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Original Article

Analysis of the risk factors for the short-term prognosis of acute ischemic stroke

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Abstract: This study investigated the risk factors for the short-term prognosis of acute ischemic stroke to provide a scientific evidence for improving prevention and treatment. A total of 2557 cases of acute ischemic stroke were included in the study. We collected the data on demographic characteristics, life style-related risk factors, clinical feature, and other clinical characteristics for all the participants. The outcomes were assessed using the modified Rankin scale (mRs) on day 14 or at discharge. According to the mRs score, the subjects were divided into three groups, namely, the control group (0≤mRs≤2), the disability group (3≤mRs≤5), and the death group (mRs = 6). The general conditions of these three groups were compared. An mRs score of 3≤mRs≤6 belonged to the composite outcome group. Logistic regression was also applied to analyze the risk factors of short-term prognosis. Monovariant logistic regression showed that age, on-set admission, hospital stays, temperature, heart rate, stroke subtype, hypertension, hyperglycemia, history of heart disease, history of atrial fibrillation, history of cerebral stroke, drinking, count of WBC, count of mononuclear leucocyte, and rate of neutrophile granulocyte were statically significant. To further control the confounding factors, multivariant logistic regression analysis was carried out. The result showed that age, on-set admission, hospital stays, temperature, heart rate, hyperglycemia, history of atrial fibrillation, and cerebral stroke history were related to the short-term prognosis. Age, on-set admission, hospital stays, temperature, heart rate, hyperglycemia, history of atrial fibrillation, and cerebral stroke history were the risk factors of the short-term prognosis of acute ischemic stroke.

Keywords: Acute ischemic stroke, prognosis, risk factors

Introduction

Approximately 15 million stroke events occur worldwide each year; two-thirds of these events occur in people living in low-income and middle-income countries. Stroke is expected to be the second leading cause of death and disability in developed regions in 2020 [1-3]. The advent of social aging in China results in increasing incidence of acute ischemic stroke. Demographic transition resulting from adaptation of westernized lifestyle is also likely to increase the burden of stroke in developing economies [1-3].

Given the high prevalence, disability rate, and mortality of acute ischemic stroke, its prognosis has been closely focused. The ability to accurately predict the outcome in stroke victims is important for clinical practice to aid clinical treatment and care [4-7]. It can also be used to select specific management strategies and set realistic therapeutic goals to improve discharge planning as well as anticipate the need for rehabilitation and community support [4, 5, 8].

Early in-hospital mortality following stroke is usually directly related to the stroke itself, whereas factors related to hospitalization and complication of being hospitalized influence death [1-3]. The outcome of ischemic stroke is influenced by many factors. Despite the considerable number of clinical studies conducted, questions on the importance of the determinants of outcome after stroke still exist. Age and severity of stroke are well-established predictors of stroke survival [9, 10], but many stud-

ies also suggest other less-reliable prognostic factors. The most commonly reported predictors include the presence of atrial fibrillation, diabetes, hypertension, glucose level on admission, and previous ischemic cerebrovascular disease [4-6, 9-11].

Few large sample studies have been conducted in China. In most of these studies, only the survival and death groups were compared, or the effect of just a single factor on prognosis was investigated. In this paper, we retrospectively reviewed 2,557 cases of acute ischemic stroke and analyzed the related prognostic factors to provide a scientific basis for its prevention and treatment.

Materials and methods

Subjects

A total of 2,557 patients with acute ischemic stroke were enrolled in this study. These patients were hospitalized in the Neurology Department of Zhongshan Hospital affiliated to Dalian University from January 1, 2009 to December 31, 2012. They were surveyed using a questionnaire. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Affiliated Zhongshan Hospital of Dalian. Written informed consent was obtained from all participants.

Retrospective cohort study

The following diagnostic criteria were applied: 1) China guideline for cerebrovascular disease prevention and treatment; 2) diagnostic criteria of hypertension (systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg); 3) diagnostic criteria of high blood glucose [fasting plasma glucose >5.6 mmol/L (110 mg/dL)]; and 4) diagnostic criteria of dyslipidemia [serum total cholesterol (TC) ≥5.72 mmol/L; triglyceride (TG) ≥1.7 mmol/L; high-density lipoprotein cholesterol (HDL-C) <1.04 mmol/L; low-density lipoprotein cholesterol (LDL-C) ≥4.14 mmol/L]. Dyslipidemia included any abnormal elevated levels of the above lipids.

Inclusion criteria were as follows: 1) initial or recurrent acute ischemic stroke; 2) acute cerebral infarction diagnosed with computed tomography scan or magnetic resonance imaging; and 3) patients aged 40 years or older.

Exclusion criteria were as follows: 1) a definite history of cancer or autoimmune disease; 2) infections before hospitalization; 3) severe liver and kidney diseases; and 4) disability or difficulty with daily activities due to any cause before the onset of acute ischemia stroke.

Information on demographic data, lifestyle, clinical manifestation, medical history, past history, physical examination, secondary examinations, laboratory tests, imaging presentations, and so on was collected. Smoking was defined as continuous smoking of one or more cigarettes per day on average for one or more years. Drinking was defined as continuous drinking 50 g or more of alcohol weekly (beer and fruit wine should be calculated according to equivalent alcohol content) for one or more years.

Laboratory tests, including routine blood (automatic blood cell analyzer; SYSMEX-XE-2100, Japan), biochemical indices (automatic biochemistry analyzer; SIEMENS-ADVIA2400, Germany), and blood coagulation (Destiny Max, automatic coagulation analyzer; Trinity Biotech, Ireland), were detected within 24 h after the patients were admitted to the hospital.

Definition of outcomes

Upon discharge, the patients were assessed by a well-trained neurologist using the modified Rankin scale (mRs). If the hospital stay lasted for more than 14 days, the score on the 14th day was evaluated as the outcome. If the patients survived until discharge, mRs ≥3 indicated disability. If a patient died, the cause of death was determined by the Identification Committee of our hospital. The attending physician then filled out the registration form of dead cases and death certificate as well as the death-related information in the case report form. Disability or death was defined as a composite outcome.

Statistical analysis

We established the database with EpiData3.1 software. The database was verified by the professional staffs separately for two times. Inconsistent data, once noticed, would be corrected by certain personnel according to the

Table 1. Distribution of subtypes and outcomes

Subtypes	No outcome group		Disability group		Death group		Total
	Frequency	Percent (%)	Frequency	Percent (%)	Frequency	Percent (%)	
Cerebral infaction	1455	77.72	373	19.93	44	2.35	1872
Cerebral embolism	164	63.08	81	31.15	15	5.77	260
Lacunar infarction	369	86.82	47	11.06	9	2.12	425
Total	1988	77.75	501	19.59	68	2.66	2557

original questionnaire. 0≤MRs≤2 was categorized into the control group (no outcome group). 3≤MRs≤5 was categorized into the disability group. MRs = 6 was divided into the death group. 3≤MRs≤6 was divided into the composite outcome group of death and disability. We compared the general conditions of patients in the control group, the disability group and the death group. Analysis of variance was used for the continuous data of normal distribution. Non-parametric test was used for data of skewed distribution. Numeration data were compared with chi-square test. Univariate and multivariate logistic regression analyses were applied to calculate the Odds ratio (OR) and 95% Confident interval (95% CI) of different risk factors when the composite group is compared with the control group. SAS9.2 software was applied for statistical analysis. Two-tailed $P<0.05$ indicates significant difference.

Results

Distribution of subtypes and outcomes

As shown in **Table 1**, 2,557 cases of acute ischemic stroke were recruited into this study. The control group included 1,988 cases (77.75%), with a mean age of 68.82 ± 10.89 years. The disability group included 501 cases (19.59%), with a mean age of 71.27 ± 10.85 years. Sixty-eight patients (2.66%) died with a mean age of 75.38 ± 9.94 years. A total of 569 cases (22.25%) had composite outcomes.

Baseline data

Table 2 shows the baseline data of patients with different outcomes including the following information: age, gender, onset-admission time (h), hospital stay, body temperature, SBP, DBP, heart rate, blood glucose, blood urea, serum creatinine, white blood cell count, monocyte count, neutrophil ratio, thrombocytocrit, TC, TG, LDL-C, HDL-C, total bilirubin, direct bilirubin, indirect bilirubin, uric acid, fibrinogen, history of hypertension, history of diabetes mellitus, history of heart disease (non-atrial fibrillation), history of atrial fibrillation, history of stroke, smoking, and drinking.

The disability group was significantly different from the non-outcome group in mean age and fasting plasma glucose ($P<0.05$). The death and non-outcome groups were significantly different in mean age, fasting plasma glucose, SBP, heart rate, serum creatinine, and uric acid ($P<0.05$). The three groups were significantly different in the distribution of onset-admission time, hospital stay, white blood cell count, neutrophil ratio, total bilirubin, direct bilirubin, urea, and fibrinogen ($P<0.05$). The three groups were also significantly different in the constituent ratio of the history of diabetes, atrial fibrillation, stroke, smoking, and drinking ($P<0.05$).

Risk factors

Univariate analysis of the factors associated with composite outcomes (disability, death) of acute ischemic stroke: non-conditional logistic regression analysis.

The unconditional logistic analysis showed that the composite outcome of patients with acute ischemic strock was associated with the following factors: age, stroke subtype, onset-admission time, hospital stay, body temperature, heart rate, hypertension, high blood glucose, history of heart disease, history of atrial fibrillation, history of stroke, drinking, white blood cell count, monocyte count, and neutrophil ratio. The other factors were not associated with the composite outcome (**Table 3**).

Multivariate analysis of the factors associated with composite outcomes (disability, death) of acute ischemic stroke: non-conditional logistic analysis.

Table 2. The baseline data of patients with different outcomes

	No outcome group		Disability group		Death group	
Age[1]	1965	68.82 (10.89)	499	71.27 (10.85)*	68	75.38 (9.94)#
Gender (male)[3]	1965	1186 (60.36)	499	296 (59.32)	68	33 (48.53)
Onset-admission time (H)[2]	1965	48 (24,96)	499	31 (7,80)	68	19.5 (4.0, 110.5)^
Hospital stay (day)[2]	1965	11 (10,13)	499	13 (10,16)	68	10.0 (4.5, 15.5)^
Breath (n)[1]	1965	17.76 (1.06)	499	18.13 (1.99)*	68	18.82 (3.55)#
Body temperature (°C)[1]	1965	36.48 (0.26)	499	36.54 (0.41)	68	36.55 (0.42)
Sbp (mmHg)[1]	1965	150.35 (21.40)	499	151.56 (22.82)	68	160.47 (28.41)#
Dbp (mmHg)[1]	1965	87.92 (10.99)	499	87.80 (12.46)	68	89.87 (16.13)
Heart rate (n/min)[1]	1965	76.71 (7.22)	499	78.16 (11.78)	68	82.37 (15.78)#
Blood glucose (mmol/l)[1]	1965	6.50 (2.63)	499	7.31 (3.34)*	68	7.54 (3.62)#
Cr (mmol/l)[1]	1963	78.16 (41.52)	498	78.86 (45.11)	68	101.36 (96.07)#
Urea (mmol/l)[1]	1952	6.45 (4.05)	497	6.90 (5.32)	68	9.08 (9.13)#
White blood cell count (10^9/l)[2]	1965	6.40 (5.40, 7.80)	499	7.10 (5.60, 8.90)	68	8.25 (5.80, 12.90)^
Monocyte count (10^9/l)[2]	1965	0.40 (0.30, 0.52)	499	0.41 (0.30, 0.57)	68	0.40 (0.27, 0.60)
Neutrophil ratio (%)[2]	1965	61.10 (54.50, 57.95)	499	67.50 (59.50, 75.00)	68	72.20 (62.70, 86.50)^
Thrombocytocrit (fl)[2]	1965	10.60 (10.00, 11.20)	499	10.60 (10.10, 11.20)	68	10.90 (10.00, 11.85)
Tc (mmol/l)[2]	1965	4.80 (4.065, 5.64)	499	4.77 (3.99, 5.46)	68	4.80 (3.93, 5.28)
Tg (mmol/l)[2]	1965	1.42 (1.05, 2.03)	499	1.40 (1.00, 2.02)	68	1.38 (0.99, 1.89)
Ldlc (mmol/l)[2]	1965	2.85 (2.30, 3.58)	499	2,87 (2.22, 3.50)	68	2.82 (2.26, 3.38)
Hdlc (mmol/l)[2]	1965	1.13 (0.94, 1.35)	499	1.10 (0.93, 1.31)	68	1.14 (0.98, 1.38)
Tbil (umol/l)[2]	1963	15.80 (12.50, 20.00)	499	16.50 (12.80, 21.40)	68	19.50 (14.20, 24.90)^
Dbil (umol/l)[2]	1963	4.50 (2.00, 7.00)	499	4.80 (2.00, 7.60)	68	6.00 (3.70, 8.75)^
Ibil (umol/l)[2]	1963	11.0 (7.90, 15.00)	499	11.60 (7.40, 16.20)	68	12.00 (8.65, 17.45)
Blood uric acid (mmol/l)[2]	1965	318.65 (259.20, 387.05)	498	304.95 (245.00, 377.00)	68	350.60 (271.60, 420.70)^
Fb (g/l)[2]	1961	3.03 (2.61, 3.47)	499	3.17 (2.76, 3.85)	68	3.28 (2.67, 4.06)^
The history of hypertension (n, %)	1959	1442 (73.61)	499	365 (73.15)	68	45 (66.18)
The history of diabetes mellitus (n, %)	1953	616 (31.54)	496	194 (39.11)	68	27 (39.71)&
The history of heart disease (non-atrial fibrillation) (n, %)	1951	183 (9.38)	495	59 (11.92)	68	12 (17.65)&
The history of atrial fibrillation (n, %)	1950	138 (7.08)	494	67 (13.56)	68	18 (26.47)&
The history of stroke (n, %)[3]	1963	522 (26.59)	499	153 (30.66)	68	25 (36.76)&
The history of smoking (n, %)[3]	1962	254 (12.95)	498	46 (9.24)	68	14 (20.59)&
The history of drinking (n, %)[3]	1961	149 (7.60)	498	19 (3.81)	68	6 (8.83)&

Notes: Missing value is existence in the no outcome group and disability group; 1. indicate that when the variable is normal distribution of measurement data, we count the mean value and standard deviation in every group. 2. indicate that when the variable is not normal distribution of measurement data, we count the median and range interquartile in every group. 3. indicate that when the variable is enumeration data, we count the constituent ratios in every group. *The disability group was significantly different from the non-outcome group (P<0.05); #The death group was significantly different from the non-outcome group (P<0.05); ^Population distribution is different in the 3 groups, P<0.05; &Constituent ratio is different in the 3 groups, P<0.05.

Table 3. Univariate analysis of the factors associated with composite outcomes Non-conditional logistic regression analysis

Influence factor	B	S.E	Wald	*OR*	*OR* 95% *CI*	*p*
Gender (male)	0.0965	0.0968	0.9949	1.10	0.91-22	0.3185
Age (Every ten years old)	0.2578	0.0458	31.6483	1.29	1.18-42	<0.0001
Region (city)	-0.2125	0.2088	1.0356	0.81	0.54-22	0.3089
Stroke subtype						
Cerebral infaction	-	-	-	-	-	-
Cerebral embolism	0.7396	0.1407	27.6100	2.10	1.59-2.76	<0.0001
Lacunar infarct	-0.6332	0.1539	16.9197	0.53	0.39-0.72	<0.0001
Onset-admission time						
<6 h	-	-	-	-	-	-
6-24 h	-0.3444	0.1647	4.3728	0.71	0.51-0.98	0.365
>24 h	-0.7800	0.1174	44.1799	0.46	0.36-0.58	<0.0001
Hospital stay (>7)	-0.1999	0.1761	46.4284	0.301	0.21-0.43	<0.0001
Body temperature	0.6145	0.1508	16.5978	1.85	1.38-2.48	<0.0001
Heart rate (10)	0.2431	0.0537	20.5227	1.27	1.15-1.42	<0.0001
Hypertension	0.2161	0.0959	5.0757	1.24	1.03-1.50	0.0243
High blood glucose	0.5117	0.0968	27.9229	1.67	1.38-2.02	<0.0001
History of hypertension	-0.0658	0.1069	0.3790	0.936	0.76-1.16	0.5382
History of diabetes	0.0442	0.0610	0.5261	1.04	0.93-1.18	0.4683
History of heart disease	0.3324	0.1488	4.9904	1.39	1.04-1.87	0.0255
History of atrial fibrillation	0.8501	0.1472	33.3627	2.34	1.75-3.12	<0.0001
History of stroke	0.2336	0.1039	5.0553	1.26	1.03-1.55	0.0246
Smoking	-0.2264	0.1522	2.2129	0.80	0.59-1.07	0.1369
Drinking	-0.5763	0.2216	6.7626	0.562	0.36-0.87	0.0093
TC	-0.1622	0.1518	1.1409	0.85	0.63-1.14	0.2855
TG	-0.1586	0.1233	1.6550	0.85	0.67-1.09	0.1983
LDL-C	-0.0888	0.1466	0.3667	0.91	0.69-1.22	0.5448
HDL-C	0.1534	0.0972	2.4911	1.17	0.96-1.41	0.1145
White blood cell count						
≤5.45	-	-	-	-	-	
5.45-6.60	-0.1156	0.1454	0.6325	0.89	0.67-1.18	0.4264
6.60-8.10	-0.0.460	0.1426	0.1042	0.95	0.72-1.29	0.7469
≥8.10	0.7432	0.1309	32.2377	2.10	1.63-2.72	<0.0001
Continuous	0.2546	0.0435	34.2709	1.290	1.19-1.41	<0.0001
Monocyte count						
≤0.30	-	-	-	-	-	
0.30-0.40	-0.3349	0.1410	5.6405	0.71	0.54-0.94	0.0175
0.40-0.54	-0.2104	0.1344	2.4504	0.81	0.62-1.05	0.1175
≥0.54	0.0814	0.1316	0.3831	1.08	0.84-1.40	0.5359
Continuous	0.0403	0.0432	0.8714	1.04	0.96-1.13	0.3506
Neutrophil ratio						
≤55.60	-	-	-	-	-	
55.60-62.40	0.3889	0.1599	5.9184	1.47	1.08-2.02	0.0150
62.40-70.00	0.6353	0.1549	16.8175	1.89	1.39-2.56	<0.0001
≥70.00	1.4734	0.1451	103.1334	4.36	3.28-5.80	<0.0001
Continuous	0.4292	0.0457	116.1698	1.64	1.50-1.79	<0.0001
Thrombocytocrit						
≤10.0	-	-	-	-	-	

10.0-10.6	0.1362	0.1433	0.9031	1.15	0.86-1.51	0.3420
10.6-11.2	0.0624	0.1447	0.1863	1.06	0.80-1.41	0.6660
≥11.2	0.2537	0.1427	3.1611	1.29	0.97-1.70	0.0754
Continuous	0.0684	0.0448	2.3251	1.071	0.98-1.17	0.1273

Table 4. Multivariate analysis of the factors associated with composite outcomes Non-conditional logistic analysis

Influence factor	B	S.E	Wald	OR	OR 95% CI	p
Age (Every ten years old)	0.2111	0.0478	19.6662	1.24	1.13-1.36	<0.0001
Onset-admission time						
<6 h	-	-	-	-	-	-
6-24 h	-0.5878	0.1389	17.8984	0.56	0.43-0.68	<0.0001
>24 h	-0.6128	0.1167	27.5883	0.54	0.42-0.73	<0.0001
Hospital stay (>7)	-1.1112	0.1871	35.2668	0.33	0.23-0.47	<0.0001
Body temperature	0.4219	0.1592	7.0273	1.52	1.16-2.08	0.0080
Heart rate (10)	0.0134	0.0054	6.0673	1.01	1.00-1.02	0.0138
High blood glucose	0.4673	0.1005	21.6327	1.60	1.31-1.94	<0.0001
History of atrial fibrillation	0.5718	0.1577	13.1532	1.77	1.30-2.41	0.0003
History of stroke	0.2411	0.1095	4.8461	1.27	1.03-1.58	0.0277

To further control the confounding factors, we further analyzed the statistically significant risk factors in univariate logistic regression as moderators for multivariate model fitting. Seven factors, including stroke subtype, history of hypertension, atrial fibrillation and stroke, drinking, white blood cell count, monocyte count, and neutrophil ratio, were gradually removed. The adverse prognosis was associated with the following factors: age (OR = 1.24; 95% CI: 1.13-1.36), body temperature (OR = 1.52; 95% CI: 1.16-2.08), onset-admission time, hospital stay (OR = 0.33; 95% CI: 0.23-0.47), heart rate (OR = 1.01; 95% CI: 1.00-1.02), high blood glucose (OR = 1.60; 95% CI: 1.31-1.94), history of atrial fibrillation (OR = 1.77; 95% CI: 1.30-2.41), and history of stroke (OR = 1.27; 95% CI: 1.03-1.58). With each additional 10 years of age, the risk of a composite outcome increased by 24%. The increase of 1 degree Celsius in body temperature also increased the risk of outcome by 52%. Onset-admission time was a protective factor (6-24 h: <6 h, OR = 0.56, 95% CI: 0.43-0.68; ≥24 h: <6 h, OR = 0.54, 95% CI: 0.42-0.73). The length of hospital stay was also a protective factor. Prolonged hospital stay reduced the incidence of composite outcomes. The increase of heart rate by 10 beats per minute increased the risk of adverse outcomes. This risk increased by 60% in patients with high blood glucose levels than those with normal glucose levels at admission. It also increased by 77% in patients with a history of atrial fibrillation compared with that in the control group. Patients with a history of stroke exhibited 27% more risk of adverse outcomes (**Table 4**).

Discussion

In China, approximately 1.6 million stroke patients will die every year, exceeding heart disease as the second leading cause of death and adult disability [12]. China has 2.5 million new stroke cases each year and 7.5 million stroke survivors [13]. Given the high prevalence, disability rate, and mortality of acute ischemic stroke, its prognosis has been closely focused. The ability to accurately predict the outcome in stroke victims is important for selecting specific management strategies and setting realistic therapeutic goals; it can also be used to improve discharge planning and anticipate the need for rehabilitation and community support [4, 5, 8].

Few studies have investigated the prognosis of stroke. In most of these studies, only the survival and death groups were compared, or the effect of just a single factor on prognosis was investigated. In the present study, we defined disability and death as composite outcomes

and compared the risk factors for composite outcomes with those of the control group. We performed multivariate analysis to achieve more comprehensive results. In univariate non-conditional logistic analysis, a number of factors (age, stroke subtype, onset-admission time, hospital stay, body temperature, heart rate, blood pressure, high blood glucose, history of heart disease, history of atrial fibrillation, history of stroke, drinking, white blood cell count, monocyte count, and neutrophil ratio) were statistically significant. However, in multivariate logistic regression, only eight variables, including age, onset-admission time, hospital stay, body temperature, heart rate, high blood glucose, history of atrial fibrillation, and history of stroke, were associated with the prognosis.

A number of studies have demonstrated that age is a predictor of mortality and poor prognosis [14, 15]. Sene Diouf *et al*. conducted a prospective cohort study including 170 cases in 2003 and 2005 and indicated that old age is an independent risk factor of poor prognosis [14]. González *et al*. reported that 55.7% of patients older than 80 years and 73.8% of patients less than 80 years were discharged with mRs ≤2 after ischemic stroke [15]. In the present study, the univariate analysis demonstrated that the incidence of poor prognosis increased with the increase of age (OR = 1.29; 95% CI: 1.18-1.42). The results of multivariate logistic regression analysis also showed that age was the main factor of poor prognosis (OR = 1.24; 95% CI: 1.13-1.36). Poor constitution, accompanied hypertension, diabetes, hyperlipemia, cardiac disease, and higher incidence of complications contribute to the suboptimal recovery of elder patients.

Onset-admission time is also an important independent risk factor for the prognosis of patients with stroke. Long pre-hospital delay reduces the benefit of thrombolytic therapy in acute cerebral infarction. Many studies reported that ultra-early thrombolytic therapy and recanalization of the culprit vessel are critical for optimal prognosis [16, 17]. However, the results of our study showed that the prognosis of patients who arrived to the hospital within 6 h after onset was worse than those who arrived after more than 6 h. The following reasons may help explain this phenomenon. 1) Patients who received treatment immediately after onset tend to be critically ill. Despite standard management, their prognosis is still suboptimal. 2) Currently, thrombolysis is poorly accepted by patients and their families, which contributes to the poor outcome. The results of this study also showed that longer hospital stay of more than 7 days is protective for the prognosis. Because longer hospital stay indicates relatively better affordability, these patients are more likely to receive standard and sufficient treatment.

In recent years, a considerable number of data indicate that fever is an independent risk factor for the early prognosis of acute cerebral infarction. Saini *et al*. studied 5305 cases of patients with acute stroke and confirmed that fever has an important function in the prognosis of acute ischemic stroke. Higher temperature within one week after onset indicates worse prognosis. The later the body temperature elevated within a week, the worse the outcome. Massive cerebral infarction and infection are the main causes for fever. Active temperature control can effectively improve poor prognosis [18]. Our study showed that with the increase of body temperature, the incidence of poor prognosis correspondingly increased (OR = 1.52; 95% CI: 1.16-2.08). Body temperature may have a vital function in the the following mechanisms: 1) release of excitatory neurotransmitters (e.g., the contents of glutamate, glycine, and γ-aminobutyric acid in patients with higher body temperature increase 10 times than those with normal body temperature after acute cerebral infarction); 2) production of reactive oxygen species; 3) degradation of cytoskeletal protein; 4) changes of blood-brain barrier; and 5) hyperpyrexia, which aggravates the depolarization of ischemic neurons and further expands the volume of infarction [18-20].

The development of cerebrocardiac syndrome following acute cerebral infarction is the main cause of death in the acute phase. Change in heart rate is one of the important aspects [21, 22]. The results of this study showed that with the increase of heart rate, the risk of composite outcome also increased (OR = 1.01; 95% CI: 1.00-1.02), which result may be associated with the occurrence of adverse events, such as myocardial ischemia, myocardial infarction, and heart failure. The association between other types of arrhythmia and these adverse

events in this study was not investigated. This study limitation needs to be improved in future studies.

Hyperglycemia at admission is an independent risk factor for the short-term prognosis of acute ischemic stroke. The increase of blood glucose levels resulted in the increase of the risk of composite outcomes (OR = 1.60; 95% CI: 1.31-1.94), which is consistent with the report of other studies [23-25]. Hyperglycemia in acute ischemic stroke may be due to pre-existing diabetes or stress. Hyperglycemia can aggravate ischemic cerebral damage, leading to poor prognosis. The main mechanism is the elevation of plasma glucose level, which exacerbates the mitochondrial damage in the cerebral ischemic penumbra, contributing to the acidosis in the infarct lesion. The enhanced release of glucocorticoids in vivo stimulates the inflammatory reaction in the ischemic area and the reperfusion zone, aggravating the damage. Glucocorticoids can increase blood viscosity, decrease erythrocyte deformability, and induce vasodilation paralysis, which inhibits recanalization [23-25]. Moreover, hyperglycemia causes severe damage to the blood-brain barrier and aggravates cerebral edema, resulting in sustained brain damage [26]. Moderate control of blood glucose in acute ischemic stroke patients is very important to improve the neurological outcome. A considerable number of studies proved that diabetes mellitus is an independent risk factor for the short-term prognosis of acute ischemic stroke [27]. However, the results of this study did not show any significance may be because of the better blood glycemic control or other reason. Further study is expected to provide an identical conclusion.

Atrial fibrillation is not only a risk factor for ischemic stroke [28], but also a risk factor for early adverse outcomes after stroke [29]. Wang also reported this conclusion [30]. The poor prognosis in patients with atrial fibrillation is related to their massive cerebral infarction, severe condition, poor collateral circulation around the lesion, and high recurrence rate of cerebral infarction, as well as their primary heart disease. The results of this study showed that atrial fibrillation is a risk factor for the early adverse outcomes after stroke (OR = 1.77; 95% CI: 1.30-2.41), which is consistent with previous findings. Therefore, secondary prevention treatment of atrial fibrillation is significant for these patients. The results also suggested that patients with a history of stroke are more likely to have a poor outcome (OR = 1.27; 95% CI: 1.03-1.58). This finding is inconsistent with the prospective study of Zhenhua *et al*. They reviewed 234 cases of patients and reported that history of stroke is not a risk factor of early adverse outcomes of ischemic stroke. The difference of results may be attributed to their limited sample size.

In summary, many factors affect the prognosis of stroke. In this large sample study, we demonstrated that age, onset-admission time, hospital stay, body temperature, heart rate, high blood glucose, history of atrial fibrillation, and history of stroke are the main prognostic factors of the poor prognosis of acute ischemic stroke. In clinical practice, physicians can further intervene with the factors to improve prognosis. Our future investigation aims to conduct a prospective cohort study to confirm these results.

Disclosure of conflict of interest

None.

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