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Analysis of onset-to-door time and its influencing factors in Chinese patients with acute ischemic stroke during the 2020 COVID-19 epidemic: a preliminary, prospective, multicenter study

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Abstract

Background Pre-hospital delay in China is a serious issue with unclear relevant reasons, seriously impeding the adoption of appropriate measures. Herein, we analyzed the onset-to-door time (ODT) in Chinese patients with acute ischemic stroke (AIS) and its influencing factors.

Methods We prospectively recruited 3,459 patients with AIS from nine representative tertiary general hospitals in China between January and June 2022. Patients were divided into ODT ≤ 3 h and ODT > 3 h groups. Following single-factor analysis, binary logistic regression analysis was performed to evaluate the risk factors leading to pre-hospital delay.

Results In total, 763 (21.83%) patients arrived at the hospital within 3 h of onset. After adjusting for confounding factors, the risk factors for ODT were residence in rural areas (odds ratio [OR]: 1.478, 95% credibility interval [CI]: 1.024–2.146) and hospital transfer (OR: 7.479, 95% CI: 2.548–32.337). The protective factors for ODT were location of onset ≤ 20 km from the first-visit hospital (OR: 0.355, 95% CI: 0.236–0.530), transportation by emergency medical services (OR: 0.346, 95% CI: 0.216–0.555), history of atrial fibrillation (OR: 0.375, 95% CI: 0.207–0.679), moderate stroke (OR: 0.644, 95% CI: 0.462–0.901), and severe stroke (OR: 0.506, 95% CI: 0.285–0.908).

Conclusions Most patients with AIS fail to reach a hospital within the critical 3-h window. The following measures are recommended to reduce pre-hospital delays: reasonable distribution of hospitals accessible to nearby residents, minimizing interhospital transfer, paying attention to patients with mild stroke, and encouraging patients to use

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ambulance services. Pre-hospital delays for patients can be reduced by implementing these measures, ultimately improving the timeliness of treatment and enhancing patient prognosis. This study was carried out amid the COVID-19 pandemic, which presented challenges and constraints.

Keywords Acute ischemic stroke, Onset-to-door time, Pre-hospital delay, Current situation, Risk factors, China

Background

Acute ischemic stroke (AIS) is a common acute cerebrovascular disease with high disability and mortality rate [1]. Restoring vascular recanalization and improving tissue perfusion within the time window is the key to a successful treatment. Intravenous thrombolysis (IVT) within 3 h of AIS onset can effectively improve prognosis without a significantly increased risk of death [2]. Pre-hospital delay in AIS in China is common [3–9]. However, the impact of the Coronavirus Disease 2019 (COVID-19) pandemic, which began in January 2020 [10], on these delays and their influencing factors remain unclear. This lack of clarity further impedes the formulation of improvement measures.

The global burden of stroke has increased markedly over the past 20 years, especially in developing countries [11]. In China, stroke has become the leading cause of death over the past 30 years [12]. The median onset-to-door time (ODT) for AIS in China is 15 h, and only a quarter of patients reach the hospital within 3 h [13], which is obviously longer than that in developed Western nations. Compared to those in the United States, patients in China are more prone to experiencing pre-hospital delays (1318 min vs. 644 min), resulting in a lower thrombolysis rate (2.5% vs. 8.1%) [14]. In contrast, stroke burden and mortality have declined in many developed countries, largely due to improvements in stroke prevention and acute stroke care.

Many factors are associated with ODT in patients with AIS, including age, sex, residential status, educational level, medical history, transportation to the hospital, and efficiency of emergency medical services (EMS) [5, 15, 16]. Patients' understanding and recognition of stroke symptoms are critical for shortening the ODT [17]. EMS has been shown to reduce pre-hospital delays [18]. Pre-hospital delays differ greatly between China and developed countries, owing to the differences in education, culture, socioeconomic status, medicine, and health [19].

This study aimed to analyze the current situation of ODT in Chinese patients with AIS and its influencing factors through a large-scale, multicenter study and provide evidence for government health departments to make scientific decisions so that more patients can receive timely and optimal treatment, improving prognosis.

Methods

Study design

This study was a multicenter, large-sample, prospective, and observational study.

Study participants

A total of 3495 patients with AIS were recruited from nine hospitals (including Fushun Central Hospital, Wuzhou Workers' Hospital, Huaihua First People's Hospital, Inner Mongolia Autonomous Region People's Hospital, the First Affiliated Hospital of Shaoyang Medical College, Xiangxi Tujia and Miao Autonomous Prefecture People's Hospital, Affiliated Hospital of Yan'an University, Yueyang Central Hospital, and Zhuzhou Central Hospital) certified as "stroke centers" [20] by the China National Stroke Prevention Project Committee Commission from January to June 2022.

The data collection and entry personnel in all sub-centers had professional knowledge of stroke and were trained by the project manager. AIS was diagnosed according to the guidelines [21], and intracranial hemorrhage was excluded using head computed tomography or magnetic resonance imaging [22]. The stroke subtype was based on the trial of Org 10,172 in acute stroke treatment (TOAST) classification of stroke [23].

Inclusion criteria

- 1) Age \geq 18 years;
- 2) AIS diagnosis;
- 3) Stroke onset \leq 7 days on admission;
- 4) provision of consent to participate in this program.

Exclusion criteria

- 1) Diagnosis of transient ischemic attack, AIS occurring in hospitals, active malignancy, iatrogenic AIS, or cerebral venous sinus thrombosis.
- 2) Life expectancy less than 3 months; and
- 3) Diagnosed with severe mental disorders, cognitive disorders, or other conditions.

The ODT was defined as the time from the onset of stroke symptoms to admission to the hospital emergency department or outpatient clinic. For patients whose onset time was uncertain (e.g., wake-up stroke), the last known asymptomatic time was taken as the onset time.

Study variables and groups

The variables studied included sex, age, educational level, residence status, medical insurance, wake-up stroke, first symptom of AIS, distance between onset location and first-visit hospital, transfer method for patients, whether an inter-hospital transfer was performed, medical history, pre-onset modified Rankin scale (mRS) score, stroke severity (according to the National Institutes of Health Stroke Scales [NIHSS] first score after onset, moderate and severe stroke have NIHSS score 5–14 and NIHSS score 15–42 respectively) [24], patient's knowledge about AIS, and TOAST classification. The division of patients based on ODT is crucial for stratifying stroke care and predicting outcomes [25]. Therefore, patients with AIS were categorized into the $ODT \leq 3$ h group and $ODT > 3$ h group accordingly.

Definition of AIS's initial symptoms

In this section, we outline a comprehensive understanding of various symptoms encountered in AIS cases, ranging from common manifestations, such as vomiting or unconsciousness, to more specific indicators, including diplopia or dysarthria. The initial symptoms of AIS are defined as follows [26, 27]: (1) Vomiting: Involuntary expulsion of stomach contents through the mouth or nasal cavity. (2) Unconsciousness: Lack of response to external stimuli, coma, or other non-alert states. (3) Paralysis: Complete loss of voluntary motor function, which may affect specific body parts or one side. (4) Diplopia: Simultaneous perception of two images of the same object. (5) Aphasia: Loss or impairment of the ability to express or understand language, characterized by difficulties in speaking, expressing oneself, or understanding others. (6) Dysarthria: Unclear speech or difficulty in pronouncing words due to impaired neuromuscular control. (7) Drooping of the angle of the mouth: Noticeable drooping of one side of the mouth corner, resulting in an asymmetrical facial expression. (8) Headache: Persistent pain or discomfort experienced in the head. (9) Paresthesia: Abnormal sensations felt on the skin, such as numbness, tingling, or burning, without obvious stimulation. (10) Vertigo: Sensation of spinning or movement of the surrounding environment or oneself, often accompanied by balance disorders. (11) Other symptoms included visual disturbances that are difficult to classify within the categories mentioned above. Detailed symptom information can be provided upon entry of specific data.

ODT calculation method

In this study, we typically documented the precise time when the patient or a witness first noticed stroke symptoms, such as sudden weakness, speech difficulties, or visual disturbances. Alternatively, when the onset time of symptoms was unclear, the following methods were

used: (a) When the patient woke up with symptoms, the time before sleep when the last symptom-free period was confirmed was considered as the onset time of symptoms [28, 29]. (b) When the exact time of symptom onset cannot be determined, the time of the last confirmed symptom-free period was considered as the onset time of symptoms [28, 29]. Subsequently, the time of the patient's arrival at the outpatient department or emergency room, specifically at the triage entrance [30], was documented. The ODT was calculated by subtracting the recorded onset time of stroke symptoms from the time of arrival at the healthcare facility's door. For instance: (1) Unconsciousness: If the patient lost consciousness, the time when symptoms started was determined based on witness accounts or when the patient was found. This time was considered as the onset time, and then the time when the patient arrived at the hospital was recorded to calculate ODT. (2) Headaches: For localized headaches, the time when the patient or witnesses noticed the headache starting was considered the onset time. Following this, the time of arrival at the hospital was recorded to calculate ODT.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, N.Y., USA). The measured data with normal distribution are expressed as the mean \pm standard deviation, and the independent-sample *t*-test was used for between-group comparisons. When data does not follow a normal distribution, quartiles are used to describe the data. Categorical variables are presented as counts and percentages, and the differences between the two groups were analyzed using the chi-squared test. Firstly, the differences between the $ODT \leq 3$ h group and the $ODT > 3$ h group were analyzed using single-factor analysis; subsequently, the variables with significant differences were included in the binary logistic multivariate analysis, which typically yields confidence intervals for parameter estimates and conducts multicollinearity tests on the variables within the multivariable model. All statistical tests were two-sided, and the threshold for statistical significance was set at $P < 0.05$.

Results

Overview of ODT in patients with AIS (Table 1)

A total of 3495 patients with AIS were recruited, and the average is 1,698.88 min (range, 9–10,062 min), and the median is 883 min (Q1=181 min, Q3=2555 min). There were 763 patients (21.83%) with $ODT \leq 3$ h and 2732 patients (78.17%) with $ODT > 3$ h. Specifically, the number of patients with ODT 3–6 h, 6–12 h, 12–24 h, 24–72 h, and > 72 h accounted for 12.26%, 13.18%, 19.02%, 23.10%, and 10.61% of all patients with AIS,

Table 1 Baseline characteristics and single factor analysis of ODT in patients with acute ischemic stroke

		ODT ≤ 3 h, %	ODT > 3 h, %	P value
Number of cases		763, 21.83%	2732, 78.17%	
Gender	Male	520, 68.15%	1841, 67.39%	0.690
	Female	243, 31.85%	891, 32.61%	
Age, y		67.02 ± 11.22	65.51 ± 11.58	0.011
Whether patients lived alone	Yes	38, 4.98%	112, 4.10%	0.289
	No	725, 95.02%	2620, 95.90%	
Residential location	City	521, 68.28%	1341, 49.08%	0.000
	Rural and other areas	242, 31.72%	1391, 50.92%	
Medical insurance	Yes	638, 83.62%	2315, 84.74%	0.450
	No	125, 16.38%	417, 15.26%	
Educational level	Illiterate	32, 4.19%	219, 8.02%	0.000
	Primary or junior high school	397, 52.03%	1462, 53.51%	
	High school or junior college	293, 38.40%	835, 30.56%	
	University or above	41.5, 38%	216, 7.91%	
Whether patient or his family knew the stroke emergency map				
	Yes	37, 4.85%	115, 4.21%	0.444
	No	726, 95.15%	2617, 95.79%	
Whether patient or his family visited the WeChat official account of the stroke emergency map				
	Yes	14, 1.83%	35, 1.28%	0.250
	No	749, 98.17%	2697, 98.72%	
Wake-up stroke	Yes	118, 15.47%	488, 17.86%	0.122
	No	645, 84.53%	2244, 82.14%	
Distance between onset location and first-visit hospital	>20 km	135, 17.69%	1161, 42.50%	0.000
	≤ 20 km	628, 82.31%	1571, 57.50%	
Transfer method for patients	Emergency Medical Services	143, 18.74%	136, 4.98%	0.000
	Reaching hospital by oneself	620, 81.26%	2596, 95.02%	
Whether inter-hospital transfer was carried out	Yes	10, 1.31%	259, 9.48%	0.000
	No	753, 98.69%	2473, 90.52%	
Medical history				
Smoking	Present	222, 29.10%	741, 27.12%	0.281
	Absent	541, 70.90%	1991, 72.88%	
Drinking	Present	149, 21.85%	447, 17.48%	0.009
	Absent	533, 78.15%	2110, 82.52%	
Diabetes	Present	148, 19.40%	712, 26.06%	0.000
	Absent	615, 80.60%	2020, 73.94%	
Diabetes duration, y		7.58 ± 6.92	7.90 ± 6.26	0.586
Hypertension	Present	478, 62.65%	1774, 64.93%	0.243
	Absent	285, 37.35%	958, 35.07%	
Hypertension duration, y		9.29 ± 8.82	8.13 ± 7.07	0.003
Hyperlipidemia	Present	69, 15.20%	428, 23.14%	0.000
	Absent	385, 84.80%	1422, 76.86%	
TIA or ischemic stroke	Present	329, 43.12%	1172, 42.90%	0.913
	Absent	434, 56.88%	1560, 57.10%	
Atrial fibrillation	Present	89, 11.66%	126, 4.61%	0.000
	Absent	674, 88.34%	2606, 95.39%	
Pre-onset mRS score		0.43 ± 1.01	0.38 ± 0.92	0.237

Table 1 (continued)

		ODT ≤ 3 h, %	ODT > 3 h, %	P value
First symptom of AIS	Vomit	34, 4.46%	109, 3.99%	0.565
	Unconscious	77, 10.09%	107, 3.92%	0.000
	Paralysis	580, 76.02%	1998, 73.13%	0.110
	Diplopia	6, 0.79%	40, 1.46%	0.146
	Aphasia	93, 12.19%	152, 5.56%	0.000
	Dysarthria	276, 36.17%	844, 30.89%	0.006
	Drooping of angle of mouth	39, 5.11%	139, 5.09%	0.979
	Headache	8, 1.05%	78, 2.86%	0.004
	Paresthesia	100, 13.11%	306, 11.2%	0.473
	Vertigo	107, 14.02%	471, 17.24%	0.034
TOAST classification of stroke	Other symptoms	115, 15.07%	522, 19.11%	0.011
	LAA stroke	396, 51.90%	1204, 44.07%	0.000
	Cardiogenic stroke	126, 16.51%	220, 8.05%	
	SAO stroke	195, 25.56%	1139, 41.69%	
	SOE	17, 2.23%	51, 1.87%	
	Unexplained stroke	29, 3.80%	118, 4.32%	
Stroke severity	Mild stroke	380, 49.80%	1798, 65.81%	0.000
	Moderate stroke	283, 37.09%	787, 28.81%	
	Severe stroke	100, 13.11%	147, 5.38%	

ODT, onset-to-door time; AIS, acute ischemic stroke; LAA, Large-artery atherosclerosis; mRS, modified Rankin scale; SAO, Small artery occlusion; SOE, Stroke of other determined etiology; TOAST, Trial of Org 10,172 in Acute Stroke Treatment; y, year; TIA, Transient ischemic attack

Emergency Medical Services primarily involve the use of ambulances to transport patients

Medical insurance include social and commercial insurance

No smoking refers to not smoking at present or in the past

No drinking refers to not drinking at present or in the past

Mild, moderate, and severe strokes are defined as NHISS score of 0–4, 5–14 and 15–42, respectively

respectively (Fig. 1). There were 2,317 patients (66.29%) with ODT ≤ 24 h and 1178 patients (33.71%) with ODT > 24 h.

Baseline characteristics and single-factor analysis of ODT in patients with acute ischemic stroke (Table 1)

Older patients (65.84 ± 11.52 years), lived in the city, had high educational qualifications, had a distance of > 20 km between onset location and the first-visit hospital, reached the hospital by ambulance, and had no inter-hospital transfer had higher ODT ($P < 0.05$).

There were significant differences in medical history (including current drinking, diabetes, hypertension duration, hyperlipidemia, and atrial fibrillation), the first symptom of AIS (including unconsciousness, aphasia, dysarthria, headache, and vertigo), TOAST classification of stroke, and stroke severity between ODT ≤ 3 h group and ODT > 3 h group ($P < 0.05$).

Analysis of delayed ODT (> 3 h) with binary logistic regression analysis

Living in rural areas (OR: 1.478, 95% CI: 1.024–2.146) and existing interhospital transfer (OR: 7.479, 95% CI: 2.548–32.337) were risk factors for ODT (Table 2).

Distance between the onset location and first-visit hospital ≤ 20 km (OR: 0.355, 95% CI: 0.236–0.530),

transportation of patients by EMSs (OR: 0.346, 95% CI: 0.216–0.555), history of atrial fibrillation (OR: 0.375, 95% CI: 0.207–0.679), moderate stroke (OR: 0.644, 95% CI: 0.462–0.901), and severe stroke (OR: 0.506, 95% CI: 0.285–0.908) were protective factors for ODT.

Discussion

Our study demonstrated that only about one-fifth of patients with AIS could reach the hospital within 3 h of symptom onset, and the pre-hospital delay was significant. Some characteristics of pre-hospital delay are risk factors for ODT, such as living in rural areas and existing inter-hospital transfer; meanwhile, distance of ≤ 20 km between onset location and the first-visit hospital, transportation of patients by EMSs, and history of atrial fibrillation and moderate and severe stroke were protective factors for ODT.

Comparison of ODT in China and developed countries

This study showed that the median of ODT was 852 min (range, 215–2459 min), and 21.83% of patients had ODT ≤ 3 h. A multicenter study in the United States showed that 21–40% of patients with AIS reach the hospital within 3 h of symptom onset [31]. In a 2006 study that included 62 subcenters in China that showed similar results, the median ODT was 15 h [13]. Our findings

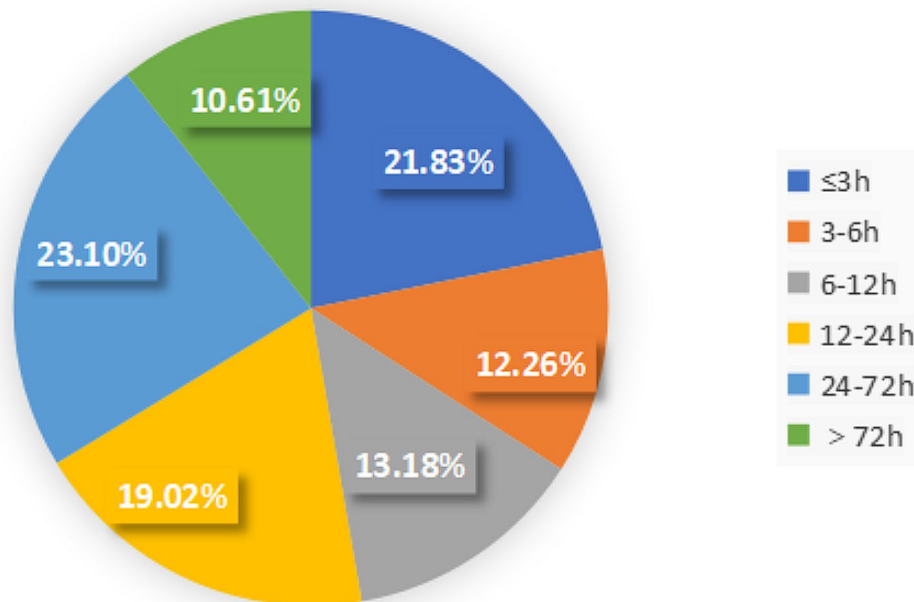


Fig. 1 Distribution ratio of ODT in patients with acute ischemic stroke
ODT: onset-to-door time

Table 2 Analysis of delayed onset-to-door time (> 3 h) with binary logistic regression analysis

	Adjusted Odds Ratio	95% confidence interval	P-value
Living in rural- areas	1.478	1.024–2.146	0.038
Distance between onset location and the first-visit hospital ≤ 20 km	0.355	0.236–0.530	0.000
Transportation- using EMS	0.346	0.216–0.555	0.000
Existing inter-hospital transfer	7.479	2.548–32.337	0.001
History of Atrial fibrillation	0.375	0.207–0.679	0.001
Moderate stroke	0.644	0.462–0.901	0.010
Severe stroke	0.506	0.285–0.908	0.021

Moderate and severe strokes are defined as NHISS score of 5–14 and 15–42, respectively

EMS, emergency medical service; The adjusted covariates include Gender, Age, Educational level, Drinking, Diabetes, Hyperlipidemia, First symptom of AIS, and TOAST classification of stroke

reveal that ODT has not shown much reduction after more than 10 years and is still 3–6 h longer than that in developed countries [30]. Furthermore, a study in 2012–2013 indicated that patients in China experienced more pre-hospital delays compared to those in the United States (1318 min vs. 644 min) [14]. There is a significant difference between ODTs in China and those in developed countries [9, 15, 32, 33].

The World Health Organization's MONICA manual provides standardized guidelines for registering stroke events [26]. These guidelines ensure that stroke cases are consistently defined and registered, facilitating accurate

comparisons across different populations and regions. The MONICA project has played a crucial role in standardizing the registration of acute stroke events, enabling uniform data collection and analysis [26]. Research has demonstrated that adherence to the MONICA criteria for stroke registration is essential for quality control and accurate event validation [34]. The protocols established by the MONICA project have been widely adopted in various studies for registering stroke events, highlighting the broad acceptance and utility of these guidelines [35]. The standardized approach to stroke event registration outlined in the MONICA manual is critical for ensuring the accuracy and consistency of data collected across diverse populations and periods.

Over time, the accuracy of patients' and witnesses' recollection of the onset time may diminish, posing a challenge in determining the ODT accurately. We have therefore implemented the following measures to address recall bias in our study design: utilizing standardized questionnaires and interview methods. Additionally, we observed that most patients experience an ODT of less than 1 day. Therefore, we argue that including all patients in the primary analysis, even those with an onset of illness exceeding 24 h, can offer a more comprehensive depiction of the actual situation.

Residential area type and ODT

This study showed that living in rural areas was a risk factor for ODT. Only 8.18% of patients in rural areas in

China reached the hospital within 3 h [36], while 45.8% of patients in urban areas reached the hospital within 3 h [37]. Compared with patients in urban areas, those in rural areas are typically older and have lower levels of education, poor housing conditions, and high poverty rates.

China's economic and healthcare service development has been uneven. Medical and health services supply in China has obvious differences in spatial distribution [19], and the eastern region has the highest medical and health services supply level, followed by the western and central regions. Patients in some parts of China experienced pre-hospital delays owing to poor economic and sanitary conditions [3]. In rural areas, insufficient medical resources, low levels of medical care, and fewer medical staff members make it extremely difficult to meet the needs of patients with stroke. In addition, rural residents have limited access to medical knowledge about first aid; this often results in patients missing the optimal stroke treatment time [38]. The coverage and reimbursement rates of medical insurance in rural areas are lower than those in urban areas, and the frequency of rural patients visiting hospitals is also low [39, 40], which may also result in longer ODTs in rural areas compared with in urban areas.

Distance between onset location and the first-visit hospital and ODT

Our study showed that the distance between the onset location and the initial hospital ≤ 20 km was associated with shorter ODT. Long distances are an important factor delaying patient transport. Improving transport efficiency is a solution that the EMS plays a crucial role in achieving. EMS most closely affects ODT [6]. When there is an optimal EMS, the median ODT can be reduced to 151 min, and the proportion of patients reaching the hospital within 3 h can be increased to 54% [6]. However, EMS usage adds to medical costs; therefore, EMS construction is not feasible in some areas. The awareness of patients regarding EMS usage is also relatively low, and the proportion of patients with AIS using it in China is extremely low, as shown in this study; our results are also consistent with the findings of Wang et al. [14].

Stroke severity and ODT

Our findings showed that patients with moderate or severe stroke were more likely to reach the stroke center within 3 h after onset. Similar results have been reported by Iversen et al. [41]. Patients with moderate or severe stroke were more likely to arrive at the hospital promptly and receive reperfusion therapy. The more serious the stroke, the more it is likely to attract patients' and bystanders' attention; this was associated with a higher probability of using EMS. Our research suggests that

patients with mild strokes often experience more delays, which can be attributed to several factors: (1) Atypical Symptoms: Mild strokes may manifest with subtle or non-specific symptoms that patients may not immediately recognize as indicative of a stroke. (2) Minimization of symptoms: Patients with mild strokes may diminish the severity of their symptoms or attribute them to other less serious conditions, delaying their decision to seek medical attention. (3) Fear or denial: Some patients may experience fear or denial about the possibility of experiencing a stroke. This psychological barrier can prevent them from promptly seeking medical care. (4) Neglect: Patients with mild strokes may perceive their symptoms as less urgent and may prioritize other obligations over seeking immediate medical attention. Thus, we emphasize the importance of concentrating on patients with mild stroke and the significance of timely referrals.

Bystanders are more likely to notice typical stroke symptoms such as limb weakness, speech disturbance, and walking difficulties [42]. It has been reported that living alone increases admission delay, and the recognition of symptoms by bystanders may shorten it [43]. The onset of symptoms can influence a patient's decision-making. When dysarthria or decreased muscle strength were the first symptoms, the rate of hospital visits increased significantly within 4.5 h ($P < 0.01$) [6, 44, 45]. The more prominent the impact of the first symptom on daily living, the easier it is to attract the attention of patients and their families, the stronger the desire to seek medical attention, and the shorter the ODT. Only 53.8% of patients with posterior circulation stroke reach the hospital within 3 h, compared to 68.4% of patients with anterior circulation stroke [7]. Compared with dysphagia and limb weakness caused by posterior circulation stroke, posterior circulation stroke often presents with non-specific symptoms such as dizziness, vertigo, and nausea, which are easily attributed to poor rest, anxiety, and failure. Cryptogenic stroke is common in young people [46]. However, young patients often ignore the possibility of stroke onset, which leads to a pre-hospital delay. Patients often choose self-observation when stroke occurs and only visit the hospital if the symptoms persist or worsen because of the inability to identify stroke in an accurate and timely manner [13]. Recognizing symptoms of stroke is an independent factor associated with early arrival [47].

Transportation of patients to hospital and ODT

Most patients in our study chose to go to the hospital by themselves, which increased the probability of inter-hospital transfer and caused pre-hospital delays. There are two main specific situations of interhospital transfer: (1) Patients who independently seek medical attention may arrive at a hospital without a stroke center, necessitating their transfer to one. (2) In our study, patients

who utilized an ambulance were directly transported to a stroke center. However, interhospital transfers may occur for these patients if the initial hospital cannot administer mechanical thrombectomy treatment. Only one in eight patients with stroke in China arrived at the hospital via EMS [48], compared to 59.6% in the DASH II study [49]. Our study showed that patients who visited the hospital via EMSs (ambulances) had shorter ODTs. Moreover, many studies have demonstrated a reduction in pre-hospital delays via EMS [50, 51]. The 2019 AHA/ASA guidelines indicate that patients with stroke who use EMS arrive at the emergency department earlier, and more eligible patients receive IVT [27]. A stroke emergency map (an intelligent EMS that can guide ambulances to transport patients more effectively) in China has effectively shortened the ODT and improved the thrombolysis rate [52].

Atrial fibrillation (AF) and ODT

Our study demonstrated that patients with AF are not prone to pre-hospital delays, given that strokes resulting from atrial fibrillation tend to be more severe [53, 54]. Cardiac stroke typically occurs abruptly with evident symptoms. Patients often experience obvious discomfort, which helps in raising the alert faster, causing them to seek medical attention in time. The multivariate regression analysis revealed that AF was an independent factor associated with early arrival [47]. AF and a history of coronary artery disease accelerated the presentation to the hospital [13]; sudden onset of symptoms, loss of consciousness, recognition of symptoms as stroke, and feelings of fear and panic were associated with hospital arrival within 3 h.

The impact of the COVID-19 pandemic on patients with stroke

The COVID-19 pandemic has markedly impacted patients with stroke, affecting different aspects of stroke care. Studies have demonstrated a decrease in hospital admissions for transient ischemic attacks and mild to moderate stroke during the COVID-19 era [55, 56]. Additionally, the pandemic has disrupted the chain of acute stroke care, resulting in potential risks such as decreased thrombectomy rates [57, 58] and modifications in the acute stroke care pathway [59]. Furthermore, the pandemic has caused a delay in patients with AIS seeking treatment at stroke centers [4]. Both pre- and post-hospital delays have been considerably prolonged, and the number of patients receiving intravenous thrombolysis treatment has decreased [60].

Moreover, a higher occurrence of severe strokes and an increased in-hospital mortality rate have been observed during the COVID-19 pandemic [61]. The pandemic has also raised concerns about the collateral damage

on stroke emergency services, as well as the necessity to reorganize stroke networks in order to provide optimal care while mitigating the risk of transmission [55]. In conclusion, the COVID-19 pandemic has had a multifaceted impact on patients with stroke, affecting various aspects of stroke care, including hospital admissions, acute stroke care pathways, delayed presentation, and treatment.

Limitations

The stroke population recruited in each subcenter of this study had certain regional characteristics; therefore, generalization of the research conclusions was affected to some extent. This study lacks detailed information on imaging, timing of EMS notification, and adjustment for socioeconomic factors. These limitations may have specific implications for interpreting and inferring research results: (1) Lack of imaging information: Inability to accurately assess disease severity and progression. (2) Lack of information on EMS notification time: Inability to determine the timeliness of patient medical assistance and the absence of a reference for optimizing emergency response systems. (3) Failure to adjust for socioeconomic factors: Socioeconomic status may influence patients' healthcare-seeking behavior. Neglecting socioeconomic factors may introduce bias, potentially leading to an overestimation or underestimation of the impact of certain factors. Lastly, the COVID-19 pandemic presented significant challenges for this study. Lockdown restrictions and safety concerns led to limited data collection, resulting in a smaller sample size.

Conclusions

Pre-hospital delays for patients with AIS are a serious medical and social issue that needs immediate attention. The majority (approximately four in five) of patients with AIS fail to reach the hospital within a 3-h prime time for stroke treatment, leaving much room for improvement in this regard. Reasonable distribution of hospitals that provide treatments to residents staying nearby, minimizing interhospital transfers, paying special attention to patients with moderate or severe stroke, and encouraging patients to reach the hospital by ambulance are recommended measures that can help reduce pre-hospital delays. The findings should be interpreted considering the constraints imposed by the COVID-19 pandemic. Future longitudinal studies could investigate the lasting effects of the pandemic on the research topic.

Abbreviations

AF	Atrial fibrillation
AIS	Acute ischemic stroke
EMS	Emergency medical services
IVT	Intravenous thrombolysis
mRS	Modified Rankin scale
NHSS	National Institutes of Health Stroke Scales

ODT Onset-to-door time
TOAST Trial of Org 10,172 in acute stroke treatment

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Author contributions

LC, LR, and XW designed the study. LC, FC, LQ and RX performed the research. XS and LR provided advice on the study. YL, WQ and SL analyzed the data. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics review board of the First Affiliated Hospital of Shenzhen University (No. 20200727003-FS01-XZ2022). Informed written/verbal consent was obtained from all participants. It was performed per the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Zhou M, Wang H, Zeng X, Yin P, Zhu J, Chen W, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for

the global burden of disease study 2017. *Lancet*. 2019;394:1145–58. [https://doi.org/10.1016/S0140-6736\(19\)30427-1](https://doi.org/10.1016/S0140-6736(19)30427-1)

- Hacke W, Kaste M, Fieschi C, Toni D, Lesaffre E, von Kummer R, et al. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). *JAMA*. 1995;274:1017–25.
- Wang Y, Wu D, Zhou Y, Zhao X, Wang C, Wang Y. Thrombolysis in the emergency department in China: results from an emergency department registry in 7 urban hospitals. *Chin J Stroke*. 2009;4:23–8. <https://doi.org/10.3969/j.issn.1673-5765.2009.01.005>. [Chinese].
- Schirmer CM, Ringer AJ, Arthur AS, Binning MJ, Fox WC, James RF, et al. Delayed presentation of acute ischemic strokes during the COVID-19 crisis. *J Neurointerv Surg*. 2020;12:639–42. <https://doi.org/10.1136/neurintsurg-2020-016299>
- Teo KC, Leung WCY, Wong YK, Liu RKC, Chan AHY, Choi OMY, et al. Delays in stroke onset to hospital arrival time during COVID-19. *Stroke*. 2020;51:2228–31. <https://doi.org/10.1161/STROKEAHA.120.030105>
- Rossmagel K, Jungehülsing GJ, Nolte CH, Müller-Nordhorn J, Roll S, Wegscheider K, et al. Out-of-hospital delays in patients with acute stroke. *Ann Emerg Med*. 2004;44:476–83. <https://doi.org/10.1016/j.annemergmed.2004.06.019>
- Sommer P, Seyfang L, Posekany A, Ferrari J, Lang W, Fertl E, et al. Prehospital and intra-hospital time delays in posterior circulation stroke: results from the Austrian stroke unit registry. *J Neurol*. 2017;264:131–8. <https://doi.org/10.1007/s00415-016-8330-x>
- Khatri P, Yeatts SD, Mazighi M, Broderick JP, Liebeskind DS, Demchuk AM, et al. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: an analysis of data from the interventional management of stroke (IMS III) phase 3 trial. *Lancet Neurol*. 2014;13:567–74. [https://doi.org/10.1016/S1474-4422\(14\)70066-3](https://doi.org/10.1016/S1474-4422(14)70066-3)
- Tong D, Reeves MJ, Hernandez AF, Zhao X, Olson DM, Fonarow GC, et al. Times from symptom onset to hospital arrival in the get with the guidelines–stroke program 2002 to 2009: temporal trends and implications. *Stroke*. 2012;43:1912–17. <https://doi.org/10.1161/STROKEAHA.111.644963>
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382:1199–207. <https://doi.org/10.1056/NEJMoa2001316>
- Katan M, Luft A. Global burden of stroke. *Semin Neurol*. 2018;38:208–11. <https://doi.org/10.1055/s-0038-1649503>
- Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, et al. Prevalence, incidence, and mortality of stroke in China: results from a nationwide population-based survey of 480 687 adults. *Circulation*. 2017;135:759–71. <https://doi.org/10.1161/CIRCULATIONAHA.116.025250>
- Jin H, Zhu S, Wei JW, Wang J, Liu M, Wu Y, et al. Factors associated with prehospital delays in the presentation of acute stroke in urban China. *Stroke*. 2012;43:362–70. <https://doi.org/10.1161/STROKEAHA.111.623512>
- Wangqin R, Laskowitz DT, Wang Y, Li Z, Wang Y, Liu L, et al. International comparison of patient characteristics and quality of care for ischemic stroke: analysis of the China national stroke registry and the American Heart Association get with the guidelines–stroke program. *J Am Heart Assoc*. 2018;7:e010623. <https://doi.org/10.1161/JAHA.118.010623>
- Tanaka Y, Nakajima M, Hirano T, Uchino M. Factors influencing pre-hospital delay after ischemic stroke and transient ischemic attack. *Intern Med*. 2009;48:1739–44. <https://doi.org/10.2169/internalmedicine.48.2378>
- Lee EJ, Kim SJ, Bae J, Lee EJ, Kwon OD, Jeong HY, et al. Impact of onset-to-door time on outcomes and factors associated with late hospital arrival in patients with acute ischemic stroke. *PLoS ONE*. 2021;16:e0247829. <https://doi.org/10.1371/journal.pone.0247829>
- Fang J, Yan W, Jiang GX, Li W, Cheng Q. Time interval between stroke onset and hospital arrival in acute ischemic stroke patients in Shanghai, China. *Clin Neurol Neurosurg*. 2011;113:85–8. <https://doi.org/10.1016/j.clineuro.2010.09.004>
- Keskin O, Kalemöçlü M, Ulusoy RE. A clinic investigation into prehospital and emergency department delays in acute stroke care. *Med Princ Pract*. 2005;14:408–12. <https://doi.org/10.1159/000088114>
- Chen B, Jin F. Spatial distribution, regional differences, and dynamic evolution of the medical and health services supply in China. *Front Public Health*. 2022;10:1020402. <https://doi.org/10.3389/fpubh.2022.1020402>
- Chao B, Cao L, Tu W, Wang L. Construction of national stroke center network system. *Int J Biomed Eng*. 2019;42:363–66. <https://doi.org/10.3760/cmaj.issn.1673-4181.2019.05.001>. [Chinese].

21. Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerschalk BM, et al. 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*. 2013;44:870–947. <https://doi.org/10.1161/STR.0b013e318284056a>
22. The World Health Organization MONICA Project. (monitoring trends and determinants in cardiovascular disease): a major international collaboration. WHO MONICA project principal investigators. *J Clin Epidemiol*. 1988;41:105–14. [https://doi.org/10.1016/0895-4356\(88\)90084-4](https://doi.org/10.1016/0895-4356(88)90084-4)
23. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*. 1993;24:35–41. <https://doi.org/10.1161/01.str.24.1.35>
24. Chang KC, Tseng MC, Weng HH, Lin YH, Liou CW, Tan TY. Prediction of length of stay of first-ever ischemic stroke. *Stroke*. 2002;33:2670–4. <https://doi.org/10.1161/01.str.0000034396.68980.39>
25. Kamal H, Assaf S, Kaban M, El Maissi R, Salhab D, Rahme D, et al. Evaluation of stroke pre-hospital management in Lebanon from symptoms onset to hospital arrival and impact on patients' status at discharge: a pilot study. *BMC Neurol*. 2022;22:494. <https://doi.org/10.1186/s12883-022-03018-0>
26. Stegmayr B, Vinogradova T, Malyutina S, Peltonen M, Nikitin Y, Asplund K. Widening gap of stroke between east and west. Eight-year trends in occurrence and risk factors in Russia and Sweden. *Stroke*. 2000;31:2–8. <https://doi.org/10.1161/01.str.31.1.2>
27. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344–418. <https://doi.org/10.1161/STR.0000000000000211>
28. Saver JL, Fonarow GC, Smith EE, Reeves MJ, Grau-Sepulveda MV, Pan W, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. *JAMA*. 2013;309:2480–8. <https://doi.org/10.1001/jama.2013.6959>
29. Strbian D, Ahmed N, Wahlgren N, Lees KR, Toni D, Roffe C, et al. Trends in door-to-thrombolysis time in the safe implementation of stroke thrombolysis registry: effect of center volume and duration of registry membership. *Stroke*. 2015;46:1275–80. <https://doi.org/10.1161/STROKEAHA.114.007170>
30. 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;4:187–99. <https://doi.org/10.1111/j.1747-4949.2009.00276.x>
31. Majersik JJ, Smith MA, Zahuranec DB, Sánchez BN, Morgenstern LB. Population-based analysis of the impact of expanding the time window for acute stroke treatment. *Stroke*. 2007;38:3213–7. <https://doi.org/10.1161/STROKEAHA.107.491852>
32. Faiz KW, Sundseth A, Thommessen B, Rønning OM. Prehospital delay in acute stroke and TIA. *Emerg Med J*. 2013;30:669–74. <https://doi.org/10.1136/34eme-rmed-2012-201543>
33. Matsuo R, Yamaguchi Y, Matsushita T, Hata J, Kiyuna F, Fukuda K, et al. Association between onset-to-door time and clinical outcomes after ischemic stroke. *Stroke*. 2017;48:3049–56. <https://doi.org/10.1161/STROKEAHA.117.018132>
34. Angerud KH, Brulin C, Näslund U, Eliasson M. Patients with diabetes are not more likely to have atypical symptoms when seeking care of a first myocardial infarction. An analysis of 4028 patients in the Northern Sweden MONICA Study. *Diabet Med*. 2012;29:e82–7. <https://doi.org/10.1111/j.1464-5491.2011.03561.x>
35. Truelsen T, Bonita R. Epidemiological transition of stroke in China? *Stroke*. 2008;39:1653–4. <https://doi.org/10.1161/strokeaha.107.510552>
36. Zeng R, He X, Zhang J. Analysis of influencing factors of delayed thrombolytic therapy for acute cerebral infarction in rural areas of a hospital. *Chin Rural Health Service Adm*. 2016;36:394–7. [Chinese].
37. Bi Q, Zhang Z, Zhang WW, Li Q. Study on prehospital time and influencing factors of stroke patients in 15 Chinese cities. *Chin J Epidemiol*. 2006;27:996–9. <https://doi.org/10.3760/j.issn:0254-6450.2006.11.019>. [Chinese].
38. Yi J, Zhuo C, Yan X. Status quo and countermeasures of the popularity of emergency medical knowledge in China rural areas. *Chin Rural Health Service Adm*. 2014;34:366–8. [Chinese].
39. Kozera G, Chwojnicki K, Gójska-Grymajło A, Gąsecki D, Schminke U, Nyka WM, et al. Pre-hospital delays and intravenous thrombolysis in urban and rural areas. *Acta Neurol Scand*. 2012;126:171–7. <https://doi.org/10.1111/j.1600-0404.2011.01616.x>
40. Lu Z, Fang Y, Wang Z, Wang X, Yang H, Wang L. Social determinants of pre-hospital delays after onset of stroke. *Chin J Health Manage*. 2014;8:40–3. <https://doi.org/10.3760/cma.j.issn.1674-0815.2014.01.012>. [Chinese].
41. Iversen AB, Blauenfeldt RA, Johnsen SP, Sandal BF, Christensen B, Andersen G, et al. Understanding the seriousness of a stroke is essential for appropriate help-seeking and early arrival at a stroke centre: a cross-sectional study of stroke patients and their bystanders. *Eur Stroke J*. 2020;5:351–61. <https://doi.org/10.1177/2396987320945834>
42. Nowacki P, Nowik M, Bajer-Czajkowska A, Porebska A, Zywicka A, Nocoń D, et al. Patients' and bystanders' awareness of stroke and pre-hospital delay after stroke onset: perspectives for thrombolysis in West Pomerania Province, Poland. *Eur Neurol*. 2007;58:159–65. <https://doi.org/10.1159/000104717>
43. Derex L, Adeleine P, Nighoghossian N, Honnorat J, Trouillas P. Factors influencing early admission in a French stroke unit. *Stroke*. 2002;33:153–9. <https://doi.org/10.1161/hs0102.100533>
44. Gonzalez-Aguines A, Cordero-Pérez AC, Cristobal-Niño M, Pérez-Vázquez G, Góngora-Rivera F, GECEN Investigators. Contribution of onset-to-alarm time to prehospital delay in patients with ischemic stroke. *J Stroke Cerebrovasc Dis*. 2019;28:104331. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104331>
45. Terecoasă EO, Radu RA, Negrilă A, Enache I, Cășaru B, Tiu C. Pre-hospital delay in acute ischemic stroke care: current findings and future perspectives in a tertiary stroke center from Romania—a cross-sectional study. *Med (Kaunas)*. 2022;58:1003. <https://doi.org/10.3390/medicina58081003>
46. Fonseca AC, Ferro JM. Cryptogenic stroke. *Eur J Neurol*. 2015;22:618–23. <https://doi.org/10.1111/ene.12673>
47. Song D, Tanaka E, Lee K, Sato S, Koga M, Kim YD, et al. Factors associated with early hospital arrival in patients with acute ischemic stroke. *J Stroke*. 2015;17:159–67. <https://doi.org/10.5853/jos.2015.17.2.159>
48. Gu HQ, Rao ZZ, Yang X, Wang CJ, Zhao XQ, Wang YL, et al. Use of emergency medical services and timely treatment among ischemic stroke. *Stroke*. 2019;50:1013–6. <https://doi.org/10.1161/STROKEAHA.118.024232>
49. Mathews R, Peterson ED, Li S, Roe MT, Glickman SW, Wiviott SD, et al. Use of emergency medical service transport among patients with ST-segment-elevation myocardial infarction: findings from the national cardiovascular data registry acute coronary treatment intervention outcomes network registry-get with the guidelines. *Circulation*. 2011;124:154–63. <https://doi.org/10.1161/CIRCULATIONAHA.110.002345>
50. Tong X, Wiltz JL, George MG, Odom EC, Coleman King SM, Chang T, et al. A decade of improvement in door-to-needle time among acute ischemic stroke patients, 2008 to 2017. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004981. <https://doi.org/10.1161/CIRCOUTCOMES.118.004981>
51. Davis NW, Buchwald N, Farooqui A, Khanna A. Factors that influence door-to-needle administration for acute stroke patients in the emergency department. *J Neurosci Nurs*. 2021;53:134–9. <https://doi.org/10.1097/JNN.0000000000000590>
52. Ye S, Hu S, Lei Z, Li Z, Li W, Sui Y, et al. Shenzhen stroke emergency map improves access to rt-PA for patients with acute ischaemic stroke. *Stroke Vasc Neurol*. 2019;4:115–22. <https://doi.org/10.1136/svn-2018-000212>
53. Dahl OE. New oral antithrombotics: focus on dabigatran, an oral, reversible direct thrombin inhibitor for the prevention and treatment of venous and arterial thromboembolic disorders. *Vasc Health Risk Manag*. 2012;8:45–57. <https://doi.org/10.2147/VHRM.S26482>
54. Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, et al. Long-term survival after ischemic stroke in patients with atrial fibrillation. *Neurology*. 2014;82:1033–7. <https://doi.org/10.1212/WNL.0000000000000248>
55. Diegoli H, Magalhães PSC, Martins SCO, Moro CHC, França PHC, Safanelli J, et al. Decrease in hospital admissions for transient ischemic attack, mild, and moderate stroke during the COVID-19 era. *Stroke*. 2020;51:2315–21. <https://doi.org/10.1161/STROKEAHA.120.030481>
56. Luo W, Li J, Li Z, Luo X, Chen M, Cai C. Effects of the COVID-19 pandemic on reperfusion therapy for acute ischemic stroke patients in Huizhou City, China. *Neurol Sci*. 2021;42:467–73. <https://doi.org/10.1007/s10072-020-04938-w>
57. Rudilosso S, Laredo C, Vera V, Vargas M, Renú A, Llull L, et al. Acute stroke care is at risk in the era of COVID-19: experience at a comprehensive stroke center in Barcelona. *Stroke*. 2020;51:1991–5. <https://doi.org/10.1161/STROKEAHA.120.030329>
58. Al Kasab S, Almallouhi E, Alawieh A, Jabbour P, Sweid A, Starke RM, et al. Alarming downtrend in mechanical thrombectomy rates in African American patients during the COVID-19 pandemic—insights from STAR. *J Neurointerv Surg*. 2021;13:304–7. <https://doi.org/10.1136/neurintsurg-2020-016946>

59. Kim TJ, Kim BJ, Gwak DS, Lee JS, Kim JY, Lee KJ, et al. Modification of acute stroke pathway in Korea after the coronavirus disease 2019 outbreak. *Front Neurol*. 2020;11:597785. <https://doi.org/10.3389/fneur.2020.597785>
60. Gu S, Dai Z, Shen H, Bai Y, Zhang X, Liu X, et al. Delayed stroke treatment during COVID-19 pandemic in China. *Cerebrovasc Dis*. 2021;50(6):715–21. <https://doi.org/10.1159/000517075>
61. Katsanos AH, Palaiodimou L, Zand R, Yaghi S, Kamel H, Navi BB, et al. Changes in stroke hospital care during the COVID-19 pandemic: a systematic review and meta-analysis. *Stroke*. 2021;52:3651–60. <https://doi.org/10.1161/STROKEAHA.121.034601>

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