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## Predictive Value of A2HD Scoring for Transient Symptoms Associated with Infarction

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**Background:**

Effective early management of cerebral infarction patients with transient ischemic attack (TIA) is undermined by an inability to predict who is at highest risk of stroke.

**Material/Methods:**

A total of 577 TIA patients with symptoms lasting no more than 1 hour were prospectively investigated and divided into a TIA group and a transient symptoms associated with infarction (TSI) group based on diffusion-weighted magnetic resonance imaging findings after hospital admission. The baseline characteristics, symptoms of TIA, features of disease onset, and findings from clinical examinations were compared between the 2 groups. Factors related to TSI were further analyzed.

**Results:**

Of 577 TIA patients, 127 patients were in the TSI group and 450 were in the TIA group. Anterior circulation events, hemiplegia, aphasia, multiple seizures, maximal duration, atrial fibrillation, and hypointense plaques were included as risk factors for stroke in a model of multivariate analysis, and results showed that hemiplegia, aphasia, multiple seizures, and atrial fibrillation were independent risk factors for TSI. In the final mode, the area under the curve (AUC) was 0.766 (95% confidence interval: 0.729–0.800). According to the A2HD score and odds ratio, hemiplegia (score 2), aphasia (score 2), multiple seizures (score 2), and atrial fibrillation (score 1) were scored, and any increment in the score increased the risk for cerebral infarction by 1.893-fold (95% confidence interval: 1.643–2.181).

**Conclusions:**





Risk of TSI seems to be highly predictable. The A2HD score can be used in clinical practice to identify high-risk cerebral infarction patients with TIA who need emergency diagnosis and treatment.

**MeSH Keywords:**

**Aphasia • Atrial Fibrillation • Hemiplegia • Ischemic Attack, Transient • Recurrence • Symptom Assessment**

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## Background

In 2016, cardiovascular and cerebrovascular diseases were the leading chronic, non-infectious fatal diseases. From 2006 to 2016, the mortality rate related to cardiovascular and cerebrovascular diseases increased by 14.5%. In China, the morbidity and mortality rates of cerebral stroke are higher than those of ischemic heart disease and malignancies; and cerebral stroke is the leading cause of death [1]. The World Health Organization declared the theme for World Stroke Day to be “Stroke Prevention” with the slogan “What’s your reason for preventing stroke?” Thus, stroke prevention is an imperative challenge in clinical practice.

Transient ischemic attack (TIA) is widely accepted to be a predictor of cerebral stroke. In 2015, Wang et al. [2] conducted a national survey of more than 90 000 patients and showed that the incidence of TIA was as high as 2.27%. Studies from 2000–2003 [3,4] have indicated that the risk for ischemic stroke and acute coronary events within 3 months of TIA range from 12–20%. Timely and appropriate treatment of TIA may reduce the risk for cerebral stroke from 2.28–9.32% to 0.73–3.05% within 90 days [5]. Thus, TIA is an early warning event that should be promptly managed by emergency clinicians and also represents the optimal time for secondary prevention of stroke.

The American Stroke Society (ASS) defines TIA as a brief episode of neurological dysfunction caused by focal ischemia in the brain, spinal cord, or retina without evidence of acute cerebral infarction. Here, cerebral infarction is defined as the presence of hyperintense signals observed by diffusion-weighted imaging (DWI) [6,7]. However, the ASS TIA guidelines are based on a summary of 19 studies involving 1117 patients, which determined the rate of hyperintense signals on DWI to be about 39% (25–67%) in clinical TIA patients.

Thereafter, several clinical studies have reported that cranial magnetic resonance imaging (MRI) findings indicate the presence of acute cerebral infarction in patients with clinical symptoms of TIA. Purroy et al. [8] found that the rate of positive MRI-DWI findings was 46.1% within 7 days of initial clinical diagnosis of TIA. Tanislav et al. [9] investigated 829 patients diagnosed with TIA by MRI-DWI and found acute cerebral infarction in 121 patients (15%).

As early as 2005, Ay et al. [10] proposed the concept of transient symptoms associated with infarction (TSI), which refers to the complete resolution of signs and symptoms within 24 hours in the presence of acute cerebral infarction seen on DWI. Tong et al. [11] found that the risk for TIA and stroke within 7 days in TSI patients was 10 times higher than that in TIA patients. In clinical practice, clinicians should pay attention to TSI with symptoms of TIA.

Currently, the differential diagnosis between TSI and TIA is based on cranial MRI-DWI. However, MRI-DWI examination is expensive, and the equipment available for diagnosis of TIA is present in less than one third of all hospitals [12]. Thus, in the absence of MRI-DWI (e.g., in the emergency department), diagnoses should be based on clinical symptoms, signs, and medical history, and thrombolysis or interventional therapy should be administered within the appropriate time window to reduce the incidence of neurological dysfunction.

In this study, patients who were admitted to the Department of Neurology due to symptoms of TIA were retrospectively reviewed, and the clinical characteristics of TSI were explored, with the aim of providing evidence for future diagnosis of TSI in emergency situations.

It should be noted that there is currently no research showing that any risk stratification tool has the ability to recognize the risk of acute stroke [13].

## Material and Methods

### Patients

Patients diagnosed with clinical TIA were recruited from the Department of Neurology at the Tenth People’s Hospital in Shanghai, China, between January 2014 and March 2017. Clinical TIA was diagnosed according to the diagnostic criteria developed by ASS in 2009. Patients with neurological dysfunction due to cerebral hemorrhage or other non-vascular causes (space-occupying lesions, subdural hematoma, epidural hematoma, hypoglycemia, or epilepsy) diagnosed by computed tomography (CT) were excluded. In addition, patients who were unable to receive MRI and a CT angiogram (CTA) were also excluded from this study. The investigation adhered to the tenets of the Declaration of Helsinki.

### General characteristics

A form was used to collect general characteristics: general clinical characteristics (gender, age, history of ischemic heart disease, history of atrial fibrillation (AF), history of ischemic cerebrovascular disease, hypertension, diabetes mellitus, hyperlipidemia, and smoking status); clinical characteristics of TIA (duration, times, and clinical manifestations); imaging findings (cranial MRI within 24 hours of admission, cranial CTA within 72 hours of admission); findings from blood work (white blood cell count, platelet count, and levels of C-reactive protein, fibrinogen, D-dimer, glycated hemoglobin, alanine aminotransferase, creatinine, potassium, sodium, troponin T, and brain natriuretic peptide).

## CTA

All patients received cranial CTA within 48 hours of admission (Siemens Dual Source CT Scanner). Scanning was performed from the aortic arch to the top of the head. The following blood vessels were examined: carotid, internal carotid, anterior cerebral, middle cerebral, posterior cerebral, vertebral, and basilar arteries. Artery stenosis was assessed with the North American Symptomatic Carotid Endarterectomy Trial Collaborators as follows: normal or mild stenosis (0–29%), moderate stenosis (30–69%), severe stenosis (70–99%), or occlusion (100%). Stenosis (%) was calculated, as follows:  $[1 - \text{arterial diameter at the most evident point of stenosis} / \text{arterial diameter at the site distal to stenosis}] \times 100$ . The cases of moderate to severe stenosis of major vessels were assessed by experienced clinicians in the Department of Radiology and Department of Neurology based on the medical history, clinical characteristics, and imaging findings.

## MRI

All patients received cranial MRI (Siemens 3.0T Avanto MRI) within 48 hours of admission, and sequences progressed in the following order: T2-weighted imaging (WI), fluid-attenuated inversion recovery (FLAIR) T1 WI, FLAIR T2 WI, MRI-DWI, and MRI apparent diffusion coefficient (–ADC) imaging.

## Statistical analysis

Statistical analysis was performed with SPSS for Windows 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM Corp.). Risk factors for TIA and cerebral infarction were analyzed with univariate and multivariate analyses. For univariate analysis, comparisons between 2 groups were performed with Student's *t*-test (normal distribution) or the Mann-Whitney U test (non-normal distribution); qualitative data were compared with the chi-square test. For multivariate analysis, TIA or cerebral infarction served as a dependent variable, and risk factors that were associated with a value of  $P < 0.05$  in univariate analysis served as independent variables for logistic regression analysis. A value of  $P < 0.05$  was considered statistically significant.

## ABCD and ABCD2 scoring

ABCD scoring was carried out according to the clinical characteristics of patients, as follows: 1) age ( $>60$  years, 1 point); 2) blood pressure at first assessment after TIA [systolic blood pressure (SBP)  $>140$  mmHg and/or diastolic blood pressure (DBP)  $>90$  mmHg, 1 point]; 3) unilateral weakness, 2 points; speech impairment without weakness, 1 point; other symptoms, 0 points; 4) duration of symptoms ( $\geq 60$  minutes, 2 points; 10–59 minutes, 1 point,  $<10$  minutes, 0 points). For ABCD2 scoring,

diabetes (yes, 1 point; no, 0 points) was included in addition to the abovementioned parameters.

## A2HD scoring

The results of multivariate analysis showed hemiplegia, aphasia, multiple epilepsy, and atrial fibrillation as independent risk factors for TSI. The A2HD score was defined as follows according to the odds ratio: hemiplegia (2 points), aphasia (2 points), multiple epilepsy (2 points), and AF (1 point).

## Results

### Comparisons of general characteristics between TIA group and TSI group

A total of 577 patients diagnosed with TIA between January 2014 and March 2017 in the Department of Neurology were included in this study. According to the findings from cranial MRIs, these patients were divided into a TIA group ( $n=450$ ) and a TSI group ( $n=127$ ).

### General clinical characteristics

There were significant differences in anterior circulation events and AF between the TIA group and the TSI group ( $P < 0.05$ ). There were no marked differences in gender, age, hypertension, diabetes, ischemic heart disease, ischemic cerebrovascular diseases, and smoking between the 2 groups ( $P > 0.05$ ) (Table 1).

### Clinical characteristics

There were significant differences in hemiplegia, aphasia, double seizure, and maximum duration between the TIA group and the TSI group ( $P < 0.05$ ) (Table 2).

### Imaging findings

There were significant differences in hypointense carotid plaques between the TIA group and the TSI group ( $P < 0.05$ ). There were no marked differences in carotid plaques, bilateral plaques, hyperintense and isointense carotid plaques, maximum plaque thickness, and severe stenosis of the responsible vessel between the 2 groups ( $P > 0.05$ ) (Table 3).

### Blood work

There were significant differences in LDL-C between the TIA group and the TSI group ( $P < 0.05$ ). There were no marked differences in white blood cells, platelets, C-reactive protein, D-dimer, fibrinogen, glycosylated hemoglobin, total cholesterol, triglycerides, alanine aminotransferase, creatinine, potassium,

**Table 1.** General clinical characteristics.

Variables	TIA (n=450)	TSI (n=127)	$\chi^2/Z/T$	P value
Anterior circulation (%)	218 (48.44)	88 (69.29)	17.282	0.000
Gender, male (%)	146 (32.44)	26 (20.47)	5.397	0.067
Age >65 years	222 (49.33)	51 (40.16)	3.345	0.067
Hypertension (%)	325 (72.22)	83 (65.35)	2.256	0.133
Diabetes (%)	114 (25.33)	37 (29.13)	0.740	0.390
Ischemic heart disease (%)	76 (16.89)	19 (14.96)	0.268	0.605
Atrial fibrillation (%)	27 (6.00)	17 (13.39)	7.670	0.006
Ischemic cerebrovascular disease (%)	138 (30.67)	48 (37.80)	2.304	0.129
Smoking (%)	155 (34.44)	51 (40.16)	1.408	0.235

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction.

**Table 2.** Clinical characteristics.

Variables	TIA (n=450)	TSI (n=127)	$\chi^2/Z/T$	P value
Hemiplegia (%)	202 (44.89)	94 (74.02)	33.634	0.000
Aphasia (%)	81 (18.00)	57 (44.88)	39.334	0.000
Maximal duration (min)	10 (3–30)	20 (5–30)	–2.194	0.028
Multiple seizures (%)	140 (31.11)	74 (58.27)	31.306	0.000

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction.

**Table 3.** Imaging findings.

Variables	TIA (n=450)	TSI (n=127)	$\chi^2/Z/T$	P value
Carotid plaques (%)	310 (68.89)	95 (74.80)	1.574	0.210
Bilateral plaques (%)	217 (48.22)	65 (51.18)	0.322	0.570
Hyperintensity (%)	283 (62.89)	81 (63.78)	0.024	0.877
Isointensity (%)	260 (57.78)	76 (59.84)	0.153	0.696
Hypointensity (%)	14 (3.11)	9 (7.09)	4.067	0.044
Maximal plaque thickness (cm)	1.80 (0.00–2.50)	2.00 (0.00–2.60)	–1.578	0.115
Severe stenosis of responsible vessel (%)	168 (37.33)	40 (31.50)	1.464	0.226

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction.

sodium, troponin-T, or brain natriuretic peptide precursor between the 2 groups ( $P>0.05$ ) (Table 4).

### ABCD scores

There were significant differences in the ABCD and ABCD2 scores between the TIA group and the TSI group ( $P<0.05$ ) (Table 5).

### Univariate analysis of risk factors in the TIA group and TSI group

Univariate analysis revealed significant differences in general clinical characteristics (anterior circulation events and AF), clinical symptoms (hemiplegia, aphasia, multiple seizure events, and maximum duration), imaging findings (hypointense carotid plaques), blood work (LDL-C), ABCD and ABCD2 scores between the TIA group and TSI group ( $P<0.05$ ). The incidence of

**Table 4.** Blood work findings.

Variables	TIA (n=450)		TSI (n=127)		$\chi^2/Z/T$	P value
WBC	6.19	(5.30–7.42)	6.38	(5.39–7.75)	–1.207	0.228
PLT	201.50	(166.00–237.00)	208.00	(168.00–249.00)	–1.434	0.152
CRP	3.30	(3.27–3.40)	3.30	(3.27–3.40)	–1.586	0.113
DD	0.27	(0.19–0.54)	0.26	(0.19–0.44)	–1.156	0.248
FIB	2.60	(2.32–2.85)	2.59	(2.30–3.00)	–0.070	0.944
HGB	5.80	(5.50–6.50)	5.80	(5.50–6.40)	–0.187	0.852
TCH	4.51	(3.81–5.18)	4.66	(3.99–5.36)	–1.759	0.079
TG	1.38	(0.97–1.82)	1.32	(0.96–1.73)	–0.951	0.342
LDL-C	2.68	(2.09–3.33)	2.79	(2.31–3.48)	–2.033	0.042
ALT	15.50	(11.10–20.73)	16.60	(11.00–22.10)	–1.070	0.285
CR	75.80	(63.20–88.18)	75.00	(64.00–85.30)	–0.742	0.458
K	3.95	(3.74–4.17)	3.91	(3.70–4.13)	–1.010	0.313
Na	143.00	(141.00–144.00)	142.00	(140.00–144.00)	–1.518	0.129
TNT	0.008	(0.005–0.012)	0.007	(0.005–0.013)	–0.875	0.382
BNP	87.30	(46.78–188.43)	79.30	(45.80–188.00)	–0.375	0.708

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction; WBC – white blood cell; PLT – platelets; CRP – C-reactive protein; DD – D-dimer; FIB – plasma fibrinogen; HGB – hemoglobin A1c; TCH – total cholesterol; TG – triglyceride; LDL-C – low density lipoprotein-cholesterol; ALT – alanine aminotransferase; CR – creatinine; K – serum potassium; Na – serum sodium; TNT – troponin T; BNP – type B natriuretic peptide.

**Table 5.** ABCD scores.

Variables	TIA (n=450)		TSI (n=127)		$\chi^2/Z/T$	P value
ABCD	3	(2–4)	4	(3–5)	–4.008	0.000
ABCD2	3	(2–4.25)	4	(3–5)	–4.014	0.000

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction.

anterior circulation events, AF, hemiplegia, aphasia, multiple seizures, maximum duration, ABCD score, ABCD2 score, and LDL-C in the TSI group was markedly higher than in the TIA group. However, there were no marked differences in general clinical characteristics (gender, age, hypertension, diabetes, ischemic heart disease, ischemic cerebrovascular diseases, and smoking), imaging findings (carotid plaques, bilateral plaques, hyperintense and isointense carotid plaques, maximum plaque thickness, and severe stenosis of the responsible vessel), and blood work (white blood cell count, platelet count, and levels of C-reactive protein, D-dimer, fibrinogen, glycated hemoglobin, total cholesterol, triglycerides, alanine aminotransferase, creatinine, potassium, sodium, troponin-T, and brain natriuretic peptide precursor) between the 2 groups ( $P>0.05$ ).

**Multivariate logistic regression analysis of risk factors in the TIA group and the TSI group**

Data related to anterior circulation events, hemiplegia, aphasia, multiple seizures, maximal duration, AF, and hypointense plaques were included for multivariate analysis (Table 6). Results showed hemiplegia, aphasia, multiple seizures, and AF were independent risk factors for TSI.

**Predictive value of the A2HD score in the TSI group**

In the final model, the area under the curve (AUC) was 0.766 (95% confidence interval: 0.729–0.800) (Table 7). The A2HD score was defined according to the odds ratio, as follows: hemiplegia (2 points), aphasia (2 points), multiple seizures (2 points), AF (1 point). Any increment in the score increased the

**Table 6.** Multivariate logistic regression analysis of risk factors in TIA and TSI groups.

Variables	Odds ratio	95% confidence interval	P value
Hemiplegia	3.400	2.132–5.423	0.000
Aphasia	3.581	2.260–5.674	0.000
Multiple seizures	3.583	2.293–5.601	0.000
Atrial fibrillation	2.459	1.202–5.028	0.014

TIA – transient ischemic attack; TSI – transient symptoms associated with infarction.

**Table 7.** Predictive value of A2HD score in TSI-AUC.

AUC	0.766
Standard error	0.0224
95% CI	0.729–0.800
Z statistic	11.882
P value (area=0.5)	<0.0001

TSI – transient symptoms associated with infarction; AUC – area under the curve; CI – confidence interval.

**Table 8.** Predictive value of A2HD score in TSI – Youden index.

Youden index J	0.4252
Threshold	>2
Sensitivity	70.08
Specificity	72.44

TSI – transient symptoms associated with infarction.

**Table 9.** Predictive value of A2HD score in TSI – sensitivity and specificity.

Threshold	Sensitivity	95% CI	Specificity	95% CI	+LR	–LR
≥0	100.00	97.1–100.0	0.00	0.0–0.8	1.00	
>0	95.28	90.0–98.2	31.11	26.9–35.6	1.38	0.15
>1	94.49	89.0–97.8	32.44	28.1–37.0	1.40	0.17
>2	70.08	61.3–77.9	72.44	68.1–76.5	2.54	0.41
>3	65.35	56.4–73.6	75.56	71.3–79.5	2.67	0.46
>4	24.41	17.2–32.8	96.67	94.6–98.1	7.32	0.78
>5	17.32	11.2–25.0	98.00	96.2–99.1	8.66	0.84
>6	0.79	0.02–4.3	99.78	98.8–100.0	3.54	0.99
>7	0.00	0.0–2.9	100.00	99.2–100.0		1.00

TSI – transient symptoms associated with infarction; CI – confidence interval.

**Table 10.** The incidence of TSI in different scores of A2HD score.

Scores (incidence)	Scores (incidence)	Multiple	OR	95% CI
<1 (4.11%)	≥1 (8.07%)	6.831	9.108	3.917–21.174
<2 (4.58%)	≥2 (28.30%)	6.179	8.233	3.747–18.091
<3 (10.44%)	≥3 (41.78%)	4.002	6.157	3.996–9.489
<4 (11.46%)	≥4 (43.01%)	3.753	5.831	3.816–8.910
<5 (18.08%)	≥5 (67.39%)	3.727	9.365	4.865–18.026
<6 (19.23%)	≥6 (70.97%)	3.690	10.267	4.594–22.945
<7 (1.915%)	≥7 (50.00%)	2.282	3.563	0.221–57.374

TSI – transient symptoms associated with infarction; OR – odds ratio; CI – confidence interval.



**Table 11.** Comparison between the A2HD and ABCD2 scores.

Difference in area	0.152
Standard error a	0.0284
95% CI	0.0959–0.207
Z statistic	5.335
P value	$P < 0.0001$

CI – confidence interval.

risk for cerebral infarction by 1.893-fold (95% confidence interval: 1.643–2.181) (Tables 8, 9).

The incidence of TSI was 10.44% in patients with a score  $< 3$  and 41.78% in those with a score  $\geq 3$ . The incidence of TSI in patients with a score  $\geq 3$  was 4.002-fold higher than in those with a score  $< 3$  (odds ratio: 6.157; 95% confidence interval: 3.996–9.489) (Table 10).

#### Comparison between the A2HD and ABCD2 scores

The AUC of the A2HD score was 0.152 higher than that of ABCD2 ( $P < 0.0001$ ) (Table 11).

## Discussion

TIA is one of the acute diseases encountered in the Department of Neurology. In some patients, TIA may progress into cerebral infarction, causing irreversible neurological dysfunction. In 2007, Giles et al. [14] and Wu et al. [15] investigated early risk for stroke after TIA by meta-analysis, and their results showed that the pooled risk for stroke was 3.1–3.5% and 5.2%, at 2 and 7 days after TIA, respectively.

TSI is an independent entity between TIA and acute cerebral infarction. Prabhakaran et al. [16], Ay et al. [17] and Calvet et al. [18] found that the risk for acute cerebral infarction was 3.6–16.2% within 7 days after TSI, suggesting that TSI patients have a high risk for stroke after TSI. Mikulik et al. [19] reported 2 unique TSI cases. Neither patient received intravenous thrombolysis or interventional therapy due to resolution of symptoms at the hospital visit. These patients were admitted and diagnosed with TIA, but it progressed into acute cerebral infarction; hemorrhage transformation was found in 1 patient who then received surgical intervention for decompression, with a poor prognosis.

As outlined in the Guideline for the Early Treatment of Acute Ischemic Stroke developed by the ASS in 2013, about one-third of patients who do not receive intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) due to

resolution of stroke symptoms upon visit to the hospital will have a poor prognosis. Thus, the rapid and spontaneous resolution of neurological symptoms is not an absolute contradiction to thrombolysis, but a relative contradiction. The guideline recommends that clinicians should balance the pros and cons of intravenous thrombolysis with rtPA before its use [20]. A study from the University of Kentucky showed patients with ischemic stroke could still benefit from thrombolysis, although vascular occlusion was not shown on magnetic resonance angiograms [21]. Therefore, we need to identify these TSI patients in a short period of time and actively give them intravenous thrombolytic therapy.

Compared to patients with acute myocardial infarction, a homological indicator (such as troponin, which rapidly increases soon after myocardial infarction) cannot be used for the timely and accurate diagnosis of cerebral infarction when patients lack symptoms of TIA or cerebral infarction at the hospital. DWI has been widely accepted as the most important imaging technique for the differential diagnosis of acute cerebral infarction and TIA, and the sensitivity and specificity of DWI are 88–100% and 86–100%, respectively, for the diagnosis of acute cerebral infarction [22]. After cerebral stroke, the ischemic brain is characterized by cytotoxic edema, water diffusion decreases, and ADC values decrease, leading to hypointensities on ADC images and hyperintensities on DWI images. In experimental animals with cerebral stroke, the diffusion limitation occurred as early as 10 minutes after infarction, but in humans, it occurred 30 minutes after infarction and peaked at 8–32 hours. Thus, the diagnosis of cerebral infarction may still be missed even though DWI can be conducted within the time window for thrombolysis. Morita et al. [23] reported that DWI within 3 hours of infarction lacked diagnostic features in 32.3% of cerebral infarction patients (confirmed diagnosis was made by MRI 24 hours later). Shono et al. [24] reported that re-examination by DWI was needed when DWI that was performed 2 hours after TIA lacked diagnostic features. Brazzelli et al. [25] summarized 47 studies involving 9078 patients, reported between 1995 and 2012, and their results showed that MRI-DWI could identify new cerebral infarction in 34.3% of patients diagnosed with TIA by specialists, suggesting that TIA patients without clinical symptoms may still have TSI. In studies with a sample size  $> 20$ , 29% (23.2–34.6%) of patients were diagnosed with TSI. In this study, patients diagnosed with TIA on admission were reviewed, and 22% were diagnosed with TSI.

Thus, although cranial MRI-DWI is a key technique in the differential diagnosis of TIA and acute cerebral infarction, a diagnosis of TIA cannot depend on imaging alone. The clinician should carefully review the patient's medical history and examine for characteristics of TIA, especially when the disease is still within the time window for successful thrombolysis.

Al-Khaled et al. [26], Fujinami et al. [27], Ohara et al. [28], Hoshino et al. [29], and Miyagi et al. [30] found that the incidence of cerebral infarction in patients with TSI during hospitalization was higher than in those with general TIA, and that hemiplegia, aphasia, and AF were independent risk factors for TSI. This study also revealed that TIA characteristics and medical history were also independent predictive risk factors for TSI. There is evidence showing that patients with repeat ischemic attacks and multiple characteristics are more likely to develop cerebral infarction compared to TIA patients with minimal characteristics [31,32]. In our study, repeat ischemic attacks were also an independent risk factor for TSI.

Scoring systems have been developed for the assessment of risk for stroke after TIA, and the ABCD and ABCD2 scoring systems are the most widely used [33,34]. In our Department of Neurology, these systems have been employed for evaluating the indicators for admission and assessing therapeutic strategies. In the present study, ABCD and ABCD2 scores in TSI patients were significantly higher than in TIA patients (4 versus 3,  $P=0.000$ ). In addition, the AUC of the A2HD score was 0.766 (95% CI, 0.729–0.800) for the prediction of risk for TSI, which was significantly higher than that of the ABCD2 score (difference: 0.152, 95% CI 0.0959–0.207,  $P<0.0001$ ). Thus, we speculate that A2HD scoring is better than ABCD2 scoring for the differential diagnosis of TIA and TSI.

There were limitations in this study. First, this was a single center study, and our findings must be confirmed in additional studies with larger sample sizes. Second, medical histories were obtained from patients or their relatives, and reviews of medical histories in the emergency department might have been biased due to time constraints. Third, some patients with TIA

or mild symptoms might have been diagnosed with cerebral infarction and subsequently excluded from this study, which would have reduced the proportion of study participants with TSI. Finally, the primary purpose of this study was to identify TSI patients more easily in the emergency department, so that more stroke patients in the time window could benefit from intravenous thrombolysis. We hope to increase the long-term follow-up of these patients in the next study to see if A2HD score has a higher predictive value for stroke recurrence.

## Conclusions

This study showed that TIA patients had a high likelihood of having TSI when the patients presented with hemiplegia, aphasia, multiple seizures, and concomitant AF, especially when the A2HD score was higher than 3. Although DWI is a determinant technique for diagnosing TIA, clinicians should emphasize the review of medical history, clinical characteristics, and findings from other adjunctive examinations when DWI is unavailable or yields negative findings; this may validate the diagnosis and identify patients who are suitable for emergent thrombolysis.

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## Conflict of interest

None.

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