

Original Article

CHA2DS2-VASc can better predict short-term prognosis in acute ischemic stroke patients with non-valvular atrial fibrillation

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Abstract: Background: CHADS2 and CHA2DS2-VASc scores are validated tools for assessing stroke risk in patients with atrial fibrillation. We aimed to investigate the correlation of CHA2DS2-VASc and CHADS2 scores with short-term prognosis in acute ischemic stroke patients with non-valvular atrial fibrillation (NVAf) in elderly patients. Methods: A total of 216 patients with non-valvular atrial fibrillation were enrolled in this study. Consecutive ischemic stroke patients with non-valvular atrial fibrillation who were hospitalized within 7 days after stroke were registered. Patients were divided into 3 groups on the basis of CHADS2 scores (0, 1, 2 to 6) and CHA2DS2-VASc score (0, 1, 2 to 9). And recovery was assessed by modified Rankin Scale (mRS) at 3 months follow-up (mRS \leq 2 reflected good prognosis and mRS \geq 3 implicated unfavorable outcome). After screening the risk factors affecting prognosis using univariate analysis, the correlation of CHADS2 and CHA2DS2-VASc scores for short-term prognosis was estimated using Logistic regression model. Results: A total of 206 cases (95.3%) were included in the study. The groups with CHADS2 scores of 0, 1, and 2-6 points contained 31, 83, and 92 cases, respectively, while the groups with CHA2DS2-VASc scores of 0, 1, and 2-9 points had 22, 78, and 106 cases, respectively. There were 89 (43.2%) patients with good prognoses and 117 (56.8%) with poor prognoses. The proportion of high-risk group was significantly higher ($P<0.01$) while that of low-risk group significantly lower as stratified by CHA2DS2-VASc score than by CHADS2 scores ($P<0.01$). High-risk (≥ 2) CHADS2 and CHA2DS2-VASc scores are both associated with 3-month poor functional outcomes (CHADS2: OR 2.85, 1.32-4.05; CHA2DS2-VASc: OR 3.24, 1.32-6.98) after adjusting for baseline differences in age, sex and neurological impairment. The CHA2DS2-VASc score is better than the CHADS2 score in estimating 3-month stroke outcomes in acute ischemic stroke patients with nonvalvular atrial fibrillation. Conclusions: The CHA2DS2-VASc score appears to be a simple tool for identifying patients at lower risk of poor outcomes and serious cardiac complications within 3 months following ischemic stroke in patients with AF.

Keywords: Stroke, atrial fibrillation, CHADS2 score, CHA2DS2-VASc score, prognosis

Introduction

Atrial fibrillation (AF) is one of the most common clinical arrhythmias, with a prevalence of 1% in the general population, but it increases with age and can be as high as 9% for individuals 80 years old and older [1]. Domestic data report that the risk of non-AF stroke in the general population is 2.36%, while the annual prevalence of stroke in patients with AF is 4.1%; 17.5% of strokes occur among hospitalized patients with AF each year [2, 3]. Therefore, the risk of ischemic stroke among patients with AF is significantly higher than that for patients without AF, and AF-related ischemic stroke is

associated with higher morbidity and mortality rates. Thus, an accurate assessment of the risk of stroke in patients with non-valvular atrial fibrillation (NVAf) followed by personalized prevention measures is highly clinically relevant [2, 3]. For current clinical practice, many researchers have proposed various methods for predicting the risk of ischemic stroke in patients with AF; the CHADS2 and CHA2DS2-VASc scores are the two most widely used [4, 5]. Conventionally, the CHADS2 score has been used for risk assessment, while the CHA2DS2-VASc scoring system is a new method for assessing the risk of stroke in patients with NVAf, and some researchers believe that the latter is a better

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prediction method [6]. Research has shown that the CHA2DS2-VASc scoring system can more accurately assess the risk of stroke in patients with AF [7]. However, the differences between these two methods for assessing the short-term prognosis of patients with AF and stroke have not been evaluated. Therefore, the objective of this study was to investigate the predictive value of the CHADS2 and CHA2DS2-VASc scores for assessing the short-term prognosis of elderly patients with AF and ischemic stroke in order to evaluate the advantages and disadvantages of both methods.

Materials and methods

General information

In the geriatric ward of Xuanwu Hospital of Capital Medical University, there were 216 patients at least 65 years of age with AF who were diagnosed with ischemic stroke from June 2011 to August 2013 (124 men [57.4%]; 92 women [42.6%]; age range, 65-92 years; mean age, 82.88 ± 5.68 years). Inclusion criteria for our study included: cases of AF diagnosed by electrocardiogram (ECG) results on admission or 24-h Holter monitoring, except for cases of rheumatic heart disease and other valvular heart disease, heart valve replacement surgery, and dilated cardiomyopathy by ECG; cases of infarction that met the diagnostic criteria for ischemic stroke [8], clinical signs and symptoms of stroke, and the responsible lesion was found via brain computed tomography (CT) and/or magnetic resonance imaging (MRI); and the course of the disease was less than 7 days. All other cases associated with neurological diseases, transient ischemic attack (TIA), severe valvular heart disease, chronic infectious diseases, recent infection or surgery, cancer, severe damage to vital organs, or circulatory system diseases were excluded from the study. This research was approved by the Committee of Research Ethics of our hospital, and all participants or their authorized representatives provided informed consent to participate.

Methods

Data collection: The following baseline data were collected for each patient: sex, age, AF type, and anticoagulant therapy (primarily antiplatelet and anticoagulant drugs). We also

noted the laboratory diagnosis (based on results of the first examination after admission) and physical examination data, which included blood pressure, heart rate, liver and kidney function results, glucose levels, lipid levels, blood coagulation data, ECG results, Holter ECG monitoring results, Doppler ECG results, and cranial CT/mRI results. Finally, we also noted any history of stroke, coronary heart disease, hypertension, diabetes, heart failure, and kidney disease.

Evaluation: The CHADS2 score [9] was based on the presence of heart failure, hypertension, diabetes, and age ≥ 75 years. One point was given for each of those factors. Two points were given for a history of stroke or a history of ischemia. The total score ranged from 0 to 6 points.

The CHA2DS2-VASc score [9] was based on the presence of heart failure, hypertension, age of 65-74 years, diabetes, vascular disease, and female sex. One point was given for each of these factors. Two points were given for age ≥ 75 years or a history of stroke. The total score ranged from 0 to 9 points.

Stroke risk assessment was based on the patient data collected. Patients were categorized into three groups based on CHA2DS2-VASc and CHADS2 scores: the low-risk group (0 points), moderate-risk group (1 point), and high-risk group (≥ 2 points).

Prognostic assessment: During hospitalization, patients were treated according to conventional medical practice after assessment. Outpatient follow-ups were carried out regularly after the patients were discharged from the hospital. The outpatient follow-ups were performed by a well-trained postgraduate candidate in neurology, who used telephone and in-person blinded interviews to assess the medical situations of the patients three months after being discharged from the hospital. A modified Rankin Scale (mRS) assessment was used to assess prognosis. mRS scores of 0-2 points were considered to indicate a good prognosis, while scores of 3-6 points were considered to indicate a poor prognosis.

Statistical methods

SPSS 17.0 statistics software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

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Table 1. Baseline characteristics of patients ($\bar{x}\pm s$)

Variable	CHADS2			ANOVA/ χ^2	CHA2DS2-VAS			ANOVA/ χ^2
	Low-risk group (n=31)	Moderate-risk group (n=83)	High-risk group (n=92)	P value	Low-risk group (n=22)	Moderate-risk group (n=78)	High-risk group (n=102)	P value
Age	69.2±4.7	75.9±7.7	85.6±5.3	0.02	68.9±3.2	76.6±5.4	84.9±4.6	0.01
Systolic BP (mm Hg)	130.5±22.1	131.0±25.5	138.4±38.6	0.57	130.0±19.5	132.5±26.3	136.6±34.1	0.52
Diastolic BP (mm Hg)	76.5±12.3	78.6±15.1	81.0±16.5	0.78	80.6±10.5	80.5±13.2	81.5±18.6	0.89
Heart rate (beats/min)	67.1±12.2	68.4±12.4	69.2±12.1	0.52	66.5±12.4	69.3±12.3	70.2±12.6	0.45
Cr (mmol/L)	66.5±11.2	89.4±12.5	10.23±28.0	0.02	64.±122.6	78.5±16.5	126.0±26.2	0.01
BUN (mmol/L)	5.49±1.34	5.62±1.17	5.99±1.02	0.68	5.46±1.32	5.59±1.22	5.95±1.12	0.56
TC (mmol/L)	4.09±0.82	4.17±1.16	4.36±1.00	0.36	4.03±0.78	4.16±1.03	4.54±1.06	0.38
TG (mmol/L)	1.38±0.38	1.59±0.24	1.88±0.26	0.02	1.26±0.28	1.58±0.32	1.94±0.46	0.01
Fasting glucose (mmol/L)	7.9±4.1	8.2±4.5	9.6±5.3	0.04	7.2±3.90	8.1±4.6	9.8±5.4	0.02
LDL-cholesterol (mmol/L)	2.2±1.0	2.3±1.2	2.8±1.5	0.03	2.1±0.9	2.2±1.2	2.9±1.7	0.02
BNP (ng/L)	124±45	369±64	767±97	0.01	102±38	287±56	816±89	0.00
hs-CRP (mg/L)	1.06±0.31	1.45±0.58	1.72±1.05	0.08	1.12±0.35	1.56±0.62	1.92±1.03	0.06
WBC ($10^9/L$)	5.24±1.78	5.32±1.65	6.58±2.46	0.07	5.36±1.56	5.41±1.87	6.73±2.52	0.06
Hemoglobi (g/L)	130.6±3.1	130.2±6.4	132.8±8.2	0.29	128.5±4.2	131.2±7.6	136.3±8.6	0.17
LVEF (%)	63.34±9.00	63.01±9.76	62.08±8.34	0.32	63.58±9.12	63.07±9.47	62.18±7.34	0.28

Table 2. Clinical data comparisons of patients with 3-month good and poor prognoses (n, %)

Variable	Good functional outcomes (mRS \leq 2) (n=89)	Poor functional outcomes (mRS \geq 3) (n=117)
Age ($\bar{x}\pm s$)	72.8±7.7 ^b	81.6±8.0
Female [(n (%))]	33 (37.1) ^a	56 (47.9)
Smoking [(n (%))]	29 (32.6)	41 (35.0)
Hyperlipidemia [(n (%))]	32 (36.0)	43 (36.8)
Hypertension [(n (%))]	56 (62.9)	87 (74.4)
Diabetes mellitus [(n (%))]	27 (30.3) ^a	58 (49.6)
Coronary heart disease [(n (%))]	49 (55.1)	68 (58.1)
Heart failure [(n (%))]	10 (11.2) ^a	28 (23.9)
Stroke/TIA [(n (%))]	8 (9.0) ^b	35 (29.9)
peripheral vascular disease [(n (%))]	18 (20.2)	30 (25.6)
CHADS2 ($\bar{x}\pm s$)	1.29±0.82 ^a	3.42±1.62
CHA2DS2-VASc ($\bar{x}\pm s$)	2.65±1.06 ^a	5.35±1.79

Compared with patients of poor functional outcomes, ^aP<0.05, ^bP<0.01.

All measurement data were presented as mean \pm standard deviation, and all enumeration data were presented as rates. All measurement data were analyzed by ANOVA. All enumeration data were analyzed by the χ^2 test. The t-test was used to compare differences between independent groups. Data that were found to be statistically significant via univariate analysis were analyzed by a multivariate logistic regression analysis. By using the CHADS2 and CHA2DS2-VASc scores as the

grouping variables, the assessments using the CHADS2 and CHA2DS2-VASc scores were compared for their ability to predict the three-month prognosis. P<0.05 was considered statistically significant.

Results

General clinical data

A total of 216 cases of NVAF-ischemic stroke were collected; 10 cases (4.6%) were lost to follow-up. Among the 206 cases that fulfilled the inclusion criteria of this study, there were 136 cases with a history of hypertension (66.0%), 98 with diabetes mellitus (47.6%), 37 with a history of congestive heart failure (18.0%), 42 with a history stroke, TIA, or thromboembolism (20.4%), and 56 with a history of vascular disease (27.2%). Based on CHADS2 score assessments, 31 patients (15.4%) were assigned to the low-risk group (0 point), 83 (40.3%) to the moderate-risk group (1 point), and 92 (44.6%) to the high-risk group (2-6 points). Based on the CHA2DS2-VASc score assessments, 22 patients (10.6%) were assigned to the low-risk group (0 points), 78 (37.9%) to the moderate-risk group (1 point),

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Table 3. CHADS2 and CHA2DS2-VASc scores on 3-month poor prognosis [(n (%))]

		N	Poor functional outcomes
CHADS2	Low-risk group	31	13 (41.9)
	Moderate-risk group	83	42 (50.6) ^a
	High-risk group	92	62 (67.4) ^b
CHA2DS2-VASc	Low-risk group	22	7 (31.2)
	Moderate-risk group	78	36 (46.2) ^a
	High-risk group	106	74 (69.8) ^b

Compared with low-risk group, ^aP<0.05, ^bP<0.01.

and 106 (51.5%) to the high-risk group (2-9 points). According to the baseline data comparison among the three groups categorized by the two assessment methods, the mean age of the high-risk groups were the highest, while the differences in sex, smoking habits and history of hyperlipidemia were not statistically significant (**Table 1**).

Clinical data comparisons of patients with 3-month good and poor prognoses

The differences in patients' age, sex, history of stroke, and CHADS2 and CHA2DS2-VASc scores between the good and poor prognosis groups were statistically significant (P<0.05). Differences in smoking habits, hypertension, hyperlipidemia, diabetes, coronary heart disease, heart failure, and history of peripheral vascular disease were not statistically significant (**Table 2**).

CHADS2 and CHA2DS2-VASc scores on 3-month good and poor prognosis

In this study, according to the mRS score 3-months after the onset of the acute ischemic stroke, 89 patients (43.2%) were categorized into the good prognosis group, while 117 (56.8%) were categorized into the poor prognosis group. The CHADS2 scores of the good and poor prognosis groups were 1.29±0.82 points and 3.42±1.62 points (t=2.014, P=0.028) respectively, while the CHA2DS2-VASc scores for these groups were 2.65±1.06 points and 5.35±1.79 points (t=2.436, P=0.012) respectively.

There were 18 patients (58.0%) in the low-risk group based on the CHADS2 score with a good prognosis, and 13 (41.9%) with a poor prognosis.

Among patients in the moderate-risk group, 41 (46.0%) had a good prognosis, and 48 (54.0%) had a poor prognosis. Among patients in the high-risk group, 30 (34.9%) had a good prognosis, and 56 (65.1%) had a poor prognosis.

Based on CHA2DS2-VASc scores, among patients in the low-risk group, 15 (68.1%) had a good prognosis, and 7 (31.2%) had a poor prognosis. Among patients in the moderate-risk group, 42 (53.8%) had a good prognosis, and 36 (46.2%) had a poor prognosis. Among patients in the high-risk group, 32 (30.2%) had a good prognosis, and 74 (69.8%) had a poor prognosis. The ratios of patients with good and poor prognoses in each group were significantly different (**Table 3**).

Analysis of relevant factors for short-term prognosis of patients with NVAF and ischemic stroke

Univariate analysis showed that age, sex, diabetes, history of heart failure, history of stroke, and CHADS2 and CHA2DS2-VASc scores were associated with the prognosis (P≤0.01). A multivariate logistic regression analysis performed on the factors shown to be statistically significant by the univariate analysis showed that age and CHADS2 and CHA2DS2-VASc scores were each independent predictors of poor prognosis in patients after 3 months disease onset (**Table 4**).

Discussion

The use of the CHADS2 score was first proposed in 2001 to assess the risk of stroke in patients with AF. It included history of heart failure, hypertension, age ≥75 years, diabetes, history of stroke or transient ischemic attack (TIA), and other factors as risk assessment factors. The CHADS2 scoring system allows a preliminary screening for the risk factors for stroke, providing clinicians with a simple foundation and premise for anticoagulation treatment.

However, there are certain controversies related to the CHADS2 scoring system, in that subsequent studies found that some other factors were also closely related to the occurrence of ischemic stroke. One study [10] found that age was an important risk factor for stroke and that it could be used as an independent predictive

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Table 4. Multivariable logistic regression analyses testing the effect of CHADS2 and CHA2DS2-VASc score on 3-month poor functional outcomes

Risk score component	OR	95% CI	P value	
Age ≥ 65	1.89	1.07~2.74	0.03	
Hypertension	1.16	0.77~1.63	0.52	
Diabetes	0.88	0.67~1.34	0.56	
Coronary heart disease	1.28	1.02~1.95	0.06	
Stroke	1.17	0.67~1.56	0.62	
NHIS	1.78	1.27~2.56	0.00	
CHADS2	Low-risk group	1		
	Moderate-risk group	1.45	1.06~2.08	0.04
	High-risk group	2.85	1.32~4.05	0.00
CHA2DS2-VASc	Low-risk group	1		
	Moderate-risk group	1.89	1.15~3.57	0.02
	High-risk group	3.24	1.92~6.98	0.00

CI = confidence interval.

factor for ischemic stroke. Female sex was also found to be an independent risk factor for stroke [11]. In addition, other factors, such as vascular disease, can also increase the risk of stroke in patients with AF. All of these factors can be taken into consideration for a better prediction of stroke occurrence.

In order to provide a more comprehensive assessment of the risk factors for stroke, some European experts have made some modifications to the original scoring system. Lip et al. [4] proposed the CHA2DS2-VASc score to improve the CHADS2 score by including three additional risk factors: age 65-74 years old, history of vascular disease, and female sex. The CHA2DS2-VASc score was recommended by the European Society of Cardiology in 2010. The "2014 Guideline for the Management of Patients With Atrial Fibrillation" issued by the American College of Cardiology/American Heart Association [7] has recommended the use of the CHA2DS2-VASc score as a more systematic assessment of the risk of stroke that can be used to provide guidance for the treatment and precautions of patients with AF. The CHA2DS2-VASc scoring system is a more systematic and comprehensive assessment tool for predicting the risk of stroke in patients with AF. It has the advantages of taking more relevant risk factors into consideration and of allowing a more refined risk evaluation for age based on different age ranges; thus, it allows a more individualized risk evaluation [12]. More importantly,

the CHA2DS2-VASc scoring system can be beneficial to patients by not only providing a more comprehensive assessment of risk in order to identify those at high-risk for anticoagulation therapy but also by identifying and eliminating those in the low-risk group from receiving unnecessary anticoagulation treatment. Therefore, in some aspects, the CHA2DS2-VASc score is better than is the CHADS2 score in predicting the prognosis of patients with NVAF and ischemic stroke [13].

Danish researchers Olesen et al. [14] demonstrated via a cohort study that the CHA2DS2-VASc scoring system was more accurate in predicting the risk of thromboem-

bolism and stroke in patients with AF. The CHA2DS2-VASc score is not only superior to the CHADS2 score in the ability to assess stroke risk in high-risk patients with AF, but it can also more accurately assess stroke risk in low-risk patients with a CHADS2 score of 0-1 points; hence, it is better for distinguishing the "actual low-risk" patients than is the CHADS2 score. Van Staa et al. [15] conducted a follow-up study on 79,884 patients with AF for an average duration of 2.9 years, and the results confirmed that the CHA2DS2-VASc score was better than was the CHADS2 score at predicting the risk of embolic events in patients with NVAF.

By observing the 3-month, short-term prognosis of patients with NVAF and ischemic stroke, we found a significant association of both the CHADS2 score and the CHA2DS2-VASc score with the 3-month prognosis. We found that the CHADS2 and CHA2DS2-VASc scores were associated with early improvement in NVAF with ischemic stroke by looking at the rates of stroke incidence and poor prognosis in patients with NVAF with different CHADS2 and CHA2DS2-VASc scores during follow-up. The comparative scores between the groups with good and poor prognosis were statistically significantly different. There were more cases of good prognosis when scores were lower (≤ 1 points), but as scores increased (≥ 2 points), the rates of poor prognosis after 3 months also increased, accompanied by increases in the rates of serious disability and mortality. The multivariate

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logistic regression analysis showed that the CHADS2 and CHA2DS2-VASc scores were independent predictors of poor prognosis for patients with NVAF and ischemic stroke. The OR for the CHA2DS2-VASc score was higher than that of the CHADS2 score. Although the 95% CIs overlapped, they showed that the CHA2DS2-VASc score was more predictive of short-term poor prognosis in patients with NVAF and ischemic stroke. This result showed its advantages over the CHADS2 scoring system, which might be related to the inclusion of more risk factors in the CHA2DS2-VASc scoring system. Therefore, the predictive value of the CHA2DS2-VASc score for the short-term prognosis of NVAF with ischemic stroke was higher than that of the CHADS2 score. This result is consistent with the outcomes of previous studies from China and other countries [16]. Hans et al. [17] found that the CHA2DS2-VASc score was an independent predictor of severe complications and mortality in patients with NVAF with ischemic stroke by observing 6,612 patients with AF and ischemic stroke continuously for 3 months. Their study also found that the CHA2DS2-VASc score was more predictive than was the CHADS2 score in distinguishing adverse outcomes of low-risk patients. Meanwhile, another domestic follow-up study on patients with NVAF with stroke [18] found that the CHA2DS2-VASc score had a better predictive value compared to that for the CHADS2 score on the 1-year prognosis for stroke patients after stroke onset.

In summary, the risk of poor short-term prognosis for patients with NVAF with ischemic stroke is directly correlated to the risk stratification of the CHA2DS2-VASc and CHADS2 scores. When stroke occurs in patients with NVAF, the CHA2DS2-VASc scoring system is better than is the CHADS2 score in assessing the prognosis of patients with NVAF with stroke and possesses even more advantages during the early prediction of short-term prognosis in these patients. The CHA2DS2-VASc score can help to reduce effectively the occurrence of stroke through prediction, followed by early precautions taken for patients with NVAF and ischemic stroke. Furthermore, the application of the scoring system is simple; thus, it is worthy of being promoted clinically. However, there are limitations to this study due to the small sample size and short follow-up period; hence, the

findings of this study need to be confirmed by a large-scale, long-term follow-up study.

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Disclosure of conflict of interest

None.

Abbreviations

AF, atrial fibrillation; CI, confidence interval; CT, computed tomography; ECG, electrocardiogram; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NVAF, non-valvular atrial fibrillation; OR, odds ratio; TIA, transient ischemic attack.

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