MEDICAL SCIENCE MONITOR

Duration of Symptom and ABCD^2 Score as Predictors of Risk of Early Recurrent Events after Transient Ischemic Attack: A Hospital-Based Case Series Study

Authors' Contribution:
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Data Collection B
Statistical Analysis C
Data Interpretation D
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Background: The aim of this study was to refine clinical risk factor stratification and make an optimal intervention plan to prevent ischemic stroke.

Material/Methods: Clinical data, including diffusion-weighted imaging (DWI) findings, were collected in a cohort of hospitalized transient ischemic attack (TIA) patients from January 2010 to December 2011. Recurrent cerebrovascular events after TIA, including recurrent TIA, minor stroke, and major stroke, were identified by face-to-face follow-up. A multivariate, ordinal, logistic regression model was used to determine significant predictors of recurrent events.

Results: Of 106 TIA patients, 24 (22.6%) had recurrent TIA and 20 (18.9%) had a stroke within 7 days. Hypertension, dyslipidemia, a history of ischemic stroke or TIA, and ABCD^2 score were significantly associated with the recurrent events after TIA (P<0.001, P=0.02, P<0.001, P=0.02). Hypertension (RR=9.21; 95% CI, 3.07–27.61, P<0.001) and duration of symptom (RR=1.10; 95% CI, 1.02–1.17, P=0.01) as an item of ABCD^2 score were highly predictive of the severity of recurrent events, whereas ABCD^2 score as a whole (P=0.18) proved to be less strongly predictive.

Conclusions: A history of hypertension and long duration of symptom independently and significantly predict severe recurrent events after TIA within 7 days, but a high ABCD^2 score was less strongly predictive of severe recurrent events.

MeSH Keywords: Ischemic Attack, Transient • Recurrence • Risk Assessment

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Background

Transient ischemic attack (TIA) is defined as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction [1]. TIA has long been regarded as the most important independent risk factor and the most useful warning signal of acute infarction [2–4]. It was reported that more than 10% of TIA patients had acute infarction within 90 days and half of them had acute infarction within 48 h after TIA [5]. Thus, it is important to refine the clinical risk factor stratification and develop an optimal intervention plan to prevent ischemic stroke. ABCD² score is a simple and efficient scale that covers the main clinical features and risk factors of TIA and has been validated for prediction of short-term risk of ischemic stroke after TIA, but some authors find it has many limitations [6–12]. The ABCD² score can predict the short-term risk of stroke after AC-TIA (anterior circulation TIA), but may have limited value in PC-TIA (posterior circulation TIA) [13]. In this prospective, hospital-based study, we compared the correlations between various risk factors and recurrent events after TIA. Using multiple statistical methods, we also explored the predictive value of ABCD² score in early recurrent events after TIA.

Material and Methods

General information of patients

All data were obtained from patients attending our hospital from January 2010 to December 2011 diagnosed with TIA according to the definition recommended by *AHA/ASA* in 2009, with a hospital stay longer than 7 days according to guideline recommended by ESO (European Stroke Organization). MRI examination (including DWI) and other examinations were needed to evaluate the risk factors in hospital. Patients with clinical symptoms lasting for more than 1 h and with a corresponding lesion on the T2-weighted MRI were excluded. After being admitted into hospital, antiplatelet therapy and statins were prescribed according to guidelines recommended by the NSA (National Stroke Association).

Characteristics of TIA events and risk factors were recorded by an experienced neurologist. The ABCD² score was calculated based on the characteristics of TIA by another investigator blind to the prognosis, as follows: age >60 years=1, blood pressure >140 systolic and/or >90 diastolic mm hg=1, clinical features (unilateral weakness=2, speech disturbance=1), duration of symptoms (≥ minutes=2, 10 to 59 minutes=1, <10minutes=0), and diabetes=1. Early prognosis within 7 days after TIA was assessed by another experienced physician, and classified as "no recurrent events", "recurrent TIA", "minor stroke", or "major stroke". A recurrent TIA was defined as a new neurologic

deficit in patients who had completely recovered from the initial symptoms before; with a duration <24 h and without corresponding lesions on MRI images obtained 6 h after the recurrent events. A recurrent stroke was defined as a new neurologic deficit with a corresponding new lesion on MRI obtained 6 h after the recurrent events. A "minor stroke"[14] was defined as a stroke with baseline NIHSS score <3, a score 0 or 1 on every NIHSS score item, except level of consciousness items (items 1a to 1c), which must be 0. Other strokes were regarded as "major stroke". This study was approved by the ethics committee of Shanghai Tenth People's Hospital of Tongji University.

MR protocol and criteria

All subjects were imaged with a 3.0 T MR scanner (Siemens 3.0T Magnetom Verio, Medical Solutions, Erlangen, Germany) with a standard 8-channel phased-array head coil. The MR protocol consists of T1-weighted image (repetition time/echo time=2000/9), T2-weighted image (repetition time/echo time=6000/94), FLAIR (repetition time/echo time=8500/94), and DWI (motion-probing gradients in 3 directions with b factors of 1000 s/mm²) were obtained with a slice thickness of 5.5 mm in the axial plane. A focal hyperintensity in the specific area corresponding to the clinical symptoms on DWI was regarded as the sign of recurrent stroke [15].

Data analysis

All our data were analyzed with SAS 9.2. Categorical data were analyzed by χ^2 test. Measurement data were analyzed by analysis of variance (ANOVA). A multinomial logistic regression model was constructed to analyze the predictive value of risk factors for the severity of recurrent events, with Z test to compare the χ^2 values. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Baseline characteristics

We enrolled 108 patients into this study and 2 of the 108 patients were excluded because of a history of cancer. Baseline characteristics of all subjects, including the vascular risk factors, are listed in Table 1. None of the hypertension or diabetes patients had organ damage.

Relationship between the risk factors of TIA and recurrent events

At 7 days after TIA, 24 (22.6%) patients had recurrent TIA. Twenty (18.9%) patients had recurrent stroke, of which 14 had minor stroke and 6 had major stroke. Risk factors of TIA and

Table 1. Demographic and baseline characteristics of all the subjects.

Items	Value
Age, years	67.5±11.1
Male, n (%)	70 (66.0)
Hypertension, n (%)	62 (58.5)
Diabetes or impaired glucose tolerance, n (%)	26 (24.5)
Dyslipidemia, n (%)	34 (32.1)
A history of cerebral infarction or TIA, n (%)	44 (41.5)
Current smoking, n (%)	38 (35.9)
Current drinking, n (%)	31 (29.3)
A family history of cerebral infarction or TIA, n (%)	9 (8.5)
A history of cardiovascular disease, n (%)	14 (13.2)
During of symptom, min	38.7±92.3
ABCD² score	3.76±1.09

ABCD² score were investigated within different categories of prognosis of TIA. The overall comparison and multiple comparisons among different prognoses showed that the proportions of hypertension, dyslipidemia, and history of cerebral infarction of TIA increased with the severity of recurrent events. Compared with patients with no recurrent events, these proportions were all higher in patients with recurrent events. The results also show that ABCD² score increased with the severity of recurrent events (Table 2).

Relationship between different items of ABCD² score and the severity of recurrent events

Based on the results in Table 2 showing that ABCD² score increased with the severity of recurrent events, we further analyzed the relationship between different items of ABCD² score and the severity of recurrent events. The results show that only duration of symptom increased with the severity of recurrent events (P<0.001) (Table 3).

The predictive value of duration of symptom for the severity of recurrent events

In this part, we constructed a multivariate, stepwise, logistic regression model to analyze the predictive value of duration of symptom as an item of ABCD² score for the severity of recurrent events. "No recurrent events", "recurrent TIA", "minor stroke", and "major stroke" were defined as 0, 1, 2, and 3, respectively. First, 3 variants (hypertension, dyslipidemia, and history of cerebral infarction or TIA) related to the severity of recurrent events (Table 1), together with age and sex, were included in the equation to show the severity of recurrent events (white histogram). Second, the ABCD² score was added to the predictive equation (grey histogram). Third, duration of symptom was added to the first predictive equation (black histogram). The results showed that compared to the first predictive equation, the second equation, which included ABCD², score did not show a significant improvement of the predictive value for the severity of recurrent events, whereas the third equation, which included duration of symptom, significantly improved the predictive value for the severity of recurrent events (χ^2 47.9 vs. 34.8, P=0.01) (Figure 1).

Table 2. Relationship between risk factors of TIA and early recurrent events.

Risk factors	No recurrent events (n=62)	Recurrent TIA (n=24)	Minor stroke (n=14)	Major stroke (n=6)	F value/χ^2	P value
Age, years	67.92±11.09	65.4±13.27	68.5±8.25	68.5±10.27	0.39	0.68
Male, n (%)	39 (62.9)	15 (62.5)	10 (71.4)	6 (100.0)	3.67	0.30
Hypertension, n (%)	24 (38.7)	21 (87.5)	11 (78.6)	6 (100.0)	24.89	<0.001
Dyslipidemia, n (%)	14 (22.6)	14 (58.3)	4 (28.6)	2 (33.3)	10.24	0.02
Current amoking, n (%)	27 (43.6)	8 (33.3)	2 (14.3)	1 (16.7)	5.45	0.14
Current drinking, n (%)	23 (37.1)	5 (20.8)	1 (7.1)	2 (33.3)	6.02	0.11
History of cerebral infarction or TIA, n (%)	0 (0.0)	7 (29.2)	1 (7.1)	1 (16.7)	19.51	<0.001
Family history of cardiovascular diseases, n (%)	6 (9.7)	4 (16.7)	3 (21.4)	1 (16.7)	0.81	0.61
ABCD² score	3.81±1.08	3.33±1.05	3.86±1.03	4.83±0.75	3.46	0.02

Table 3. Relationship between different items of ABCD² score and the severity of recurrent events.

| Items of ABCD² score	No recurrent events (n=62)	Recurrent TIA (n=24)	Minor stroke (n=14)	Major stroke (n=6)	F value/χ²	P value
Age (years)	67.9±11.1	65.4±13.3	68.5±8.3	68.5±10.3	0.35	0.79
Systolic pressure(mm hg)	141.8±16.1	146.9±9.4	144.6±13.1	152.5±5.2	1.58	0.20
Clinical features						
Dysarthria or aphasia, n (%)	21 (33.9)	2 (8.3)	2 (14.3)	1 (16.7)	7.32	0.06
Motor deficits, n (%)	40 (64.5)	12 (50.0)	7 (50.0)	4 (66.7)	2.20	0.53
Sensory deficits, n (%)	24 (38.7)	8 (33.3)	2 (14.3)	0 (0.0)	6.14	0.11
Duration of symptom (min)	15.3±17.3	32.8±33.0	90.4±158.2	182.2±266.2	9.51	<0.001
Diabetes mellitus, n (%)	15 (24.2)	8 (33.3)	1 (7.1)	2 (33.3)	3.55	0.31
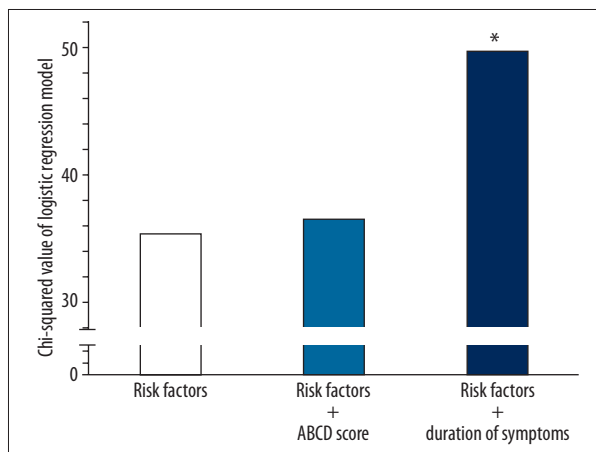
Figure 1. Predictive values of different predictive equations. Compared to the first predictive equation, the second equation, which included ABCD² score, did not show a significant improvement in predictive value for the severity of recurrent events, whereas the third equation, which included duration of symptom, significantly improved the predictive value for the severity of recurrent events. * P<0.05 *vs.* risk factors only.

Different predictive values of risk factors for the severity of recurrent events

In this part, hypertension, dyslipidemia, and history of cerebral infarction or TIA which were proven to be related to the severity of recurrent events, together with age, sex, ABCD² score, and duration of symptom, were added to the predictive equation for the severity of recurrent events. The results showed that only hypertension (RR=9.21, 95% CI=3.07–27.61, P<0.001) and duration of symptom (RR=1.10, 95% CI=1.02–1.17, P=0.01) could independently and significantly predict the severity of recurrent events, whereas no significant predictive

value of ABCD² score (P= 0.18) was found for the severity of recurrent events (Table 4).

Discussion

ABCD² score is a widely used tool for the prediction of prognosis of TIA and screening for high-risk TIA (TIA with ABCD² score>3), which was proven to be strongly predictive of recurrent TIA or stroke [16]. In a follow-up study of 500 TIA patients, Arvin et al. found that a high ABCD² score was predictive of major stroke and a low ABCD² score was predictive of recurrent TIA [17]. Our study also proved that ABCD² score increased with the severity of recurrent events. Among the items of the ABCD² score, the multivariate, stepwise, logistic regression proved that duration of symptom had the greatest contribution to the predictive value of ABCD² score for the early recurrent events. The duration of symptom could independently and significantly predict the severity of recurrent events, whereas ABCD² score as a whole was less strongly predictive for the severity of recurrent events. This difference might be caused by the transformation of duration of symptom from a continuous variable to a classified variable, which might reduce the predictive value of duration of symptom, and the weakening effect of other items of the ABCD² score. Our study showed that adding duration of symptom to the predictive equation, which included hypertension, dyslipidemia, history of cerebral infarction, and TIA, could enhance the predictive value (P=0.01), while ABCD² score could not function as duration of symptom in this model. Specifically, the risk of recurrent events increased by 5% with a 10-min increase in duration of symptom. The sensitivity analysis, which excluded some extreme values, showed that the risk of recurrent events increased by 10% with a 10-min increase of duration of symptom. Short duration of symptom was predictive of a low risk and severity of recurrent events, which could be explained by the rapid improvement of collateral circulation

Table 4. Predictive values of different risk factors for the severity of recurrent events.

	RR	95% CI	P value
Age, +10 years	0.90	0.60–1.36	0.62
Sex, 1=male; 2=female	0.54	0.21–1.39	0.20
Hypertension, (1, 0)	9.21	3.07–27.61	<0.001
Dyslipidemia, (1, 0)	1.88	0.74–4.79	0.19
History of cerebral infarction or TIA, (1, 0)	3.95	0.94–16.64	0.06
ABCD² score	0.74	0.48–1.15	0.18
Duration of symptom, +10 min	1.10	1.02–1.17	0.01

Considering that duration of symptom sometimes had extreme values, the patients with duration of symptom more than 60 min were excluded in the sensitive analysis (n=8), which proved the predictive value of duration of symptom again (RR=1.61, 95% CI=1.27–2.05, P<0.001).

and adaption of brain cells to ischemia caused by TIA [18]. It is reported that the release of glutamic acid was less in the condition of frequent transient vascular occlusion than in the condition of a relatively long occlusion [19]. This might be the mechanism of neuro-protection of short-term TIA.

It has been reported that history of hypertension is an independent risk factor of short-term cerebral infarction [20] and that that hypertension is correlated to the recurrent events of TIA. As reported, the blood pressure-based genetic risk score was associated with both baseline hematoma volume and poor clinical outcome, specifically in deep ICH [21]. Moreover, hypertension could significantly and independently influence the severity of recurrent events, which was proven by the multivariate logistic regression analysis of this study. Kovalenko et al. found that many organs can help the brain maintain normal blood pressure in acute blood loss in rats [22]. Therefore, we think the high blood pressure after TIA might be a compensatory reaction to the low blood flow volume of brain tissue, which directly suggests a condition of persistent ischemia of brain cells and a high risk of short-term cerebral infarction.

The results of the present study suggest that TIA with long duration of symptom and hypertension might need more attention

and relatively more urgent treatment; otherwise, this kind of TIA might progress to severe cerebral infarction.

We compared the predictive value of the ABCD² score as a whole and duration of symptom as an item for the severity of recurrent events, finding that duration of symptom was the main independent risk factor of the severity of recurrent events and proving its advantage for this prediction. However, due to a small sample size, we cannot make further conclusions about the predictive values of different risk factors and items of the ABCD² score, such as the predictive values for time-point of recurrent events. A more strictly designed study with larger sample size is required.

Conclusions

A history of hypertension and long duration of symptom both independently and significantly predict severe recurrent events after TIA in 7 days, while a high ABCD² score was less strongly predictive of severe recurrent events. Our findings provide evidence that the ABCD² score may predict recurrent TIA and likelihood of becoming a stroke after TIA, and also may help in clinical treatment of TIA.

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