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Risk Factors of Admission Delay after Ischemic Stroke in an Urban Tertiary Care Setting in China

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Abstract

Background: Thrombolytic therapy within 6 hours of the onset of symptoms significantly improves clinical outcomes in patients with ischemic stroke, but many patients failed to receive timely treatment in China. The factors contributing to such admission delays in China remain largely unknown. We sought to identify important risk factors of admission delay after ischemic stroke in an urban tertiary care setting in China.

Methods: In a cross-sectional study, data were collected from 273 ischemic stroke patients admitted to a major tertiary care centre in Kaifeng city, China, between July 2011 and December 2011. Admission delay was defined as admission time >6 hours from onset of symptoms to arrival at the hospital.

Results: Admission delay occurred in 163 out of 273 patients (59.7%). Bivariate analyses showed that the factors significantly influencing admission delay were place of residence, education, type of employment, type of medical insurance, time of onset of symptoms, concerns about high cost of treatment, referral from a community hospital and patient's stroke-related knowledge (P<0.05). Multivariate logistic regression analyses revealed that the significant risk factors of admission delay were referral from a community hospital, patient's poor stroke-related knowledge and living with a spouse.

Conclusions: Admission delays are common, and certain modifiable risk factors (timely patient transfer, stroke knowledge and living pattern) may be targeted to reduce the frequency of such delays for improved outcomes in ischemic stroke patients in an urban tertiary care setting in China. Large multi-center studies in China are needed to confirm the findings.

Keywords: Ischemic stroke; Admission delay; Risk factor; China

Introduction

Ischemic stroke is a major cause of death in many countries, and fatality rate in ischemic stroke patients is about 20% to 30% in China [1]. According to the third National Sampling Survey of Chinese residents on causes of death, cerebrovascular disease has become the leading cause of death in China, and stroke mortality is higher in rural areas than in urban areas [2]. Thrombolysis with intravenous recombinant tissue plasminogen activator is widely accepted as an effective treatment for ischemic stroke especially in acute phase. However, this strategy is effective only if the treatment can be initiated within the time window of about 4.5 hours after the onset of symptoms [3,4]. In China, early thrombolysis refers to the treatment initiated within 6 hours after the onset of stroke symptoms. However, many patients arrive at the hospital too late to receive effective thrombolytic therapy, and consequently miss the best treatment time window. For example, a study in the Temple of Heaven Hospital in Beijing showed that only 38% of ischemic stroke patients arrived in the hospital within 3 hours of onset of symptoms, and only about half (53.5%) of patients arrived within 6 hours [5]. Another study on Chinese farmers with acute ischemic stroke found that only 3 of 144 cases (2.1%) arrived in hospital within 6 hours of onset of symptoms [6]. Knowledge on the risk factors of admission delay is critical for developing effective preventive measures to reduce the frequency of such delays for timely treatment to decrease the risk of mortality and disability after ischemic stroke. However, the factors contributing to such admission delays in China remain largely unknown. We sought to identify important risk factors of admission delay in ischemic stroke patients in an urban tertiary care setting in China.

Methods

Ethics statement

The study was approved by the research ethics committee of Henan University. Written informed consent was obtained from all study participants.

Design and participants

This was a cross-sectional study. Ischemic stroke patients were recruited and data were collected between July 15, 2011 and December 15, 2011 at the neurology department of Hai-He Hospital of Henan University, Kaifeng, China. The hospital is the largest tertiary care center in the city, with a catchment population of about five million residents. The stroke team included neurologists and nurses specialized in acute stroke therapy. All neurologists and nurses worked six days a week. During nighttime and weekends, there were at least one neurologist and one nurse on duty.

Admission time was defined as the duration between the identification of first symptoms and arrival at the hospital's emergency room. If the study hospital was not the primary hospital for the diagnosis, the patient should not have been referred from more than one hospital to be eligible for participation in this study. The time of onset of symptoms was obtained from the patient, or any available witnesses, or extracted from the medical records. Admission delay was defined as admission time >6 hours following the onset of symptoms.

All patients were diagnosed with ischemic stroke confirmed by computed tomography (CT) or magnetic resonance imaging (MRI),

based on the fourth Chinese National Conference's recommendations on the diagnosis of cerebrovascular diseases [7]. The inclusion criteria were patients with focal neurological symptoms, age >18 years, consciousness and no serious cognitive impairment, and no serious complications at the time of diagnosis. Exclusion criteria included hemorrhagic stroke, a CT or MRI investigation revealing the primary cause of the symptoms as a transient ischemic attack, lack of informed consent, or lack of information on the time of onset of symptoms. There were no hospital deaths in the study cohort.

The study was explained to the patient and/or his/her legal guardian by a designated research staff. A standardized, structured questionnaire survey was implemented within 48 hours after admission. The questionnaire documented the patient's demographic information (age, sex, marital status, education, living pattern, type of employment), place of residence, type of medical insurance, time since stroke onset, location of stroke onset, whether the patient was referred from a community hospital, whether the patient worried about high medical treatment fees. Patient's stroke-related knowledge was assessed using a structured questionnaire focused on basic knowledge of stroke, stroke-related risk factors and stroke prevention measures [8]. The questionnaire included a total of 23 questions; a correct answer to each item received a score of 1. Stroke-related risk factor scores were assessed by blood pressure, blood cholesterol, diabetes, smoking, heart disease, overweight, physical exercise and family history. The presence of each risk factor received a score of 1, and so on. Stroke severity was assessed on admission using the National Institutes of Health Stroke Scale (NIHSS) (range 0 to 42; normal score=0) [9]. Education was classified as low (middle school and lower), medium (high school or college) and high (university bachelor or higher degree). Living patterns included living with children, living with a spouse, or living alone.

Statistical Analysis

Mean and SD are presented for continuous variables, number and proportion are presented for categorical variables. Chi-square tests were used to test for differences in the proportion of admission delay by each risk factor. Multivariate logistic regression was applied to identify significant risk factors of admission delay adjusting for other co-variables. The differences were considered to be statistically significant when $P < 0.05$. With a sample size of 273 and a baseline admission delay rate of about 50% in the literature, at an alpha error of 5%, assuming about 1/3 or more of study subjects were exposed to a risk factor of interest, the study has a power of 97% to detect a risk factor with a risk ratio of 1.5 or greater in association with the outcome (admission delay).

Results

All enrolled ischemic stroke patients (n=273) were administered a face-to-face interview within 48 hours after admission. The mean age was 62 years (SD=12). About 44.3% of patients were female, and 30.8% came from rural areas (Table 1). About 30.4% of patients had New Rural Cooperative Medical System (NRCMS) insurance, 59% had Urban Employees Basic Medical Insurance System (UEBMIS) insurance, and 6.6% had Urban Residents Basic Medical Insurance System (URBMIS) or other insurance.

Characteristic	n	%
Sex		
Male	152	55.7
Female	121	44.3
Residence		
Urban	189	69.2
Rural	84	30.8
Marital status		
Unmarried	3	1.1
Married	228	83.5
Divorced or widowed	42	15.4
Education		
Low (<high school)	188	68.9
Medium (high school or college)	75	27.5
High (University)	10	3.7
Living pattern		
With children	114	41.8
With spouse	137	50.2
Alone	22	8.1
Type of employment		
Manual workers	93	34.1
Non-manual workers	180	65.9
Type of medical insurance		
None	11	4.0
NRCMS	83	30.4
UEBMIS	161	59.0
URBMIS/other insurance	18	6.6

NRCMS= New Rural Cooperative Medical System; UEBMIS =Employees Basic Medical Insurance System; URBMIS= Urban Residents Basic Medical Insurance System

Table 1: Characteristics of ischemic stroke patients (n=273) admitted to an urban tertiary care center in Kaifeng city, China

Mean baseline NIHSS stroke severity score was 10.5 (SD 4.0), and the median was 9. About 11.7% of patients had a baseline NIHSS score > 15. Among the stroke-related risk factors, the prevalence rate was 59% for hypertension, 38.8% for hyperlipidemia, 26% for

diabetes , 30.4% for tobacco consumption, 28.6% for cardiopathy, 10.6% for obesity, 33% for family history of stroke, and 65% for no regular physical exercise.

Among the 273 study patients, 98 (35.9%) arrived at the study hospital within 4.5 hours, 110 (40.3%) within 6 hours, and 163 (59.7%) patients had admission delay (>6 hours). When the first symptoms of stroke occurred, 216 (79.1%) patients were at home, 40 (14.7%) were performing outdoor activities, 14(5.1%) were working. At the onset of stroke, 128 (46.9%) patients had limb weakness or were unable to flex limbs, 116 (42.5%) had headache or dizziness, 41 (15%) had limb numbness, 34 (12.5%) had wry mouth or drooling. Most (79.1%) patients had a bystander at the onset of stroke, but only 27.3% of bystanders recognized the symptoms of stroke.

Bivariate analyses revealed that the factors significantly (P<0.05) influencing admission delay were patient's place of residence, education, type of employment, type of medical insurance, time of onset, whether the patient was afraid of high costs of treatment, whether the patient was referred from a community hospital, and the patient's stroke-related knowledge score (Table 2).

Factor	Admission delay (>6 hours)		P*
	No	Yes	
Residence			< 0.001
Urban	89 (47.1)	100 (52.9)	
Rural	21 (25.0)	63 (75.0)	
Education			0.02
Low	65 (34.6)	123 (65.4)	
Medium	40 (53.3)	35 (46.7)	
High	5 (50.0)	5 (50.0)	
Living pattern			0.093
Living with children	54 (47.4)	60 (52.6)	
Living with spouse	50 (36.5)	87 (63.5)	
Living alone	6 (27.3)	16 (72.7)	
Type of employment			<0.001
Manual workers	25 (26.9)	68 (73.1)	
Non-manual workers	85 (47.2)	95 (52.8)	
Type of medical insurance			0.03
None	4 (36.4)	7 (63.6)	
NRCMS	22 (26.5)	61 (73.5)	
UEBMIS	77 (47.8)	84 (52.2)	
URBMIS /other insurance	7 (38.9)	11 (61.1)	
Onset time			0.007
0:00~5:59	26 (57.8)	19 (42.2)	
6:00~11:59	42 (30.9)	94 (60.1)	
12:00~17:59	25 (43.9)	32 (56.1)	
18:00~23:59	17 (48.6)	18 (51.4)	
Afraid of high medical fees			< 0.001
Yes	15 (22.1)	53 (77.9)	
No	95 (46.3)	110 (53.7)	
Referral from a community hospital			< 0.001
Yes	2 (3.5)	55 (96.5)	
No	108 (50.0)	108 (50.0)	
Stroke-related risk factors score	3.0±1.4	2.7±1.4	0.14
Patient's stroke knowledge score	14.1±5.3	11.3±5.9	< 0.001
NIHSS score	10.5±4.3	10.5±3.9	0.97

Data presented are n (%) or mean±SD.

P* values in t tests for differences in means or Chi-square tests for differences in proportions, comparing patients with versus without admission delay.

NIHSS=National Institutes of Health Stroke Scale.

Table 2: Risk factors of admission delay in ischemic stroke patients (n=273) from bivariate analyses

Among the 57 patients referred from a community hospital without a stroke care center, 28 (49.1%) were referred from private clinics, 20 (35.1%) from country hospitals, and 7 (12.3%) from township hospitals. 37 (64.9%) patients had ineffective treatment before arrival at the study hospital, 15 (26.3%) had mild remission, and 5 (8.8%) were in critical condition. 32 (56.1%) patients were referred to the study hospital because of the availability of advanced equipment, diagnosis and treatment techniques, 22 (38.6%) because of the previous attending doctor's recommendation (Table 3).

Characteristic	n	%
Residence		
Urban	20	35.1
Sex		
Male	32	56.1
Female	25	43.9
Treatment effect before the referral		
Ineffective	37	64.9
Some remission	15	26.3
Critical condition	5	8.8
Reasons for referral		
Advanced equipment	32	56.1
Doctor's suggestion	22	38.6
High reimbursement ratio	3	5.3
Admission time		
≤6 hours	2	3.5
> 6 hours	55	96.5

Table 3: Characteristics of referral patients (n=57) in the study cohort

Concerning transportation to arrive at the study hospital, only 13 (4.8%) patients used Emergency Medical Service (EMS/Ambulance), 125 (45.8%) patients arrived by personal car, 63 (23.1%) by taxi, 43 (15.8%) by bus, 16 (5.9%) by electromobile and 13 (4.8%) patients by other means of transportation.

Significant contributors to admission delay in ischemic stroke from multivariate logistic regression models are presented in Table 4. As expected, the odds of admission delay for patients who were referred from a community hospital was much greater (adjusted OR=22.8) than that of patients who arrived directly at the study hospital after onset of stroke. The higher the patient's stroke-related knowledge score, the lower the risk of admission delay (adjusted OR=0.9). The odds of admission delay was more than doubled (adjusted OR=2.2) for patients who lived with a spouse compared to those who lived with their children.

Factor	Odds Ratio	95% CI	P
Referral from a community hospital			
No	referent		
Yes	22.79	5.21-103.72	<0.001
Stroke knowledge score	0.89	0.84-0.95	0.001
Living pattern			
With children	referent		
With a spouse	2.16	1.04-4.49	0.04
Alone	2.51	0.63-10.02	0.19

Table 4: Factors remained significantly associated with admission delay (>6 hours) in ischemic stroke patients from multivariate logistic regression models

Discussion

Main findings

Admission delays are common, and certain modifiable risk factors (stroke knowledge, living pattern, and timely transfer to a tertiary care center) may be targeted to improve outcomes for ischemic stroke patients in an urban tertiary care setting in China. Caution is warranted in data interpretation since the findings were based on data from a single urban tertiary care center, and need to be confirmed in multi-center studies.

Comparisons with previous findings

The percentage of admission delay >6 hours was high (59.7%) for ischemic heart stroke patients in the study cohort in an urban tertiary care setting in China as compared to those reported in urban tertiary care centers in developed countries. For example, the percentage of admission delay >6 hours was about 25% among patients admitted to a tertiary care stroke unit in French [10] or Switzerland [11], and was 39% in a study from New Jersey, United States [12].

Our results suggest the need for setting up stroke prevention and treatment centers in township/community hospitals to reduce the need for patient transfers/referrals – a major risk factor for admission delay. About 3/4 of patients with admission delay were from rural areas. Most patients from rural areas had low education and little stroke-related knowledge, and lived far from the study hospital (about 20-50 km) which could have contributed to their high risk of admission delay.

Several studies have found that the use of emergency medical service (EMS) as the means of transportation to a hospital can provide standard and efficient first-aid outside the hospital, as well as shorten admission time, as compared to patients who failed to use EMS [13-17]. In this study, only 4.8% of patients used EMS. We speculated that most patients/family members did not have the experience in using EMS, or might not sure how to use EMS. Greater publicity of EMS is warranted to promote its use at times of need in China.

Patients referred from a community hospital were far more likely (22.8 times) to have an admission delay. Physicians in primary care hospitals could be better trained to more timely recognize the symptoms of stroke to initiate more timely transfer of patients to tertiary care centers. It has been reported that distance between the site of stroke onset and the admission hospital is important: if the distance was >5 km, the risk of admission delay would increase 1.9 times [18]. A better organized stroke care delivery system could be helpful to reduce the frequency of admission delays for improved clinical outcomes [19]. Strengthened emergency care capacity in primary care hospitals, especially in rural areas, may reduce the need for transfer referrals and improve outcomes in ischemic stroke patients.

A study in a French stroke unit showed that living alone was a contributing factor to admission delay [9], while we only observed a non-significant risk elevation (adjusted OR=2.5, p=0.19) due to the small number of patients living alone (n=22) in the study cohort. In China, old people traditionally live with family members, and very few individuals live alone. This is especially so in the city of Kaifeng with a history of several thousand years. Respecting the olds is a traditional Chinese virtue. We found that only 8.1% patients were living alone at the time of stroke onset. However, we found that admission delay more than doubled for patients living with a spouse than those living with children, suggesting that children are better than a spouse at times of medical emergency. Living with children is recommended, especially for elderly patients with cerebrovascular or cardiovascular risk to avoid admission delay at times of medical emergency.

Some previous studies showed that admission delay was not associated with patient's stroke knowledge [10,20,21]. In contrast, we found that patient's stroke knowledge was independently associated with admission delay, a finding consistent with studies in Korea and United Kingdom [22,23]. This indicates a need to improve stroke-related knowledge through public health promotion campaigns which may play an important role in reducing the rate of admission delay. Poor knowledge about stroke may delay efforts in timely seeking emergency care after stroke [24]. Timely initiation of thrombolytic therapy is important not only for decreasing mortality, but also for functional outcomes and quality of life in ischemic stroke patients [25,26].

Most studies found that NIHSS score was related to admission delay [10,11,22]. However, this study found no such association. The reasons are unclear, and deserve further investigations in urban tertiary care settings in China.

Limitations

The study is observational in nature, and thus causality could not be clearly established. The study was based on patients from a single urban tertiary care center in China. The findings are preliminary, and large multi-center studies in China are needed to confirm these findings.

Conclusions

The major risk factors contributing to admission delays among ischemic stroke patients in an urban tertiary care setting in China included referral from a community hospital, patient's poor stroke-related knowledge, and living with a spouse. These findings suggest the needs for a more efficient emergency care delivery system for more timely transfer of stroke patients, setting up stroke care centers in community hospitals, more public heath campaigns on stroke knowledge, and advocating for elderly patients with cerebrovascular risk living with their children in China.

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Conflicts of interest

None of the authors have any conflict of interest to declare.

References

1. Sarti C, Stegmayr B, Tolonen H, Mähönen M, Tuomilehto J, et al. (2003) Are changes in mortality from stroke caused by changes in stroke event rates or case fatality? Results from the WHO MONICA Project. Stroke 34: 1833-1840.

2. Chen Z (2008) The third national mortality retrospective sampling survey report of the People's Repubic of China Ministry of health. Beijing Union Medical College Press 1: 14-17.

3. Wardlaw JM, Murray V, Berge E, Del Zoppo GJ (2009) Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev : CD000213.

4. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, et al. (2008) Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 359: 1317-1329.

5. Wang S, Niu S, Wang Y, Zhang G (2002) [Evaluation of the factors leading to delay from stroke onset to arrival at hospital]. Zhonghua Nei Ke Za Zhi 41: 728-731.

6. Du P, Yang ZL (2006) Admission and prognosis of 144 patients with acute ischemic stroke from rural in China. Clin Med 26: 60-61.

7. The neuroscience society (1996) The neuro erve surgery to learn - All kinds of cerebrovascular disease diagnosis points. Chin J Neurology 29: 379.

8. Yuan DC, Fu XX, Ma BS (2003) A survey of stroke prevention and treatment knowledge in stroke patients and relatives. Chin Chronic Disease Prev & Control 17:211-213.

9. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, et al. (1989) Measurements of acute cerebral infarction: a clinical examination scale. Stroke 20: 864-870.

10. Derex L, Adeleine P, Nighoghossian N, Honnorat J, Trouillas P (2002) Factors influencing early admission in a French stroke unit. Stroke 33: 153-159.

11. Agyeman O, Nedeltchev K, Arnold M, Fischer U, Remonda L, et al. (2006) Time to admission in acute ischemic stroke and transient ischemic attack. Stroke 37: 963-966.

12. Lacy CR, Suh DC, Bueno M, Kostis JB (2001) Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology (S.T.R.O.K.E.). Stroke 32: 63-69.

13. Kuster GW, Bueno Alves M, Cendoroglo Neto M, Silva GS (2013) Determinants of emergency medical services use in a Brazilian population with acute ischemic stroke. J Stroke Cerebrovasc Dis 22: 244-249.

14. Inatomi Y, Yonehara T, Hashimoto Y, Hirano T, Uchino M (2008) Pre-hospital delay in the use of intravenous rt-PA for acute ischemic stroke in Japan. J Neurol Sci 270: 127-132.

15. Maestroni A, Mandelli C, Manganaro D, Zecca B, Rossi P, et al. (2008) Factors influencing delay in presentation for acute stroke in an emergency department in Milan, Italy. Emerg Med J 25: 340-345.

16. Tan TY, Chang KC, Liou CW (2002) Factors delaying hospital arrival after acute stroke in southern Taiwan. Chang Gung Med J 25: 458-463.

17. Nedeltchev K, Arnold M, Brekenfeld C, Isenegger J, Remonda L, et al. (2003) Pre- and in-hospital delays from stroke onset to intra-arterial thrombolysis. Stroke 34: 1230-1234.

18. Fu Y, Fan D, Zhang Y, Liu X, Zhang X, et al. (2003) [Study of delaying hospital admission after acute stroke]. Beijing Da Xue Xue Bao 35: 299-302.

19. Kapral MK, Fang J, Silver FL, Hall R, Stamplecoski M, et al. (2013) Effect of a provincial system of stroke care delivery on stroke care and outcomes. CMAJ 185: E483-491.

20. Wester P, Rådberg J, Lundgren B, Peltonen M (1999) Factors associated with delayed admission to hospital and in-hospital delays in acute stroke and TIA: a prospective, multicenter study.Seek- Medical-Attention-in-Time Study Group. Stroke 30: 40-48.

21. Williams LS, Bruno A, Rouch D, Marriott DJ (1997) Stroke patients' knowledge of stroke. Influence on time to presentation. Stroke 28: 912-915.

22. Kim YS, Park SS, Bae HJ, Cho AH, Cho YJ, et al. (2011) Stroke awareness decreases prehospital delay after acute ischemic stroke in Korea. BMC Neurol 11: 2.

23. Mackintosh JE, Murtagh MJ, Rodgers H, Thomson RG, Ford GA, et al. (2012) Why people do, or do not, immediately contact emergency medical services following the onset of acute stroke: qualitative interview study. PLoS One 7: e46124.

24. Abilleira S, Lucente G, Ribera A, Permanyer-Miralda G, Gallofré M (2011) Patient-related features associated with a delay in seeking care after stroke. Eur J Neurol 18: 850-856.

25. de Weerd L, Luijckx GJ, Groenier KH, van der Meer K (2012) Quality of life of elderly ischaemic stroke patients one year after thrombolytic therapy. A comparison between patients with and without thrombolytic therapy. BMC Neurol 12:61.

26. Silvestrelli G, Parnetti L, Paciaroni M, Caso V, Corea F, et al.
(2006) Early admission to stroke unit influences clinical outcome.
Eur J Neurol 13: 250-255.