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ORIGINAL ARTICLE

The ABCD2 score may underestimate the short-term risk of stroke in Chinese population: A meta-analysis

Tingting Chu [1,2*], Weidong Yu [3*], Yingying Wang [1], Na Guo [1], Jinting He [1], Yankun Shao [1], Jing Mang [1], Zhongxin Xu [1]

1 Department of Neurology, China-Japan Union Hospital of Jilin University, Changchun, China
2 Department of Neurology, the 4th Hospital of Harbin Medical University, Harbin, China
3 Department of Neurosurgery, China-Japan Union Hospital of Jilin University, Changchun, China

* *These authors contributed equally*

Correspondence to: Jing Mang
Department of Neurology, China-Japan Union Hospital of Jilin University
Changchun 130033, China.
TEL: +86-15844031118; FAX: +86-431-84641026; E-MAIL: mangjing@jlu.edu.cn

Zhongxin Xu
Department of Neurology, China-Japan Union Hospital of Jilin University
Changchun 130033, China.
TEL:+86-13180802999;FAX:+86-431-84995820;E-MAIL:xuzhongxin999@aliyun.com

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Abstract

OBJECTIVES: The ABCD2 score has been commonly used to triage patients with transient ischemic attack (TIA) who are at high risk for imminent stroke. However, its accuracy in predicting short-term stroke risk among TIA patients in China remains unclear.

METHODS: All eligible studies published up to May 2014 were identified by searching Medline, PubMed, Embase, the China Knowledge Resource Integrated Database (CNKI) and the China Biological Medicine Database (CBM-disc), as well as unpublished articles manually scanned. The strength of the associations between treatments and outcomes was estimated by incorporated risk ratios (RRs) and 95% confidence intervals (CIs) using the Mantel–Haenszel statistical method.

RESULTS: Eight and 32 studies, which validated the value for predicting the risk of stroke 2 and 7 days after TIA respectively, were included. We calculated the RRs and CIs for 2- and 7-day prediction for stroke (low: RR=0.43, 95% CI=0.17–1.10, I^2=0%; moderate: RR=0.42, 95% CI=0.26–0.67, I^2=0%; high: RR=0.32, 95% CI=0.21–0.48, I^2=0%; and low: RR=0.29, 95% CI=0.20–0.44, I^2=0%; moderate: RR=0.27, 95% CI=0.23–0.33, I^2=0%; high: RR=0.22, 95% CI=0.18–0.27, I^2=1%).

CONCLUSIONS: This meta-analysis indicated that the ABCD2 score may highly under-predict the short-term occurrence of stroke after TIA for the Chinese population compared with the original model derived from Caucasian populations, which may lead to neglect of the short-term risk for stroke in the clinical practice.

INTRODUCTION

Approximately 20% of strokes are preceded by transient ischemic attacks (TIAs) according to carefully conducted population-based studies (Easton *et al.* 2009). Two clinical prediction rules (CPRs), the ABCD system and the California rule, were developed to assist clinicians in quantifying the short-term risk of stroke after TIA. In 2007, these scores were unified and refined to form the ABCD2 rule (Rothwell *et al.* 2005; Johnston *et al.* 2000; Johnston *et al.* 2007). The ABCD2 rule is recommended for use in several national guidelines and management strategies based on different populations.

Although novel CPRs, such as ABCD3, have already been derived and used, the ABCD2 score is still the most common CPR for prediction of stroke in China. CPRs always have the most high-value prediction for the original study population. While there have been some independent validation studies, which have confirmed the effectiveness of the ABCD2 score in China compared with the original study population, its predictive value for the Chinese population remains to be determined.

In this population-based study, we systematically reviewed studies that have validated the predictive value of the ABCD2 score in China during the last 6 years. We found that the ABCD2 score highly underpredicted the occurrence of short-term stroke after TIA. Our results suggest that, compared with the population (Western countries) of its initial derivation study, the ABCD2 rule may not accurately reflect the risk of stroke in China as a middle-income country.

MATERIALS AND METHODS

Search strategy

We carried out a comprehensive search of the literature by following the PRISMA Statement (Moher *et al.* 2009). Medline, PubMed, Embase, the China Knowledge Resource Integrated Database (CNKI), and the China Biological Medicine Database (CBM-disc) were searched for studies published up to May 2014. In addition to the online search, references from reviews and original unpublished articles were also manually scanned to identify further studies. No language restrictions were applied. The search terms were "transient ischemic attack" OR "TIA", and "cerebrovascular accident" OR "CVA" OR "stroke", and "ABCD" OR "score" OR "prediction" OR "prognosis" OR "risk".

Inclusion criteria. Studies included in the analysis had to meet all of the following criteria. (i) Patients were diagnosed with TIA and were at least 18 years old. (ii) For diagnostic criteria, TIA was diagnosed according to the diagnostic criteria in 2002 (Albers *et al.* 2002). (iii) The ABCD2 score was used for the prediction of stroke. (iv) For observation points, 2 or 7 days after TIA were included. (v) Studies of minor stroke or neurological deficit as the first symptom lasting for greater than 24 hours were excluded. (vi) Duplicate published research data were only used once.

Data extraction and quality assessment

Data extraction and quality assessment were independently performed by 2 reviewers (Chu T and Mang J). Two reviewers assessed the internal and external authenticity of each study. Evaluation included background/principle, study objective, study design, study objective, study variables, data source, sample size, statistical methods, study results, and study limitations. Any disagreements between the reviewers were discussed with the supervisor (Xu Z) to achieve a consensus.

Data analysis

The initial derivation study of the ABCD2 rule was used as a predictive model against which subsequent validation studies were compared. In addition, the data were divided into 3 subgroups (low-risk group: 0–3 points, moderate-risk group: 4–5 points, and high-risk group: 6–7 points), which were then assessed. Meta-analysis was performed using Review Manager (version 5.0, provided by The Cochrane Collaboration). The strength of the associations between treatments and outcomes was estimated by incorporated risk ratios (RRs) and 95% confidence intervals (CIs), which were measured by the Mantel-Haenszel statistical method. The RR score of 1 represents an accurate prediction by the ABCD2 rule, <1 represents under-prediction and >1 represents over-prediction. The heterogeneity between different studies or different subgroups was estimated using Cochran's Q test and the I^2 statistic. A significant Q test ($p \leq 0.1$) or I^2 >50% indicated significant heterogeneity. If significant heterogeneity existed, the random effects model was used for meta-analysis; otherwise, the fixed effects model was used. The presence and extent of publication bias in meta-analysis was assessed by visual inspection of the funnel plots. Both fixed and random effects were undertaken to assess the sensitivity of the enrolled studies.

RESULTS

Identification and characteristics of the studies

We retrieved a total of 2600 studies after searching from the online database (n=2589) and manual searching (n=11). After excluding 13 repeats, we obtained 2587 studies. Finally, we included 33 studies after screening the summaries, abstracts, and full text (Lin 2010; Lv *et al.* 2010; Ma *et al.* 2009; Wu *et al.* 2010; Yang 2011; Zhou & Wei 2009; Wang *et al.* 2010; Zhang *et al.* 2009; Liu *et al.* 2010; Tan *et al.* 2009; Liu *et al.* 2009; Sun 2010; Tu *et al.* 2010; Zhang *et al.* 2012; Li & Li 2011; Li & Liu 2011; Yu & He 2011; Zhu & Lu 2011; Tong & Liu 2012; Zhou 2012; Chen & Ye 2012; Cha & Wang 2012; Wang & Wan 2012; Xi & Wang 2013; Chang 2013; Lai *et al.* 2013; Lv & Wang 2013; Luo & Wu 2013; Li & Qian 2013). A

total of 32 studies mentioned 7 days and 8 studies mentioned 2 days as the observation time points (Figure 1). A total of 5074 patients were included and they were from 16 different provinces of China (Table 1).

Quality of the studies

The integrated quality of the 33 studies was relatively "not good". A few studies did not report how to use the blinding method. Some of the studies did not mention

Tab. 1. Characteristics of the studies included in the meta-analysis.

Included Study	Region	Patient Type	Study Type	Sample Size	Time End
Xue Lin, 2010 (9)	Jiangsu	Hospital	Retrospective	120	7 Days
Xiangxiong Lv, 2010 (10)	Zhejiang	Hospital	Retrospective	94	7 Days
Ting Ma, 2009 (11)	Heilongjiag	Hospital	Retrospective	432	7 Days
Bin Wu, 2010 (12)	Zhejiang	Hospital	Retrospective	176	7 Days
Guohua Yang, 2011 (13)	Hebei	Emergency Hospital	Retrospective	125	7 Days
Faming Zhou, 2009 (14)	Hunan	Hospital	Retrospective	96	7 Days
WeiqiangWang, 2009 (15)	Anhui	Hospital	Retrospective	179	7 Days
Zhen Zhang, 2009 (16)	Shandong	Hospital	Retrospective	148	2/7/90 Days
Hongshun Liu, 2010 (17)	Hebei	Hospital	Prospective	182	2/7/30 Days
Lu Zhao, 2009 (18)	Henan	Outpatient Hospital	Prospective	136	2/7Days
Chunpeng Xu, 2008 (19)	Jilin	Hospital	Retrospective	89	2/7Days
Shuhua Liu, 2009 (20)	Hebei	Emergency	Prospective	102	2 Days
Cuilan Lv, 2010 (21)	Neimenggu	Hospital	Prospective	98	2/7 Days
Weina Ju, 2010 (22)	Jilin	Hospital	Retrospective	680	7 Days
Xinshuai Sun, 2010 (23)	Henan	Emergency	Retrospective	270	7 Days
Yanyang Tu, 2011 (24)	Shanxi	Outpatient Emergency Hospital	Retrospective	362	2/7Days
Shuchun Lin, 2010 (25)	Liaoning	Hospital	Retrospective	97	2/7 Days
Fazhong Zhang, 2012 (26)	Shandong	Hospital	Retrospective	126	7 Days
Mingjun Li, 2011 (27)	Henan	Outpatient Hospital	Prospective	81	7 Days
Xiaohong Li, 2011 (28)	Liaoning	Hospital	Prospective	112	7 Days
Huiqing Yu, 2011 (29)	Hebei	Hospital	Retrospective	100	7 Days
Yingbiao Zhu, 2011 (30)	Zhejiang	Hospital	Retrospective	120	7 Days
Xingjian Tong, 2012 (30)	Liaoning	Hospital	Retrospective	132	7 Days
Song Zhou, 2012 (32)	Anhui	Hospital	Retrospective	95	7 Days
Jianguang, Chen 2012 (33)	Zhejiang	Hospital	Retrospective	83	7 Days
Dexi Cha, 2012 (34)	Anhui	Hospital	Retrospective	118	7/90 Days
JindingWang, 2012 (35)	Jiangxi	Hospital	Retrospective	106	7 Days
Hongyan Xi, 2013 (36)	Hebei	Hospita	Retrospective	96	7 Days
XinrongChang, 2013 (37)	Guangxi	Hospital	Retrospective	110	7 Days
Jianqiang Lai, 2013 (38)	Jiangxi	Hospital	Retrospective	60	7 Days
Fengqiong Lv, 2013 (39)	Hebei	Hospital	Retrospective	148	7 Days
Rong Luo, 2013 (40)	Sichuan	Hospital	Retrospective	87	7 Days
Weiyuan Li, 2013 (41)	Yunnan	Hospital	Retrospective	114	7 Days

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detailed exclusion and inclusion criteria. Some studies even used unsuitable statistical methods to evaluate the value of the ABCD2 score .The external validity of the studies was good. The main shortcoming in relation to internal validity was inadequate reporting of blinding in the included studies.

Value of the ABCD2 score within 2 days

Eight studies (n=1214) reported the 2-day risk of stroke. The ABCD2 score could predict the occurrence of stroke at 2 days across all 3 risk strata, but highly under-predicted the risk (low: RR=0.43, 95% CI=0.17–1.10, I^2=0%; moderate: RR=0.42, 95% CI=0.26–0.67, I^2=0%; and high: RR=0.32, 95% CI=0.21–0.48, I^2=0%; Figure 2).

Value of the ABCD2 score within 7 days

Thirty-two studies (n=4972) reported the 7-day risk of stroke. The ABCD2 score could predict occurrence of stroke at 7 days across all 3 risk strata, but highly under-predicted the risk (low: RR=0.29, 95% CI=0.20–0.44, I^2=0%; moderate: RR=0.27, 95% CI=0.23–0.33, I^2=0%; and high: RR=0.22, 95% CI=0.18–0.27, I^2=1%; Figure 3).

Analysis of publication bias

All of the 6 funnel plots were symmetrical. This indicates that the publication bias of the enrolled studies was small (Figure 4).

Sensitivity analysis

There is no significant difference in application of the fixed and random effects models, which confirmed that the sensitivity of the results was high.

DISCUSSION

Although stroke is the second leading cause of death worldwide, it carries an enormous financial burden in most middle-income countries, including China (Krishnamurthi *et al.* 2013). Approximately 20% of strokes are preceded by TIAs in carefully conducted population-based studies (Easton *et al.* 2009). During the last 6 years, the ABCD2 score has been widely used to help provide a more efficient method of predicting the risk of post-TIA stroke in China. The effectiveness of the ABCD2 score has been proved by many validation studies. However, the accuracy of the ABCD2 score has not been systematically reviewed in the Chinese population. This score needs to be reviewed in the Chinese population because CPRs always have the most high-value prediction for the original study population, which is the Western population in the case of the ABCD2 score.

In this meta-analysis, we systematically reviewed studies that validated the predictive value of the ABCD2 score at 2 and 7 days after TIA. To quantify estimation of the risk of post-TIA stroke by the ABCD2 score, we compared the observed number of strokes with the predicted number (using the proportion of incidence in the ABCD2 derivation study for calculations). However, we found that the ABCD2 score significantly under-predicted the risk of stroke across 3 strata in the Chinese population compared with its derivation study population. Our results suggest that the risk of stroke is underestimated when solely relying on

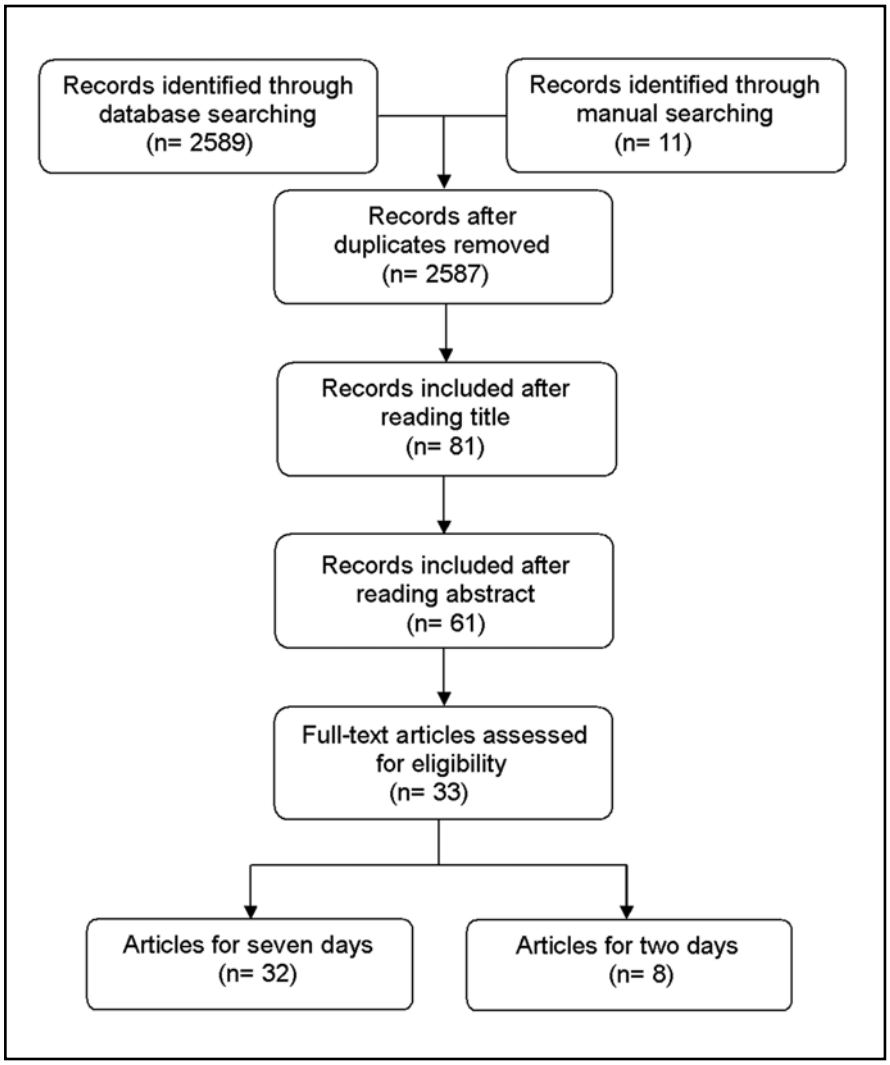

Fig. 1. Study flow diagram of the applied search strategy.

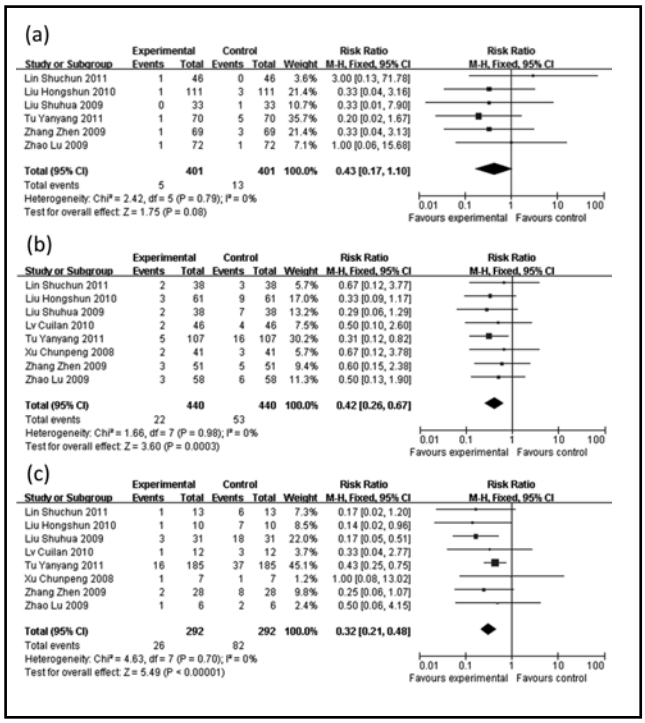

Fig. 2. (a): Prediction of the 2-day risk of stroke (low risk);
(b): Prediction of the 2-day risk of stroke (moderate risk);
(c): Prediction of the 2-day risk of stroke (high risk).

the ABCD2 score as a CPR for decision-making in the Chinese population**.**

Our conclusions are different from those in most of the validation studies in China, which may give rise to debate regarding the usefulness of the ABCD2 score. The conclusions of former validation studies always depended on the occurrence of observed stroke. Although this can demonstrate proper trends across different strata in the cohort, the prediction strength (observed number versus predicted number) remains untested. The risk of stroke within 2 days after TIA in our analysis after merging the studies was 2.7% in the low-risk group, 12% in the moderate-risk group, 28.1% in the high-risk group, and for 7 days, it was 5.2% in the low-risk group, 23.6% in the moderate-risk group, and 49.8% in the high-risk group. Interestingly, our results are consistent with some findings of studies outside of China, which found that although patients with an ABCD2 score greater than 4 are more likely to develop recurrent stoke in the short term, those with a lesser score still harbor a considerable risk for stoke (Chardoli *et al.* 2013). However, in our analysis, the risk of stroke at 2 and 7 days across the 3 strata was even higher than that in this previous study (Chardoli *et al.* 2013). Taking into consideration the rising incidence of stroke in China (Liu *et al.* 2011; Zhao *et al.* 2013), making a timely assessment of the ABCD2 rule is important because it has been validated to be useful and accurate in previous studies in China for the last 6 years.

Various reasons may be responsible for potential underestimation of risk of stroke in the clinic. First,

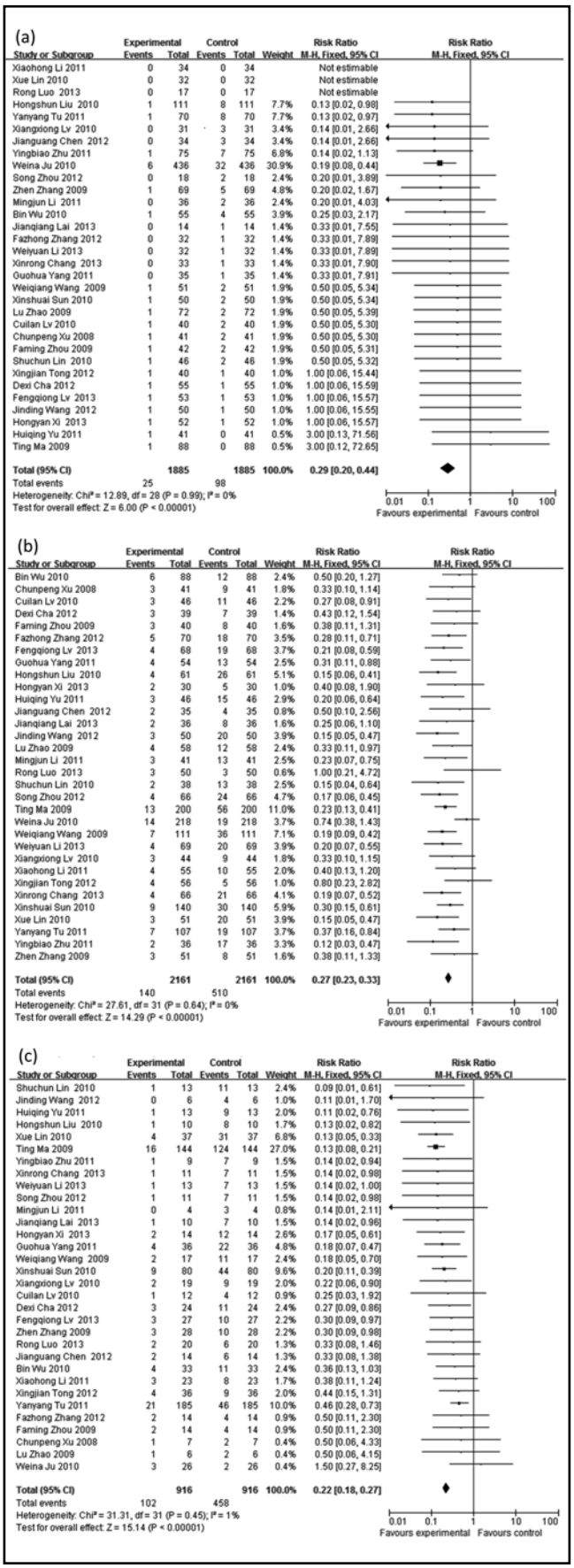

Fig. 3. (a): Prediction of the 7-day risk of stroke (low risk);
(b): Prediction of the 7-day risk of stroke (moderate risk);
(c): Prediction of the 7-day risk of stroke (high risk).

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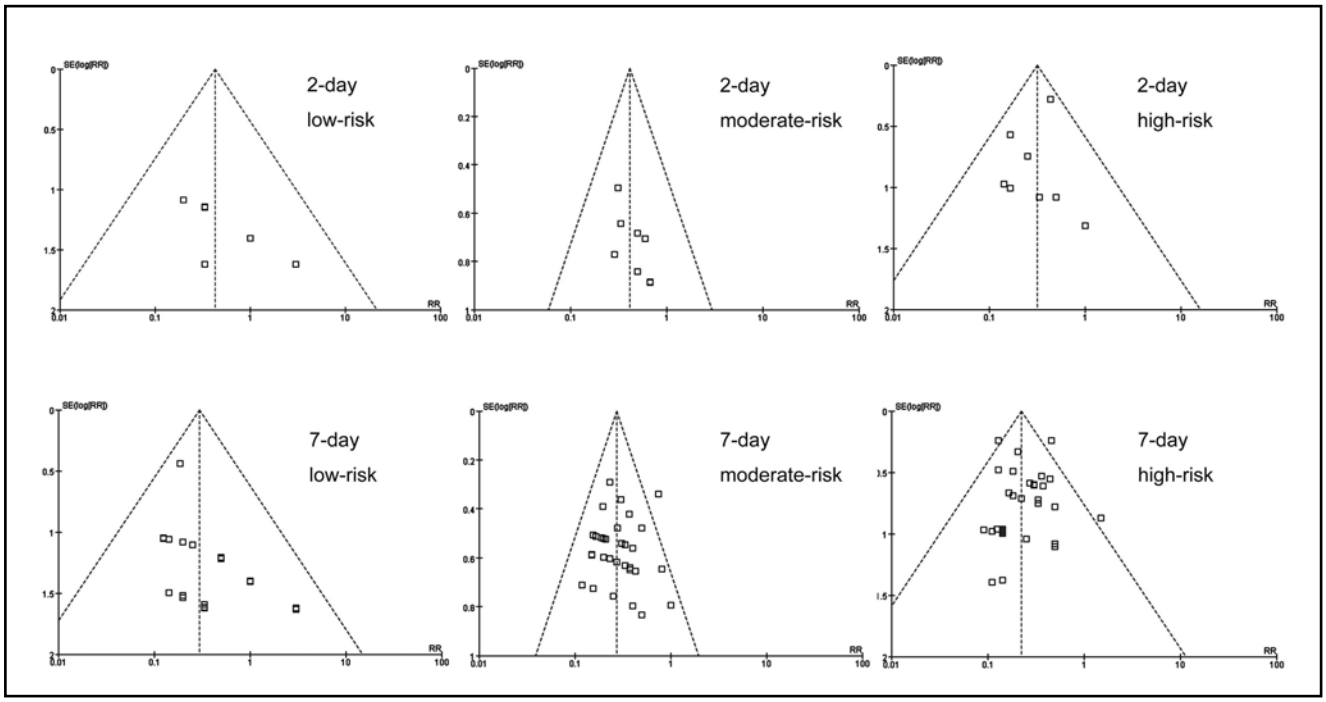

Fig. 4. Funnel plot for publication bias.

Chinese physicians may assume the role of specialized neurologists when using the ABCD2 score, but some important risk factors, especially assessment of carotid stenosis and blood flow from images, may not be considered together. The ABCD3 and ABCD3-I scores, which are superior to the ABCD2 score, have been derived and used outside of China. However, many Chinese studies of these CPRs lacked assessment of images for community TIA patients in most parts of China (Kiyohara *et al.* 2014). Second, the population in our included studies was inpatients who often had more serious clinical symptoms and more risk factors when they came to the doctor compared with the general population included in Western studies. China now faces major challenges in stroke care, such as a lack of a national policy in stroke prevention (recurrence rate of stroke remains high at 11.2%) (Liu *et al.* 2011), which implies that Chinese medical levels still lag behind developed countries. Under these conditions, introducing the ABCD2 score as an approved CPR for prevention of stroke may lead to clinical neglect, especially in community hospitals. Our findings suggest that use of the ABCD2 score in China may provide the convenience of prediction of stroke at the expense of its accuracy.

Several limitations of this study deserve mention. The studies included in this meta-analysis were not randomized controlled trials and the methodological quality was generally poor. Although the methods of the included studies were not unified as randomized controlled trials, most were still performed according to the national stroke guidelines. We attempted to use scientific methods to filter out articles of relatively high value, which were analogous to a type of quasi-randomized controlled trial for the reliable data that they presented. Our conclusions, which were based on former validation studies, may not be attributed to bias.

In conclusion, The ABCD2 score may highly underpredict the short-term occurrence of stroke after TIA for the Chinese population compared with the original model derived from Caucasian populations. This may result in neglect of the short-term risk for stroke in the clinical practice.

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