Original Article

Prehospital Identification of Stroke Subtypes in Chinese Rural Areas

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Abstract

Background: Differentiating intracerebral hemorrhage (ICH) from cerebral infarction as early as possible is vital for the timely initiation of different treatments. This study developed an applicable model for the ambulance system to differentiate stroke subtypes.
Methods: From 26,163 patients initially screened over 4 years, this study comprised 1989 consecutive patients with potential first-ever acute stroke with sudden onset of the focal neurological deficit, conscious or not, and given ambulance transport for admission to two county hospitals in Yutian County of Hebei Province. All the patients underwent cranial computed tomography (CT) or magnetic resonance imaging to confirm the final diagnosis based on stroke criteria. Correlation with stroke subtype clinical features was calculated and Bayes' discriminant model was applied to discriminate stroke subtypes.
Results: Among the 1989 patients, 797, 689, 109, and 394 received diagnoses of cerebral infarction, ICH, subarachnoid hemorrhage, and other forms of nonstroke, respectively. A history of atrial fibrillation, vomiting, and diabetes mellitus were associated with cerebral infarction, while vomiting, systolic blood pressure ≥180 mmHg, and age <65 years were more typical of ICH. For noncomatose stroke patients, Bayes' discriminant model for stroke subtype yielded a combination of multiple items that provided 72.3% agreement in the test model and 79.3% in the validation model; for comatose patients, corresponding agreement rates were 75.4% and 73.5%.
Conclusions: The model herein presented, with multiple parameters, can predict stroke subtypes with acceptable sensitivity and specificity before CT scanning, either in alert or comatose patients. This may facilitate prehospital management for patients with stroke.

Key words: Bayes' Discriminant Model; Prehospital Identification; Stroke Subtypes

INTRODUCTION

There is much evidence that the clinical outcome of ischemic stroke is significantly benefited by early recanalization of the thrombotic cerebral artery, while in cerebral hemorrhage blood pressure should be lowered rapidly.[1,2] Thus, it is crucial that these stroke subtypes are differentiated as soon as possible.

Computed tomography (CT) in the ambulance enables a significant reduction in the time to differential diagnosis,[3] while noncontrast CT scan is the gold standard for distinguishing stroke subtypes,[4] its use in rural areas is limited. In the absence of a CT scan, weighted clinical score systems such as the Allen stroke score (Guy Hospital score)[5] Siriraj stroke score (SSS)[6] and the Besson score[7] may improve the rapid diagnosis of stroke subtypes with excellent predictive value. Kolapo *et al*.[6] reported the excellent predictive value of the SSS in Nigerians in Africa. However, according to a study by Badam *et al*.,[8] the accuracy of the SSS and Guy's Hospital stroke scores was poor for distinguishing hemorrhagic from ischemic stroke for stroke patients in a rural, tertiary care hospital in India. In addition, a systematic meta-analysis by Mwita *et al*.[9] questioned the accuracy of clinical stroke scores for distinguishing stroke subtypes in resource-poor settings. To the best of our knowledge, none

Access this article online	
Quick Response Code:	**Website:** www.cmj.org
	DOI: 10.4103/0366-6999.180521

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Received: 01-12-2015 **Edited by:** Li-Shao Guo
How to cite this article: Jin HQ, Wang JC, Sun YA, Lyu P, Cui W, Liu YY, Zhen ZG, Huang YN. Prehospital Identification of Stroke Subtypes in Chinese Rural Areas. Chin Med J 2016;129:1041-6.

of these score systems have been validated in Chinese stroke patients.

China is a multiethnic nation spanning a wide geographic area, and the incidence rate of hemorrhagic stroke is relatively high, with an expanding economy and increasingly aging population. Thus, China faces significant challenges in stroke prevention and treatment. It has been estimated that only 1–3% of patients with ischemic stroke receive thrombolytic therapy,[10] due to prehospital and in-hospital delays, and among patients who did receive proper therapy, outcomes were closely associated with treatment time.[11] The ability to diagnose stroke as well as its subtypes in the field would be very helpful in routing patients to the appropriate health facility, and to prenotify the receiving hospital.

With a sensitivity of 91% and specificity of 97%, the Los Angeles Prehospital Stroke Screen (LAPSS) can efficiently aid prehospital personnel to identify acute stroke patients.[12] However, the LAPSS cannot differentiate stroke subtypes, and its application is restricted to nontrauma and noncomatose patients with stroke symptoms, while coma is very common in stroke, especially in patients with cardiac embolism or hemorrhagic stroke.[13,14]

The present study evaluated the predictive value of stroke symptoms in the early stages for differentiating patients with cerebral ischemia (CI) or intracerebral hemorrhage (ICH), regardless of the patient's state of consciousness, in rural areas of Northern China.

METHODS

Ethics statement

The Ethics Committee of Yutan County Hospital, Tangshan, China, approved the trial protocol and the participant information documents, in compliance with the *Declaration of Helsinki*. All patients or their legal representatives provided signed informed consent.

Hospital setting

The study was designed by the Department of Neurology, Peking University First Hospital. The study was conducted from 2008 to 2012, in Yutian County Hospital and Yutian Traditional Chinese Medicine Hospital in a rural area of Yutian County, Hebei Province, China. Yutian County covers an area of 1165 km^2 with a population of 660,000 and population density of 567 persons/km^2.

In this region, the two hospitals were uniquely equipped with an ambulance system. The ambulances were staffed with paramedics, nurses, and doctors. The phone number "120" was available to the populace in the region to summon emergency aid. The emergency personnel of these two hospitals was available 24 h/day and 7 days/week, to arrive on the scene by ambulance as quickly as possible upon receipt of the 120 alarm, from suspected stroke patients or any other emergency cases.

Before commencement of the study, all emergency practitioners with experience of emergency aid for at least 3 years were systematically trained regarding acute stroke identification through repeated counseling and examination and were given study data sheets.

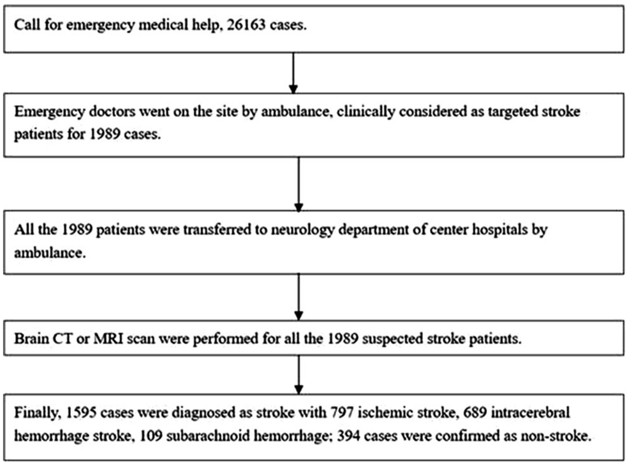
Subjects

The patient subjects targeted for this study were those for whom 120 was called for emergency aid. In addition, these patients were transported to the above two hospitals in Yutian County, including comatose or conscious patients with first-ever rapid onset of local or global neurological deficient signs of facial palsy, paralysis or anesthesia of one limb or more limbs, and difficulty of speech or critical headache.

Criteria for study exclusion were: <16 years old; with symptoms other than stroke or stroke-like syndromes; transferred to other hospitals; with repeat or recurrent stroke; or refusal to disclose medical information. For cases of patients with onsite coma, the symptoms were recorded according to the description of relatives.

Upon arrival at the patient's location, emergency personnel conducted a basic health assessment, including vital physical signs, blood pressure, capillary finger-prick blood glucose, and electrocardiogram (ECG). Other documented information included basic demographics, vomiting, consciousness, auscultation of arrhythmias, and medical history of atrial fibrillation (AF), hypertension (HTN), and Type 1 or Type 2 diabetes mellitus (DM). A quick assessment of the LAPSS scale (<3 min) for nontrauma, noncomatose patients was also completed. For comatose patients, only the basic demographics, ECG, and physical examination, including the finger-prick test of the glycemic level, were performed. The patients were then sent to either of the two hospitals by ambulance, regardless of the suspected subtype of stroke.

Cranial CT or magnetic resonance imaging was performed in all target patients at the hospitals. The final diagnosis was determined according to the clinical manifestation and the imaging results, upon discharge from the hospital. The methodology of the study is summarized by a flowchart in Figure 1.



Call for emergency medical help, 26163 cases.

Emergency doctors went on the site by ambulance, clinically considered as targeted stroke patients for 1989 cases.

All the 1989 patients were transferred to neurology department of center hospitals by ambulance.

Brain CT or MRI scan were performed for all the 1989 suspected stroke patients.

Finally, 1595 cases were diagnosed as stroke with 797 ischemic stroke, 689 intracerebral hemorrhage stroke, 109 subarachnoid hemorrhage; 394 cases were confirmed as non-stroke.

Figure 1: Flowchart of the study.

Explanatory variables

The time interval from receiving the 120 call to arrival of the ambulance was defined as the ambulance delay time. HTN was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, or current antihypertensive treatment. DM included all patients with a confirmed diagnosis of Type 1 or Type 2 DM. Coma was considered a Glasgow Coma Scale ≤8. AF was defined as having a history of AF or AF on ECG. Arrhythmia was considered an abnormal ECG wave, except AF. Confirmed stroke was defined as any acute focal neurological deficit due to a vascular event with imaging confirmed CI, ICH stroke, or subarachnoid hemorrhage.

Data collection

All the completed study datasheets were collected by the Department of Neurology, Peking University First Hospital, and the overall efficacy study sheets were monitored in a blinded manner by two neurologists to correct possible documentation errors before the analysis. For the target patients, the above two blinded neurologists reviewed the emergency department records and the neuroimaging documents to validate the final diagnosis.

Statistical analysis

Data analyses were performed using SPSS 13.0 (SPSS Corporation, USA) and SAS software 9.1 (SAS Corporation, USA) (the USA, both). Patients with acute stroke were grouped as CI or ICH. The patients with the transient ischemic attack were categorized as CI. Subarachnoid hemorrhage was not included in the hemorrhagic group, due to differences in clinical manifestation and etiology and was thus excluded from this analysis.

The Chi-squared test was applied first to evaluate the significance of associations between each of the symptom parameters and the stroke subtypes. A multivariate logistic regression analysis was performed to identify predictors of stroke subtype. Explanatory variables were selected using liberal criteria ($P < 0.20$) for inclusion in the multivariate regression model.

A subset of 85% of cases was drawn out randomly to build a Bayes' discriminant model with the significant variables from the multivariate regression, and the remaining 15% of cases were used to validate the predictive model. For all the statistical analyses, significance was accepted as $P < 0.05$.

RESULTS

From the year 2008 to 2012, 26, 163 patients were transported to the 2 study hospitals by ambulance in response to an emergency call. During this time, 1989 patients (1093 men; mean age 66 years) met the inclusion criteria for the study and were considered target patients by ambulance doctors upon initial suspicion of a stroke at the site of symptom occurrence [Table 1]. The median ambulance delay time was 39.5 min (interquartile range: 27.0–54.0 min). All the patients were hospitalized for further examination.

Among those with suspected stroke [Table 1] the discharge diagnosis was CI in 797 (40.1%), ICH in 689 (34.6%), subarachnoid hemorrhage in 109 (5.5%), and nonstroke in 394 (19.8%). The univariate analysis showed that gender and heart rate (HR, more or less than 100 beats/min) were not statistical significant discriminators between ischemic stroke and hemorrhagic stroke. Parameters that were significantly associated with CI were age ≥65 years, history of DM, history of AF, and arrhythmia. Parameters that were significantly associated with ICH were vomiting, SBP ≥180 mmHg, and DBP ≥100 mmHg.

According to the univariate analyses for patients with different stroke subtypes and stratified by state of consciousness [Table 2], in the noncomatose group the following seven variables were significantly discriminatory between infarction or hemorrhage: age ≥65 years, history of DM, history of AF, arrhythmia, vomiting, SBP ≥180 mmHg, and DBP ≥100 mmHg. In the comatose group, the following nine variables were significantly discriminatory: age, history of HTN, history of DM, history of AF, arrhythmia, vomiting, SBP ≥180 mmHg, DBP ≥100 mmHg, and HR >100 beats/min.

In the multivariate analysis model, however, arrhythmia was not statistically significant in the noncomatose stroke group, and HR was not statistically significant in the comatose stroke group [Tables 3 and 4]. Because of the correlation effect of SBP and DBP, only SBP was adopted in the Bayes' discriminant model. Consequently, in the noncomatose stroke group the following five variables of statistical significance were incorporated in the final Bayes' discriminant model: history of DM, history of AF, vomiting, and SBP. Similarly, in the comatose stroke group, the following variables were incorporated in the final Bayes' discriminant model: age, history of DM, history of AF, vomiting, and history of HTN.

Given assumption of individual's symptom values of $S = \{S1j, S2j, \ldots, Sij\}$, the probability ($P$) for CI is $P(S \mid \mathrm{CI}) = P(S1j \mid \mathrm{CI}) \times P(S2j \mid \mathrm{CI}) \times \ldots \times P(S5j \mid \mathrm{CI})$. The probability for ICH is $P(S \mid \mathrm{ICH}) = P(S1j \mid \mathrm{ICH}) \times P(S2j \mid \mathrm{ICH}) \times \ldots \times P(S5j \mid \mathrm{ICH})$. According to the formula of Bayes' conditional probability, the posterior probability for CI is:

$$P(\mathrm{CI} \mid S) = \frac{P(\mathrm{CI})P(S \mid \mathrm{CI})}{P(\mathrm{CI})P(S \mid \mathrm{CI}) + P(\mathrm{ICH})P(S \mid \mathrm{ICH})}.$$

The posterior probability for ICH is:

$$P(\mathrm{ICH} \mid S) = \frac{P(\mathrm{ICH})P(S \mid \mathrm{ICH})}{P(\mathrm{CI})P(S \mid \mathrm{CI}) + P(\mathrm{ICH})P(S \mid \mathrm{ICH})}.$$

According to the actual posterior probability of CI or ICH, an absolute binary answer of CI or ICH was made.

For noncomatose stroke patients, the conditional probability of the parameters history of AF, vomiting, DM, SBP (more than 180 mmHg or not), and age (more than 65 years or not) was multiplied to obtain the actual posterior probability of CI or ICH, as appropriate. For comatose stroke patients, the conditional probability of the parameters history of AF,

Table 1: Baseline demographics and clinical characteristics by stroke subtype (N = 1989), n (%)

Variables	Nonstroke (n = 394)	CI (n =797)	ICH (n = 689)	SAH (n =109)	χ^2	P
Male	207 (52.5)	452 (56.7)	385 (55.9)	49 (45.0)	6.6	0.09
Age ≥65 years	253 (64.2)	525 (65.9)	317 (46.0)	51 (46.8)	72.5	<0.001
History of HTN	235 (59.6)	589 (73.9)	576 (83.6)	74 (67.9)	77.5	<0.001
History of DM	45 (11.4)	114 (14.3)	29 (4.2)	7 (6.4)	45.2	<0.001
History of AF	15 (3.8)	99 (12.4)	8 (1.2)	3 (2.8)	88.1	<0.001
Coma	106 (26.9)	197 (24.7)	366 (53.1)	52 (47.7)	151.8	<0.001
Arrhythmia	46 (11.7)	134 (16.8)	64 (9.3)	19 (17.4)	20.8	<0.001
Vomiting	195 (49.5)	243 (30.5)	381 (55.3)	77 (70.6)	129.5	<0.001
SBP ≥180 mmHg	126 (32.0)	250 (31.4)	397 (57.6)	54 (49.5)	125.0	<0.001
DBP ≥100 mmHg	191 (48.5)	424 (53.2)	540 (78.4)	80 (73.4)	141.3	<0.001
HR >100 beats/min	40 (10.2)	66 (8.3)	40 (5.8)	6 (5.5)	8.0	0.05
LAPSS screening	288 (73.1)	600 (75.3)	323 (46.9)	57 (52.3)	151.8	<0.001

CI: Cerebral ischemia; ICH: Intracerebral hemorrhage; SAH: Subarachnoid hemorrhage; HTN: Hypertension; DM: Diabetes mellitus; AF: Atrial fibrillation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; LAPSS: Los Angeles Prehospital Stroke Screen.

Table 2: Univariate analysis for patients with different stroke subtypes by state of consciousness, n (%)

Variables	Noncomatose				Comatose			
	CI (n = 513)	ICH (n = 276)	χ^2	P	CI (n = 169)	ICH (n = 311)	χ^2	P
Male	302 (58.9)	165 (59.8)	0.1	0.80	85 (50.3)	162 (52.1)	0.1	0.71
Age ≥65 years	328 (63.9)	124 (44.9)	26.5	<0.001	118 (69.8)	146 (47.0)	23.2	<0.001
History of HTN	394 (76.8)	225 (81.5)	2.4	0.12	108 (63.9)	268 (86.2)	32.0	<0.001
History of DM	64 (12.5)	12 (4.3)	13.6	<0.001	28 (16.6)	14 (4.5)	20.0	<0.001
History of AF	57 (11.1)	3 (1.1)	25.7	<0.001	28 (16.6)	3 (1.0)	44.1	<0.001
Arrhythmia	69 (13.5)	17 (6.2)	9.8	<0.01	45 (26.6)	35 (11.3)	18.6	<0.001
Vomiting	148 (28.9)	153 (55.4)	53.8	<0.001	55 (32.5)	173 (55.6)	23.4	<0.001
SBP ≥180 mmHg	158 (30.8)	151 (54.7)	43.1	<0.001	52 (30.8)	191 (61.4)	41.1	<0.001
DBP ≥100 mmHg	276 (53.8)	207 (75.0)	34.0	<0.001	92 (54.4)	254 (81.7)	40.4	<0.001
HR >100 beats/min	33 (6.4)	146 (5.1)	0.6	0.44	25 (14.8)	22 (7.1)	7.4	<0.01

CI: Cerebral ischemia; ICH: Intracerebral hemorrhage; HTN: Hypertension; DM: Diabetes mellitus; AF: Atrial fibrillation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate.

Table 3: Multivariate analysis of patients with different stroke subtypes by state of consciousness

Variables	Noncomatose*		Comatose†	
	Partial regression coefficient‡	P	Partial regression coefficient‡	P
Age ≥65 years	–0.593	<0.001	–0.643	<0.01
History of DM	–1.022	<0.001	–1.293	0.001
History of AF	–2.333	<0.01	–2.489	<0.001
Vomiting	1.126	<0.001	0.927	<0.001
SBP ≥180 mmHg	0.660	<0.001	0.769	<0.001
DBP ≥100 mmHg	0.586	<0.01	0.689	0.02
History of HTN	–	–	1.148	<0.001
Arrhythmia	–	–	–0.939	<0.01

*n = 789; †n = 480; ‡CI as the reference. HTN: Hypertension; DM: Diabetes mellitus; AF: Atrial fibrillation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; –: Not applicable.

vomiting, DM, HTN, and age (more than 65 years or not) was multiplied to obtain the actual posterior probability of CI or ICH, as appropriate.

In noncomatose patients with suspected stroke, in the training set (n = 621) the discriminant function model [Table 5; variables history of AF, vomiting, history of DM, SBP ≥180 mmHg, and age ≥65 years] had a positive predictive accuracy of 75.7% for CI, 63.3% for ICH, and 72.3% overall, with a kappa (κ) value of 0.38 (95% confidence interval [*CI*], 0.31–0.46). In the validation set (n = 106), the positive predictive accuracy for CI was 78.3%, and the positive predictive accuracy of ICH was 78.4%, with an overall predictive accuracy of 79.3% and κ value of 0.54 (95% *CI*, 0.38–0.71).

In comatose patients with suspected stroke, the discriminant function model in the training set [Table 5; variables age ≥65 years, history of DM, history of AF, history of HTN, and vomiting] resulted in a positive predictive accuracy of 78.0% for CI and 74.8% for ICH, with an overall predictive accuracy of 75.4% and a κ value of 0.40 (95% *CI*, 0.31–0.48). In the validation set, the positive predictive accuracy for CI and ICH was 68.7% and 74.6%, respectively, with an overall predictive accuracy of 73.5% and a κ value of 0.34 (95% *CI*, 0.13–0.55).

Table 4: The conditional probability for patients with different stroke subtypes by state of consciousness

Variables	Noncomatose (n =789)		Comatose (n = 480)	
	CI (n = 513)	ICH (n = 276)	CI (n = 169)	ICH (n = 311)
	P (Sij $\mid$ CI)	P (Sij $\mid$ ICH)	P (Sij $\mid$ CI)	P (Sij $\mid$ ICH)
Age (S1)				
<65 years (S11)	0.36	0.55	0.30	0.53
≥65 years (S12)	0.64	0.45	0.70	0.47
History of DM (S2)				
No (S21)	0.88	0.96	0.83	0.96
Yes (S22)	0.12	0.04	0.17	0.04
History of AF (S3)				
No (S31)	0.89	0.99	0.83	0.99
Yes (S32)	0.11	0.01	0.17	0.01
Vomiting (S4)				
No (S41)	0.71	0.45	0.67	0.44
Yes (S42)	0.29	0.55	0.33	0.56
SBP (S5)				
<180 mmHg (S51)	0.69	0.45	–	–
≥180 mmHg (S52)	0.31	0.55	–	–
History of HTN (S6)				
No (S61)	–	–	0.36	0.14
Yes (S62)	–	–	0.64	0.86

Prior probability: P (CI): 513/789 = 0.65; P (ICH): 276/789 = 0.35. CI: Cerebral ischemia; HTN: Hypertension; DM: Diabetes mellitus; AF: Atrial fibrillation; ICH: Intracerebral hemorrhage; SBP: Systolic blood pressure; –: Not applicable.

Table 5: Final discharge diagnosis of stroke subtype compared to outcome predicted by the Bayes' discriminant model in the noncomatose and comatose stroke groups (n)

Predicted by the Bayes' model	Final discharge diagnosis					
	Noncomatose			Comatose		
	CI	ICH	Total	CI	ICH	Total
Training set						
CI	305	98	403	71	20	91
ICH	80	138	218	98	291	389
Total	385	236	621	169	311	480
Validation set						
CI	54	15	69	11	5	16
ICH	8	29	37	17	50	67
Total	62	44	106	28	55	83

CI: Cerebral ischemia; ICH: Intracerebral hemorrhage.

DISCUSSION

The identification of patients with different stroke subtypes as early as possible on symptom onset may help to improve prehospital management, and direct the stroke unit team to provide further stroke therapy. This study found that certain medical parameters could help doctors accurately predict stroke subtypes, regardless of the patients' conscious state, in rural areas where modern equipment is not yet available.

The overall predictive accuracy of ~75% in this study is comparable to the study of Kolapo *et al*.,[6] involving African Nigerians, but lower than the accuracy of 90% reported in Bangkok.[15] The predictive parameters validated in our study are simple to determine and rapidly applied. A small computer program could be installed in the mobile health unit or ambulance according to the conditional probability of the related parameters, and the suspected stroke subtype may be easily determined. This is very feasible in clinical practice, especially in a primary stroke care hospital.

Many studies have shown that ICH accounts for about one-third of all stroke in China, especially in the North,[16,17] a proportion that is 3-fold higher than that of Western populations. The relative preponderance of ICH was also confirmed in our study in Yutian County, located in Northern China. The proportion of ICH among the stroke patients in the present study appeared to be even higher, in which about half the patients suffered from ICH. This may be because patients with ICH generally experience more severe symptoms and therefore were more inclined to call 120 for emergency medical aid.[18,19] In addition, as a result of the small radius of medical service for the county, the emergency response reaction was very timely.

Several studies have found strong correlations between age, history of DM, AF, vomiting, and SBP and stroke subtype.[20-22] Although the risk factors and the symptoms of CI and ICH are very similar or even overlap (e.g., HTN, family history, and smoking),[23] there are still distinctive differences in the statistical weights of these features between the two stroke subtypes. In particular, patients with primary hemorrhagic stroke are likely to be younger than those with ischemic stroke.[24] Some investigators have demonstrated that a history of hyperlipidemia, cigarette smoking, and HTN could not differentiate between these two subtypes of stroke, either because they were weakly associated with CI or were similarly associated with both CI and ICH,[25] as in the present study. Nevertheless, conditions such as the history of DM and AF were more prevalent in ischemic patients than in primary hemorrhagic stroke patients.[25]

In contrast, in the present study hemorrhagic stroke patients are more likely to experience vomiting due to increasing intracranial pressure, in accord with the findings of Arboix *et al*.[26] and Runchey and McGee.[25] Early elevation of blood pressure was found very common after ICH, and a number of observational studies have shown close associations between increasing levels of blood pressure and poor outcomes.[27,28] In the present study, SBP ≥180 mmHg in noncomatose stroke patients was more related to ICH than CI. This was similar to the SSS.[6]

This study has several limitations which deserve comment. Our results were mainly based on critical acute stroke requiring emergency medical aid, and so it was difficult to extrapolate our findings to differentiate subtypes in minor stroke patients. In addition, the sample size of 1989 participants in this study may be insufficient to characterize the entire population. Given the preponderance of ICH in the Chinese population, and that only two county-level hospitals in Northern China were involved, the generalizability and external validity of the results may be questioned to some extent. However, we contend that the consistency of the study is high because of the similarity in emergency paramedic care and can be applied to primary hospitals in the Northern region of China. Finally, due to the multiplication of conditional probabilities in Bayes' discriminant models, the discriminant effect may slightly differ due to the alteration in the sample volume.

In summary, by combining traditional parameters such as paralysis with others, we can predict the stroke subtype with good positive accuracy during very early stroke onset. This may expedite the immediate management and subsequent initiation of therapy for these patients.

Financial support and sponsorship

This study was supported by a grant from the Beijing Science Committee (No. D111107003111008).

Conflicts of interest

There are no conflicts of interest.

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