, Krishnan SV, Thaha F, Balakrishnan JM, Thomas T, Palatty BU. Factors delaying management of acute stroke: an Indian scenario. *Int J Crit Illn Inj Sci.* 2017;7(4):224–230.
36. Harrison M, Ryan T, Gardiner C, Jones A. Patients' and carers' experiences of gaining access to acute stroke care: a qualitative study. *Emerg Med J.* 2013;30(12):1033–1037.
37. Shokri HM, El Nahas NM, Aref HM, et al. Factors related to time of stroke onset versus time of hospital arrival: a SITS registry-based study in an Egyptian stroke center. *PLoS One.* 2020;15(9):e0238305.
38. Sekoranja L, Griesser AC, Wagner G, et al. Factors influencing emergency delays in acute stroke management. *Swiss Med Wkly.* 2009;139(27–28):393–399.
39. Jin HQ, Zhu SN, Hao HJ, Sun YA, Huang YN. An analysis of stroke subtypes and influencing factors in different regions of China [In Chinese]. *Zhonghua Nei Ke Za Zhi.* 2012;51(3):201–205.
40. Mosley I, Nicol M, Donnan G, Patrick I, Kerr F, Dewey H. The impact of ambulance practice on acute stroke care. *Stroke.* 2007;38(10):2765–2770.

41. Kwan J, Hand P, Sandercock P. Improving the efficiency of delivery of thrombolysis for acute stroke: a systematic review. *QJM*. 2004;97(5):273–279.
42. Sobesky J, Frackowiak M, Zaro Weber O, et al. The Cologne stroke experience: safety and outcome in 450 patients treated with intravenous thrombolysis. *Cerebrovasc Dis*. 2007;24(1):56–65.
43. Lachkhem Y, Rican S, Minvielle E. Understanding delays in acute stroke care: a systematic review of reviews. *Eur J Public Health*. 2018;28(3):426–433.
44. Liu L, Kong FJ. Factors affecting the time window of thrombolytic therapy in acute ischemic stroke and intervention measures [In Chinese]. *J Neurosci Ment Health*. 2007;7(1):52–54.
45. Feng LY, Gui XX, Wang CS. Analysis of influential factors of delayed diagnosis of acute cerebral infarction [In Chinese]. *Chin J Gen Pract*. 2004;3(1):64.
46. Huang CX, Zhao SH. The effect of process management on quality control of community nursing in stroke patients [In Chinese]. *Chin Gen Pract*. 2011;14(35):4028–4031.
47. Yang HJ, Huang X, Yang CY, et al. Time window for acute stroke management: a cross-sectional study among community healthcare practitioners in primary care. *Int J Gen Med*. 2022;15:4483–4493.
48. Bhaskar S, Thomas P, Cheng Q, et al. Trends in acute stroke presentations to an emergency department: implications for specific communities in accessing acute stroke care services. *Postgrad Med J*. 2019;95(1123):258–264.
49. Nepal G, Yadav JK, Basnet B, Shrestha TM, Kharel G, Ojha R. Status of prehospital delay and intravenous thrombolysis in the management of acute ischemic stroke in Nepal. *BMC Neurol*. 2019;19(1):155.
50. Bhaskar S, Stanwell P, Bivard A, et al. The influence of initial stroke severity on mortality, overall functional outcome and in-hospital placement at 90 days following acute ischemic stroke: a tertiary hospital stroke register study. *Neurol India*. 2017;65(6):1252–1259.
51. Acker JE 3rd, Pancioli AM, Crocco TJ, et al. Implementation strategies for emergency medical services within stroke systems of care: a policy statement from the American Heart Association/American Stroke Association expert panel on emergency medical services systems and the stroke council. *Stroke*. 2007;38(11):3097–3115.
52. Yang H, Zhang J, Xie J, et al. Factors influencing pre-hospital delay among acute ischemic stroke patients in the midlands of China. *Int J Cardiol*. 2014;172(2):533–534.
53. Zakaria MF, Aref H, Abd EINasser A, et al. Egyptian experience in increasing utilization of reperfusion therapies in acute ischemic stroke. *Int J Stroke*. 2018;13(5):525–529.
54. Wang HHX, Li YT, Wong MCS. Leveraging the power of health communication: messaging matters not only in clinical practice but also in public health. *Hong Kong Med J*. 2022;28(2):103–105.
55. El Nahas NM, Shokri HM, Roushdy TM, et al. Door to needle count down: a 3-years experience in an Egyptian University Stroke Center. *Neurologist*. 2021;27(2):61–64.
56. Aref HM, Shokri H, Roushdy TM, Fathalla F, El Nahas NM. Pre-hospital causes for delayed arrival in acute ischemic stroke before and during the COVID-19 pandemic: a study at two stroke centers in Egypt. *PLoS One*. 2021;16(7):e0254228.

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