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ORIGINAL COMMUNICATION

Frequency and predictors of spontaneous hemorrhagic transformation in ischemic stroke and its association with prognosis

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Abstract Few prospective studies have examined the frequency, predictors and long-term outcomes of spontaneous hemorrhagic transformation (HT) in patients with ischemic stroke not receiving thrombolytic treatment. We prospectively enrolled a consecutive cohort of 407 patients with ischemic stroke who were admitted within one month of stroke onset. In patients who developed spontaneous HT, the area of the infarct and HT were examined by computed tomography (CT) or magnetic resonance imaging (MRI). Univariate analysis was used to correlate clinical characteristics with appearance of HT, then multivariate logistical regression was used to identify independent predictors of spontaneous HT and factors that predict 3-month prognosis of ischemic stroke. Spontaneous HT was observed in 50 patients (12.3 %), comprising 33 cases (66 %) of hemorrhagic infarction, 17 (34 %) of parenchymal hematoma, 32 (64 %) of non-symptomatic HT, and 18 (36 %) of symptomatic HT. In 40 % of HT cases, the condition was detected by CT or MRI within 4–7 days of symptom onset. Multivariate logistic regression identified atrial fibrillation (OR 4.88, 95 % CI 1.83–13.00, $P = 0.002$) and infarct area (OR 4.48, 95 % CI 1.85–10.85, $P = 0.001$) as independent predictors of HT in ischemic stroke. Multivariate analysis also found that spontaneous HT was not independently associated with a worse 3-month prognosis for ischemic stroke (OR 1.59, 95 % CI 0.38–6.69, $P = 0.527$). Spontaneous HT occurred in 12.3 % of our patients with ischemic stroke, and atrial fibrillation and large infarct area were independent predictors. Spontaneous HT was not an independent predictor of a worse 3-month prognosis for ischemic stroke.

Keywords Frequency · Prevalence · Risk factor · Ischemic stroke · Spontaneous hemorrhagic transformation

Background

Thrombolytic or antithrombotic therapy, which involves antiplatelets and anticoagulants, is widely used as an effective treatment for ischemic stroke, but it increases the risk of hemorrhagic transformation (HT). How serious a risk this poses for stroke patients is unclear because little is known about the prevalence of spontaneous HT, which occurs in the absence of thrombolytic therapy. Therefore, it is important to understand the frequency of spontaneous HT among ischemic stroke patients, as well as determine whether clinical characteristics can help guide the selection of patients for thrombolytic or antithrombotic therapy and the prediction of prognosis of patients with ischemic stroke.

Studies have identified several risk factors for HT in patients with cerebral infarction, including vascular risk factors, changes in brain imaging, infarct area, revascularization time, stroke severity, blood pressure, changes in blood glucose, platelet counts, and use of antiplatelets, anticoagulants or thrombolytic therapy [1–7, 10, 11]. Most of these studies are retrospective [1–7, 12–17], including

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several studies in China [12–17] with small cohorts of non-consecutive cases for which the inclusion criteria and method of HT diagnosis were unclear. The few prospective studies examining HT risk factors focus on thrombolysis-related HT [8, 9], for which the risk factors and prognosis may differ from those of spontaneous HT.

Here, we carried out a prospective study with consecutive patients with ischemic stroke, in which we examined the incidence, subtypes, and predictors of spontaneous HT and examined whether spontaneous HT can independently predict the prognosis of patients after ischemic stroke. Our aim was to generate insights that would help clinicians understand the characteristics and patterns of spontaneous HT among patients with ischemic stroke, as well as make more informed decisions about using antithrombotic therapy.

Methods

Subjects

Data on all patients came from the Chengdu Stroke Registry Database [18–20], which prospectively collects data on consecutive patients admitted to the Department of Neurology of West China Hospital (Chengdu, China) and followed up for long periods. This registry project was approved by the Scientific Research Department of West China hospital, which conformed to the local ethical criteria for research. The present study involved patients enrolled in the Registry between 1 March 2002 and 5 March 2005.

The criteria used to diagnose ischemic stroke, inclusion and exclusion criteria for the Registry, and methods used to collect data have been described previously [18–20]. For the present study, we also applied additional exclusion criteria, eliminating patients with hematological disorders or serious liver or renal failure, as well as patients who for any reason were unable to take care of themselves prior to stroke onset.

All patients in our study underwent computed tomography (CT) of the head within 24 h from symptoms onset and then CT or magnetic resonance imaging (MRI) of the head after three days from stroke onset or immediately in case of clinical worsening. Any changes in symptoms or signs were recorded. CT and MRI scans were evaluated by a neuroradiologist blinded to patient details, including the clinical characteristics of the stroke.

Definition of HT and its subtypes

HT in this study was defined as an infarct zone hemorrhage not detected by head CT taken initially after cerebral infarction but later confirmed by a second CT or MRI [21]. We also categorized HT into four subtypes [22]. Hemorrhagic infarct (HI) was defined either as small petechiae along the margins of the infarct or as more confluent petechiae within the infarcted area, without a space-occupying effect. Cerebral parenchymal hematoma (PH) was defined as hematoma in the infarcted area with slight or substantial space-occupying effect, or as any hemorrhagic lesion outside the infarcted area. Symptomatic HT was defined as HT with worsening clinical manifestations, e.g., headache and neurologic deficit, while asymptomatic HT referred to HT without worsening of manifestations.

Outcomes and 3-month follow-up

Data were collected on the following outcomes: HT occurrence, time from stroke onset to HT, and subtype of HT. These data were collected during the entire period of hospitalization, as well as three months after onset as part of routine scheduled visits to an outpatient clinic or by telephone interview. Prognosis was calculated for each patient at three months from stroke onset using the modified Rankin Scale (mRS): scores of 0–2 were deemed good prognosis, while scores of 3–6 were defined as poor prognosis (6 = death) [23].

Identification of HT risk factors and predictors of prognosis after ischemic stroke

Data were collected for a broad range of factors that might influence risk of spontaneous HT during ischemic stroke or 3-month prognosis after ischemic stroke. These included age, gender, time from stroke onset to admission, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation (paroxysmal or persistent), coronary heart disease (angina pectoris and/or myocardial infarction), history of stroke (previous cerebral infarction and/or hemorrhage), history of smoking and alcohol consumption, carotid stenosis (more than 50 %), score on Glasgow Coma Scale (GCS) at admission, and score on National Institutes of Health Stroke Scale (NIHSS) at admission, systolic pressure and diastolic pressure on first visit, blood glucose level on first visit, platelet count, TOAST classification, and therapy administered after stroke onset (antiplatelet, anticoagulation, thrombolysis, traditional Chinese medicine to promote blood flow or relieve blood stasis). Patients were classified as having hypertension, diabetes mellitus, or dyslipidemia if they had a definite history of the condition or if the condition was definitely diagnosed after admission to our hospital.

Data were also collected about infarct area, which was categorized as (1) small if the maximal infarct section area was <1.5 cm^2 (lacunar infarction); (2) medium, if the

maximal infarct section area was more than 1.5 cm^2 and it involved one anatomic site with blood supply from a branch of a major artery (MCA or ACA or PCA), or it involved a lesion in internal border areas; (3) massive, if the maximal infarct section area was more than 1.5 cm^2 and affected two or more major arterial areas (e.g., MCA associated with ACA areas).

Statistical analysis

Statistical analysis was conducted using SPSS 16.0 (IBM, USA). Univariate analysis was carried out to identify possible risk factors for spontaneous HT. Differences in categorical data were assessed for statistical significance using the Chi squared test; differences in continuous data showing a normal distribution, using Student's t test; and differences in ordinal data, using the Mann–Whitney non-parametric test. Factors with $P \leq 0.10$ as determined by univariate analysis were then analyzed by logistic regression. This P value threshold was less stringent than the traditional cut-off of $P < 0.05$ in order to reduce the possibility of omitting factors that may be related to prognosis [24].

As appropriate, results were reported as percentages or as odds ratios (ORs) with associated 95 % confidence intervals (95 % CI).

Results

Baseline characteristics

A total of 407 ischemic stroke patients were included in the present study. Their ages ranged from 19 to 91 years (mean 64.57 ± 12.83 years). Of the participants, 242 (59.5 %) were men with an average age of 63.74 ± 12.96 years, and 165 (40.5 %) were women with an average age of 65.79 ± 12.57 years. A total of 227 patients (55.8 %) were admitted to hospital within 24 h of stroke onset (range 0.5–24 h), while the interval from stroke onset to admission ranged from one day to one month. Only one patient used thrombolytic agents, and the patient did not develop HT during follow-up. Therefore, cases of HT in our population were considered spontaneous.

HT incidence

Of the 407 patients with ischemic stroke, 50 (12.3 %) developed HT. These patients were subjected to a second head CT or MRI scan due to worsening condition within three days of stroke onset in 11 patients (22.0 %), within 4–7 days in 20 patients (40 %), 8–14 days in 11 patients (22.0 %), and 15–30 days in 8 patients (16 %) (Fig. 1).

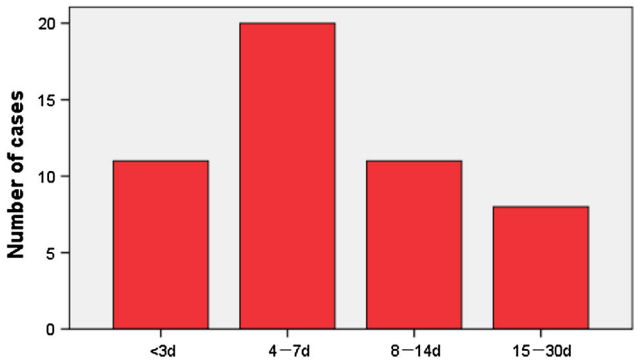

Fig. 1 Interval between admission and detection of HT among 50 patients who developed HT

Based on imaging findings, 33 of these patients (66 %) were diagnosed with HI, 17 (34 %) with PH, 32 (64 %) with asymptomatic HT, and 18 (36 %) with symptomatic HT. Of the 33 patients with HI, 6 (18.2 %) were symptomatic. Of the 17 patients with cerebral PH, 12 (70.6 %) were symptomatic, with symptoms including aggravated headache, onset or aggravation of disturbed consciousness, and aggravated neurologic deficits.

Risk factors of HT after acute ischemic stroke

We carried out univariate and multivariate analyses to identify whether any of several factors were associated with risk of HT occurrence. Some clinical parameters that we examined are meaningful only if they are assessed within 24 h of stroke onset; otherwise, they may not be relevant as factors that influence the acute stage of HT. We considered these variables to be time from stroke onset to admission, GCS score on admission, NIHSS score on admission, systolic and diastolic blood pressure on first visit, and blood glucose level on first visit. Therefore, we performed univariate and multivariate analyses using data only for the 227 patients who were admitted to hospital within 24 h of stroke onset. Baseline characteristics of these patients are shown in Table 1.

Univariate analysis

Univariate analysis was carried out using 22 possible risk factors for HT (Table 2). This analysis identified six factors that satisfied the significance threshold of $P \leq 0.10$, which were: atrial fibrillation ($P < 0.001$), TOAST classification ($P = 0.059$), infarct area ($P < 0.001$), time interval from stroke onset to admission ($P = 0.005$), GCS score on admission ($P = 0.039$), and NIHSS score on admission ($P = 0.003$).

Table 1 Characteristics of patients with ischemic stroke admitted to hospital within 24 h of stroke onset ($n = 227$)

Characteristic	
Age (mean ± SD), years	65.86 ± 13.57
Male, *n* (%)	126 (55.5)
Hypertension, *n* (%)	113 (49.8)
Diabetes mellitus, *n* (%)	32 (14.1)
Dyslipidemia, *n* (%)	31 (13.7)
Coronary heart disease, *n* (%)	37 (16.3)
Atrial fibrillation, *n* (%)	45 (19.8)
Alcohol consumption, *n* (%)	35 (15.4)
Smoking, *n* (%)	52 (22.9)
History of stroke, *n* (%)	25 (11.0)
Antiplatelet therapy after stroke onset, *n* (%)	198 (87.2)
TCM therapy after stroke onset, *n* (%)	190 (83.7)
Anticoagulation therapy after stroke onset, *n* (%)	14 (6.2)
Thrombolysis after stroke onset, *n* (%)	1 (0.44)
Platelet count (mean ± SD) × 1,000 mm^3	142.13 ± 55.35
TOAST classification, *n* (%)	
Large-artery atherosclerosis	29 (12.8)
Cardioembolism	99 (43.6)
Small-vessel occlusion	44 (19.4)
Undetermined etiology	55 (24.2)
Infarct area, *n* (%)	
Massive	37 (16.3)
Medium	125 (55.1)
Small	65 (28.6)
Consciousness (GCS score)	
14–15 (normal)	179 (78.9)
8–13 (somnolence)	41 (18.1)
0–7 (coma)	7 (3.1)
NIHSS score on admission, *n* (%)	
0–5	112 (49.3)
6–10	55 (24.2)
11–15	32 (14.1)
16–20	14 (6.2)
>20	14 (6.2)
Time interval from stroke onset to admission, (mean ± SD), h	9.72 ± 7.81
Systolic pressure (mean ± SD) on first visit, mmHg	141.2 ± 22.1
Diastolic pressure (mean ± SD) on first visit, mmHg	84.1 ± 13.7
Blood glucose on first visit (mean ± SD), mmol/L	6.83 ± 2.94

Values are reported as *n* (%) or as mean ± SD

GCS Glasgow Coma Scale, *NIHSS* National Institutes of Health Severity Scale, *TCM* traditional Chinese medicine

Table 2 Univariate analysis to identify factors that affect risk of HT in patients with ischemic stroke admitted within 24 h of stroke onset ($n = 227$)

Variable	HT ($n = 26$)	No HT ($n = 201$)	*P*
Male, *n* (%)	11 (42.3)	115 (57.2)	0.150
Age (mean ± SD), y	66.96 ± 13.10	65.72 ± 13.65	0.661
Hypertension, *n* (%)	11 (42.3)	102 (50.7)	0.418
Diabetes mellitus, *n* (%)	2 (7.7)	30 (14.9)	0.485
Dyslipidemia, *n* (%)	2 (7.7)	29 (14.4)	0.354
Coronary heart disease, *n* (%)	4 (15.4)	33 (16.4)	0.893
Atrial fibrillation, *n* (%)	15 (57.7)	30 (14.9)	<0.001*
Alcohol consumption, *n* (%)	2 (7.7)	33 (16.4)	0.384
Smoking, *n* (%)	5 (19.2)	47 (23.4)	0.635
History of stroke, *n* (%)	4 (15.4)	21 (10.4)	0.672
Antiplatelet therapy after stroke onset, *n* (%)	23 (88.5)	175 (87.1)	0.841
TCM therapy after stroke onset, *n* (%)	19 (73.1)	171 (85.1)	0.202
Anticoagulation therapy after stroke onset, *n* (%)	2 (7.7)	12 (6.0)	0.731
Platelet count,×1,000 mm^3	133.92 ± 37.30	143.19 ± 57.25	0.423
TOAST classification, *n* (%)			0.059*
Large-artery atherosclerosis	2(7.7)	27(13.4)	0.608
Cardioembolism	17 (65.4)	82 (45.8)	0.017*
Small-vessel occlusion	1 (3.8)	43 (21.4)	0.033*
Undetermined etiology	6 (23.1)	49 (24.4)	0.884
Infarct area, *n* (%)			<0.001*
Massive	14 (53.8)	23 (11.4)	
Medium	11 (42.3)	114 (56.7)	
Small	1 (3.8)	64 (31.8)	
Time interval from stroke onset to admission, (mean ± SD), h	6.17 ± 4.22	10.18 ± 7.89	0.005*
GCS score on admission, *n* (%)			0.039*
14–15	16 (61.5)	163 (81.1)	
8–13	8 (30.8)	33 (16.4)	
0–7	2 (7.7)	5 (2.5)	

Table 2 continued

Variable	HT ($n = 26$)	No HT ($n = 201$)	P
NIHSS score on admission, *n* (%)			0.003*
0–5	5 (19.2)	107 (53.2)	
6–10	8 (30.8)	47 (23.4)	
11–15	5 (19.2)	27 (13.4)	
16–20	4 (15.4)	10 (5.0)	
>20	4 (15.4)	10 (5.0)	
Systolic pressure (mean ± SD) on first visit, mmHg	140.00 ± 22.60	141.40 ± 22.08	0.762
Diastolic pressure (mean ± SD) on first visit, mmHg	84.92 ± 15.76	83.99 ± 13.41	0.743
Blood glucose on first visit (mean ± SD), mmol/L	6.54 ± 2.54	6.86 ± 2.89	0.594

HT hemorrhagic transformation, *TCM* traditional Chinese medicine

* Associated with $P \leq 0.10$ and therefore used in multivariate analysis

Multivariate analysis

The six factors identified as significant in the univariate analyses were subsequently analyzed by logistic regression (Table 3), and two were identified as independently correlated with onset of spontaneous HT: atrial fibrillation (OR 4.88, 95 % CI 1.83–13.00, $P = 0.002$) and infarct area (OR 4.48, 95 % CI 1.85–10.85, $P = 0.001$). These ORs suggest that the patients with ischemic stroke and atrial fibrillation are at nearly fivefold higher risk of spontaneous HT than are similar patients without atrial fibrillation. Since our analysis involved discrete levels of infarct area, the OR suggests that patients with ischemic stroke and massive infarcts are at about fourfold higher risk of HT than similar patients with medium infarcts.

Prognostic factors of acute ischemic stroke

Based on data just from the 227 patients who were admitted to hospital within 24 h of stroke onset, univariate analysis identified several factors associated with poor mRS score (3–6) at three months from stroke onset (Table 4). Multivariate analysis identified only NIHSS score on admission to be an independent predictor of 3-month prognosis of ischemic stroke (OR 1.35, 95 % CI 1.21–1.50, $P < 0.001$). Spontaneous HT itself did not predict a poor 3-month prognosis of ischemic stroke (OR 1.59, 95 % CI 0.38–6.69, $P = 0.527$).

Table 3 Multivariate analysis to identify factors associated with occurrence of spontaneous HT in patients with ischemic stroke admitted within 24 h of stroke onset ($n = 227$)

Factor	OR	95 % CI	P
Atrial fibrillation	4.88	1.83–13.00	0.002
TOAST classification	1.20	0.80–1.80	0.370
Infarct area	4.48	1.85–10.85	0.001
Time from stroke onset to admission	0.93	0.85–1.02	0.105
GCS score	1.08	0.84–1.39	0.560
NIHSS score	1.03	0.96–1.11	0.359

GCS Glasgow Coma Scale, *NIHSS* National Institutes of Health Severity Scale, *OR* odds ratio, *95 % CI* 95 % confidence interval

Table 4 Univariate analysis to identify factors associated with poor mRS scores within three months of initial hospital admission in patients with ischemic stroke admitted to hospital within 24 h of stroke onset ($n = 227$)

Factor	χ^2	P
Age	2.350	0.35
Gender	7.659	0.06
GCS score at admission	37.388[a]	<0.001
NIHSS score at admission	81.754	<0.001
Infarct area	19.504	<0.001
HT	5.018	0.025

GCS Glasgow Coma Scale, *NIHSS* National Institutes of Health Severity Scale, *HT* hemorrhagic transformation, χ^2 Pearson Chi squared

[a] Fisher's exact test

Discussion

We undertook this study to clarify the frequency of spontaneous HT among patients with ischemic stroke, as well as examine whether certain clinical factors correlate with risk of HT or prognosis after ischemic stroke. Among our cohort of 407 patients, incidence of HT was 12.3 %, and it was most often detected by second CT or MRI scans 4–7 days after stroke onset. Half of HT cases were asymptomatic, including most cases of hemorrhagic infarct. In contrast, most cases of cerebral parenchymal hematoma were symptomatic.

We identified spontaneous HT in 12.3 % of our patients with ischemic stroke, which falls within the broad range of incidence from 0.6 to 85 % among stroke patients reported in a recent systematic review [25]. The studies included in that review were based on diverse patient inclusion criteria, HT diagnostic criteria, stroke types, times between stroke onset and hospital admission, and stroke therapy. When we searched the literature for studies examining HT incidence and risk factors in samples of at least 100 stroke patients, most of whom were not taking thrombolytic therapy, we

Table 5 Selected observational studies on incidence and risk factors of HT among stroke patients, excluding studies involving fewer than 100 patients and studies where most patients received thrombolytic therapy

First author and year	Country	*n* (% with HT)	Exam type	Exam timing, 1st/2nd	Principal results
Lodder [1]	NL	952 (5.1)	CT	0–13 days/ND	Massive infarct correlated with HT
Okada et al. [2]	Japan	160 (40.6)	CT	<7 days/1 month	All HT were observed after thrombosis. Older age and medium or massive infarcts correlated with HT
Toni et al. [3]	Italy	150 (43)	CT or autopsy	<5 h/7 days	CT identified early signs of low density that correlated with HT independently; medium and massive infarcts were likely to cause HT
Alexandrov [4]	Canada	490 (4)	CT	On admission/ 3–5 days	Massive infarct and cardiogenic stroke were likely to cause HT
Castellanos et al. [5]	Spain	250 (15.2)	CT	<24 h/4–7 days	High plasma MMP-9 levels, cardiogenic infarct and infarct of unknown cause were independent predictors of HT
Rodríguez-Yánez et al. [6]	Spain	200 (18)	CT	<24 h/4–7 days	History of hypertension, atrial fibrillation, proteinuria and early CT signs independently correlated with HT
Paciaroni et al. [10]	Italy	1125 (9)	CT	<14 h/3–7 days	Massive infarct, cardioembolism and low platelet counts on admission independently correlated with HT
Terruso et al. [7]	Italy	240 (12)	CT	<24 h/on discharge	Infarct area correlated with HT
Kablau et al. [11]	Germany	122 (20.5)	CT/T2*WI	<12/6–60 h	HT correlated with use of tPA, watershed infarct and serious neurologic deficit on admission

HT hemorrhagic transformation, *MMP-9* matrix metalloproteinase 9, *ND* not done, *NL* Netherlands, *tPA* tissue plasminogen activator, *T2*WI* T2*-weighted gradient-echo MRI

found reported incidences to range from 5.1 % to 43 % (Table 5) [1–7, 10, 11]. In several studies in Europe, where CT is a major tool for detecting HT, incidence has been reported to be 9–18 % [5–7, 10, 11]. Taken together, these findings suggest that our incidence in China is consistent with other studies and that incidence appears not to differ significantly between Asia and the West.

These incidences are substantially higher than the values reported in multicenter, large-scale controlled trials on thrombolytic therapy using recombinant tissue plasminogen activator (NINDS, ECASS I, ECASS II and ATLANTIS) [8, 9]. In the control groups of those studies, HT incidence was reported to range from 0.6 % to 7 %. The most likely explanation for this much lower range is that the multicenter studies applied strict inclusion criteria, leading them to exclude some serious patients at high risk of HT.

Our results suggest that larger infarct area independently predicts greater risk of HT in patients with ischemic stroke, consistent with several studies in patients of other ethnicities with other types of stroke [1–4, 7, 10]. Like ours, these previous studies measured infarct area and diagnosed HT during a second CT or MRI scan. In our study, each increase from one level of infarct area to the next (small → medium → massive) meant an approximately fourfold increase in HT risk. These findings suggest that antithrombotic therapies should be prescribed with caution for patients with massive cerebral infarction, and dynamic CT/MRI monitoring may be advisable to detect HT. Future prospective studies should explore whether infarct area is causally linked to HT pathogenesis.

The present study indicated atrial fibrillation to be an independent predictor of HT. In fact, HT risk was nearly fivefold higher in patients with atrial fibrillation than in those without it. In addition, univariate analysis indicated the stroke subtype of small vessel occlusion correlated with HT risk, but multivariate analysis did not support this independent correlation. This may reflect a lack of statistical power: only one patient who suffered HT had small-vessel occlusion. We failed to find an independent correlation between cardioembolism stroke subtype and HT risk, in contrast to other studies [4, 5, 10]. One possible explanation for these discrepancies is that we typed ischemic stroke according to the TOAST classification. The TOAST system may classify some cases of cardioembolism as being of undetermined etiology (e.g., when clinical data are missing) or as having more than one etiology. Another possible explanation is that a substantial number of participants in these clinical studies may have atherosclerosis, and artery–artery embolism may develop into HT when atherosclerotic plaque detaches from the vessel wall.

Future studies should seek to take into account the possible confounder of atherosclerosis as much as possible.

We found that frequency of hypertension and systolic blood pressure on the initial visit were lower in patients who developed spontaneous HT (42 %, 140 ± 23 mmHg) than in those who did not (54.6 %, 141 ± 22 mmHg), but this difference did not achieve statistical significance (Table 2). Several studies have analyzed the relationship between hypertension and HT and have come to opposite conclusions [26–28]. A widely held view continues to be that elevated blood pressure independently predicts thrombolysis-related HT [27]. It may be that, not blood pressure per se, but rather blood pressure variability is related to HT [29, 30], which may help explain the discrepancies in the literature. Future research should examine this question.

We did not observe a significant correlation between high blood glucose at the initial visit and risk of HT. In contrast, high blood glucose, like hypertension, is considered an independent predictor of thrombolysis-related HT [31, 32]. Since we focused exclusively on spontaneous HT, future research is needed to examine whether blood glucose level acts differently during onset of the different subtypes of HT.

The present study did not find spontaneous HT to correlate independently with poor prognosis of ischemic stroke. This is consistent with the findings of a multicenter, prospective study in Italy involving 1,125 patients [10]. At the same time, however, that study reported that PH-related HT correlated with poor prognosis, which we did not observe here. This discrepancy may reflect a combination of our much smaller sample size and the use of thrombolytic drugs: in the Italian study, altogether 67 patients (6 %) received thrombolytic treatment, among which four patients developed PH, accounting for 11 % of 36 patients who developed HT. Patients with thrombolysis-related PH may have had poorer prognosis than patients with spontaneous PH. In fact, our entire sample size was much smaller than in the Italian study: for identifying prognostic factors, we relied on data from only 227 patients. We tentatively conclude that HT is not a reliable indicator of poor prognosis, but larger studies are needed to address this question definitively.

Despite the insights of the present study, its findings should be interpreted with caution because of several limitations. The work involves a relatively small sample of patients at a single hospital, although the hospital is very large in China and draws patients from an extensive surrounding area.

Conclusions

The incidence of HT in this cohort of patients with acute ischemic stroke was 12.3 %, suggesting the need to consider the risk of such a complication during treatment. Atrial fibrillation and infarct area independently correlated with risk of spontaneous HT, while spontaneous HT by itself was not an independent predictor of poor prognosis at three months after ischemic stroke. Our findings suggest that caution should be used when prescribing antithrombotic therapies to patients with massive cerebral infarction, and that dynamic monitoring by CT or MRI may help detect HT in patients who suffer acute ischemic stroke.

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Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical standard This study was approved by the Scientific Research Department of West China hospital, which conformed to the local ethical criteria for research. And all patients gave informed consent for participation in the registry.

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