

Prestroke CHA₂DS₂-VASc Score and Severity of Acute Stroke in Patients with Atrial Fibrillation: Findings from RAF Study

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Background and Purpose: The aim of this study was to investigate for a possible association between both prestroke CHA₂DS₂-VASc score and the severity of stroke at presentation, as well as disability and mortality at 90 days, in patients with acute stroke and atrial fibrillation (AF). **Methods:** This prospective study enrolled consecutive patients with acute ischemic stroke, AF, and assessment of prestroke CHA₂DS₂-VASc score. Severity of stroke was assessed on admission using the National Institutes of Health Stroke Scale (NIHSS) score (severe stroke: NIHSS ≥ 10). Disability and mortality at 90 days were assessed by the modified Rankin Scale (mRS < 3 or ≥ 3). Multiple logistic regression was used to correlate prestroke CHA₂DS₂-VASc and severity of stroke, as well as disability and mortality at 90 days. **Results:** Of the 1020 patients included in the analysis, 606 patients had an admission NIHSS score lower and 414 patients higher than 10. At 90 days, 510 patients had mRS ≥ 3 . A linear correlation was found between the prestroke CHA₂DS₂-VASc score and severity of stroke ($P = .001$). On multivariate analysis, CHA₂DS₂-VASc score correlated with severity of stroke ($P = .041$) and adverse functional outcome (mRS ≥ 3) ($P = .001$). A logistic regression with the receiver operating characteristic graph procedure (C-statistics) evidenced an area under the curve of .60 ($P = .0001$) for severe stroke. Furthermore, a correlation was found between prestroke CHA₂DS₂-VASc score and lesion size. **Conclusions:** In patients with AF, in addition to the risk of stroke, a high CHA₂DS₂-VASc score was independently associated with both stroke severity at onset and disability and mortality at 90 days. **Key Words:** Ischemic stroke—CHA₂DS₂-VASc score—severity—outcome—atrial fibrillation—scores. © 2017 National Stroke Association. Published by Elsevier Inc. All rights reserved.

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Background and Purpose

In patients with atrial fibrillation (AF), current guidelines recommend using the CHA₂DS₂-VASC score to assess the risk of stroke.¹ In retrospective studies, CHA₂DS₂-VASC score has been suggested as a predictor of severity of stroke on admission and poor outcome.²⁻⁴

The aim of this study was to investigate for a possible association between both prestroke CHA₂DS₂-VASC score and the severity of stroke at presentation, as well as disability and mortality at 90 days, in patients with acute stroke and AF.

Methods

Data for this analysis were extracted from the database of a prospective multicenter study which had enrolled consecutive patients with acute stroke and AF (the RAF study).⁵ This study, carried out between January 2012 and March 2014, enrolled 1029 consecutive patients from 29 stroke units throughout Europe and Asia.

Prestroke CHA₂DS₂-VASC score was evaluated as previously described.⁵ On admission, the severity of acute stroke was assessed using the National Institutes of Health Stroke Scale (NIHSS); all investigators were certified on the use of this scale. Disability and mortality at 90 days were assessed using the modified Rankin Scale (mRS).

Data on known stroke risk factors were collected as reported in the main paper.⁵

A cerebral computed tomography (CT) or magnetic resonance was performed on admission for all patients to exclude intracranial hemorrhage. A second cerebral CT scan or magnetic resonance was performed 48-72 hours from stroke onset. The sites and sizes of the qualifying infarcts were determined based on standard templates,^{6,7} as previously described.⁵

Statistical Analysis

The primary prespecified a priori study question was if CHA₂DS₂-VASC score had been associated with stroke severity assessed by the NIHSS at onset. Then, as a post-hoc analysis, possible correlations between CHA₂DS₂-VASC scores and outcome assessed by mRS and between CHA₂DS₂-VASC scores and lesion size were investigated.

The admission NIHSS score was evaluated both as a continuous variable for the correlation coefficient *r* analysis and as a dichotomized variable (severe stroke NIHSS ≥ 10) for the multivariate analysis.

The correlation coefficient *r*, Pearson product-moment correlation coefficient, was used to measure the strength of the linear association between CHA₂DS₂-VASC before the event and NIHSS score on admission (as continuous variable).

Correlations between prestroke CHA₂DS₂-VASC and severity of stroke were sought by multiple logistic regression after adjusting for the following variables: smoking,

hyperlipidemia, alcohol abuse, and use of statins in addition to CHA₂DS₂-VASC.

Thereafter, the probability of a receiver operating characteristic curve against NIHSS ≥ 10 as dependent variable was plotted. The area under this curve suggests an ability of the CHA₂DS₂-VASC score to predict for severe stroke, which is also referred to as the *C*-statistics (Harrell's *C*). In addition, a multiple logistic regression model including every single components of the CHA₂DS₂-VASC was performed. Stroke was defined as either nondisabling (mRS 0-2) or disabling (mRS 3-5).

The factors evaluated as independent predictors of 3-month adverse outcome (defined as mRS ≥ 3 or death) were assessed using multiple logistic regression analysis. The variables included in the model were CHA₂DS₂-VASC score, cardiovascular risk factors, reperfusion therapy, and severity of stroke on admission according to the NIHSS score.

The sites and sizes of the qualifying infarcts shown on CT scan were determined based on standard templates as follows: (1) small, when a lesion was ≤ 1.5 cm in the anterior or posterior circulation; (2) medium, when a lesion was in a cortical superficial branch of the middle cerebral artery (MCA), in the MCA deep branch, in the internal border zone territories, in a cortical superficial branch of the posterior cerebral artery, in the posterior cerebral artery branch, or in a cortical superficial branch of the anterior cerebral artery (ACA); (3) large anterior, when a lesion involved the complete territory of middle cerebral artery (MCA), posterior cerebral artery (PCA), or ACA in 2 cortical superficial branches of MCA, in a cortical superficial branch of MCA associated with the MCA deep branch, or in more than 1 artery territory (e.g., MCA associated with ACA territories); and (4) large posterior, when a lesion was ≥ 1.5 cm in the brain stem or cerebellum.⁸

A possible correlation between lesion size and CHA₂DS₂-VASC score was investigated using chi-square test (*P* for trend).

Results

Overall, 1029 consecutive patients were included in the study (mean age: 77.2 ± 9.5 years; 560 females and 469 males). The distribution of CHA₂DS₂-VASC score in the study patients is reported in Table 1.

Nine patients were excluded from the analysis as their NIHSS score was not available. Of the 1020 patients included in the analysis, 606 patients had an admission NIHSS score lower and 414 patients higher than 10. The mean NIHSS scores for each of the CHA₂DS₂-VASC scores are reported in Table 1 (*P* = .071). A linear correlation was found between severity of stroke and CHA₂DS₂-VASC score (r^2 : 0.010, *P* = .001) (Fig 1). On multivariate analysis, CHA₂DS₂-VASC score correlated with severity of stroke (odds ratio [OR]: 1.084, 95% confidence interval [CI]: 1.003-1.172, *P* = .041, for each 1-point increase). Considering the

Table 1. Stroke severity (NIHSS) and 90-day outcome according to prestroke CHA₂DS₂-VASc score

CHA ₂ DS ₂ -VASc score	Prestroke CHA ₂ DS ₂ -VASc (n = 1029)	NIHSS on admission (mean)* (n = 1020‡)	90-day mRS score ≥3† (n = 1019§)
0	17 (1.7%)	5.18 ± 5.75	4/17 (23.5%)
1	54 (5.2%)	8.30 ± 8.16	16/53 (30.2%)
2	91 (8.9%)	8.31 ± 6.70	34/90 (37.7%)
3	200 (19.4%)	8.86 ± 7.10	81/198 (40.9%)
4	243 (23.6%)	9.12 ± 7.22	125/242 (51.6%)
5	206 (20.0%)	9.67 ± 7.73	113/202 (55.9%)
6	129 (12.8%)	9.70 ± 6.50	78/129 (60.5%)
7	66 (6.4%)	10.30 ± 8.20	43/65 (66.1%)
8-9	23 (2.2%)	12.09 ± 6.68	16/23 (69.6%)

Abbreviations: mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

**P* for trend = .071.

†*P* for trend = .0001.

‡Nine patients were excluded from the analysis as their NIHSS score was not available.

§1019 patients were available for the final functional outcome analysis (10 patients were lost to follow-up).

modest correlation, a logistic regression with a receiver operating characteristic graph procedure, to get the C-statistics, was performed and it evidenced that the area under the curve was .60 (.56-0.63), *P* = .0001 for severe stroke.

When every single components of the CHA₂DS₂-VASc score were assessed for a correlation with stroke severity, only increasing age and female sex were

significantly correlated with stroke severity according to NIHSS (*P* = .007 and *P* = .001, respectively) (Table 2).

A correlation was also found between prestroke CHA₂DS₂-VASc score and lesion size. After excluding patients treated with revascularization, 70% of patients with CHA₂DS₂-VASc score of 8 or 9 had a medium-large lesion, whereas 70% of patients with CHA₂DS₂-VASc score of 0 had a small lesion (Fig 2, *P* for trend = .042).

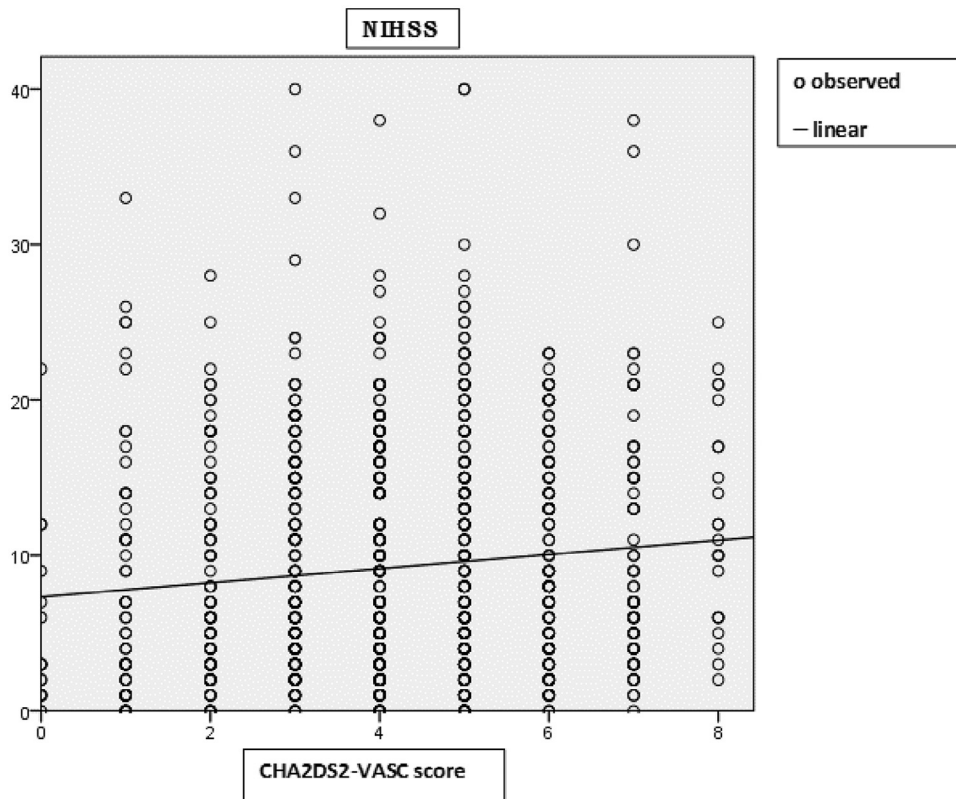
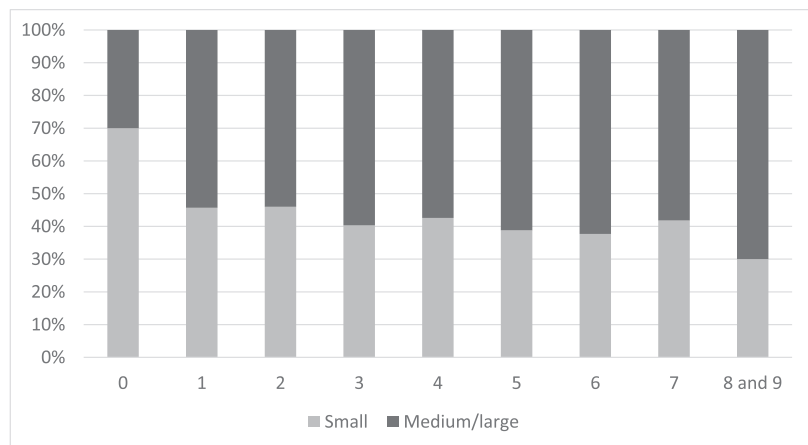


Figure 1. Linear correlation between NIHSS on admission and CHA₂DS₂-VASc score. Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

Figure 2. CHA₂DS₂-VASC score and lesion size (excluding patients treated with revascularization). *P for trend = .042.



At 90 days, 1019 patients were available for the functional outcome analysis (10 patients were lost to follow-up). The correlation between prestroke CHA₂DS₂-VASC score and 90-day outcome is reported in Table 1.

On multivariate analysis, both NIHSS score on admission and CHA₂DS₂-VASC score were correlated with disability and mortality at 90 days (mRS ≥ 3) (OR: 1.236, 95% CI: 1.197-1.277, $P < .0001$; OR: 1.278, 95% CI: 1.100-1.484, $P = .001$, respectively, for each point increase).

The administration of thrombolytic therapy and the use of statins on admission correlated with better outcome (OR: .313, 95% CI: .204-0.481, $P < .0001$; OR: .585, 95% CI: .354-0.967, $P = .036$, respectively).

Discussion

The results of our study found correlations between prestroke CHA₂DS₂-VASC score and severity of stroke at presentation, according to NIHSS, as well as between CHA₂DS₂-VASC score and 90-day mortality and disability, as measured by mRS, therein indicating that a higher CHA₂DS₂-VASC score is predictive of a worse outcome.

Moreover, in post-hoc analyses, we found, first, a correlation between higher CHA₂DS₂-VASC score and greater

lesion size. This finding could support previous studies that have reported an association between CHA₂DS₂-VASC score and major vessel occlusion in patients with acute ischemic stroke and AF.⁹ Second, our study results are also in line with past studies reporting that among the risk factors, age and female sex are more predictive of severe stroke.^{10,11}

A strength of this study was that several stroke assessment scores were prospectively utilized, and each of these scores was correlated with CHA₂DS₂-VASC score, whereas several past studies were retrospective and used only a single assessment score.^{2-4,12-14}

In conclusion, we found that an increasing CHA₂DS₂-VASC score in AF patients predicted a more severe stroke at presentation, leading to a higher rate of disability and mortality at 90 days. This result highlights the need for physicians to more regularly investigate for AF in patients with other known vascular risk factors, especially increasing age and female sex.

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Table 2. Multivariate analysis for correlation of stroke severity and any of each component of CHA₂DS₂-VASC score

	OR	P	95% CI
Age (for each year increase)	1.020	.007	1.005-1.035
Sex	.367	.001	.515-0.175
Diabetes	1.172	.296	.870-1.575
Hypertension	.759	.110	.542-1.065
Stroke/TIA/thromboembolism history	.972	.849	.723-1.306
Congestive heart failure	1.049	.777	.753-1.462
Vascular disease	1.034	.832	.760-1.406

Abbreviations: CI, confidence interval; OR, odds ratio; TIA, transient ischemic attack.

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