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Roles of the $CHADS_2$ and CHA_2DS_2-VASc scores in post-myocardial infarction patients: Risk of new occurrence of atrial fibrillation and ischemic stroke

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Abstract

Background: *Patients with myocardial infarction (MI) are at risk of the development of atrial fibrillation (AF) and ischemic stroke. We sought to evaluate the prognostic performance of the $CHADS_2$ and CHA_2DS_2-VASc scores in predicting new AF and/or ischemic stroke in post-ST segment elevation MI (STEMI) patients. Six hundred and seven consecutive post-STEMI patients with no previously documented AF were studied.*

Methods and Results: *After a follow-up of 63 months (3,184 patient-years), 83 (13.7%) patients developed new AF (2.8% per year). Patients with a high $CHADS_2$ and/or CHA_2DS_2-VASc score were more likely to develop new AF. The annual incidence of new AF was 1.18%, 2.10%, 4.52%, and 7.03% in patients with $CHADS_2$ of 0, 1, 2, and ≥ 3; and 0.39%, 1.72%, 1.83%, and 5.83% in patients with a CHA_2DS_2-VASc score of 1, 2, 3 and ≥ 4. The CHA_2DS_2-VASc score (C-statistic = 0.676) was superior to the $CHADS_2$ (C-statistic = 0.632) for discriminating new AF. Ischemic stroke occurred in 29 patients (0.9% per year), the incidence increasing in line with the $CHADS_2$ (0.41%, 1.02%, 1.11%, and 1.95% with score of 0, 1, 2, and ≥ 3) and CHA_2DS_2-VASc scores (0.39%, 0.49%, 1.02%, and 1.48% with score of 1, 2, 3 and ≥ 4). The C-statistic of the CHA_2DS_2-VASc score as a predictor of ischemic stroke was 0.601, superior to that of $CHADS_2$ score (0.573). $CHADS_2$ and CHA_2DS_2-VASc scores can identify post-STEMI patients at high risk of AF and stroke.*

Conclusions: *The $CHADS_2$ and CHA_2DS_2-VASc scores can identify post-STEMI patients at high risk of AF and ischemic stroke. This enables close surveillance and prompt anticoagulation for stroke prevention.* (Cardiol J 2014; 21, 5: 474–483)

Key words: $CHADS_2$, CHA_2DS_2-VASc, atrial fibrillation, myocardial infarction

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Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice and it is associated with an increased risk

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of ischemic stroke [1]. Patients with established coronary artery disease, particularly myocardial infarction (MI), are at substantial risk of AF development [2, 3], as well as ischemic stroke. Although anticoagulation therapy can effectively reduce the risk of thromboembolism in these patients, the arrhythmia is often not diagnosed until the patient presents with an ischemic stroke, as ischemic stroke has been reported as the first presentation in up to 25% of patients with AF [4]. This precludes the implementation of any preventive measures including anticoagulation. Early identification of patients at high risk of AF development may thus allow close surveillance and prompt initiation of oral anticoagulation to prevent stroke. To date, several scores have been developed to predict AF in the general population but daily clinical application is difficult [5, 6].

The $CHADS_2$ (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, previous Stroke) score and more recently, the CHA_2DS_2-VASc (CHA_2DS_2-Vascular disease, Age 65–74 years, Sex category) score have been validated and widely used for risk stratification of AF patients for oral anticoagulation therapy [1, 7, 8]. The individual score components not only predict ischemic stroke risk associated with AF, but have also been linked to the development of AF [5, 6, 9]. In this study, we sought to investigate whether the $CHADS_2$ and CHA_2DS_2-VASc scores can predict new-onset AF and ischemic stroke in patients with MI but no previously documented AF.

Methods

Patients

From January 1998 to December 2005, 617 consecutive patients who previously survived a ST-segment elevation MI (STEMI; > 40 days) were referred to the Cardiac Rehabilitation and Prevention Center of Tung Wah Hospital [10–14]. This is the largest rehabilitation facility in Hong Kong and serves a population of about half a million. During the study period, coronary revascularization was performed in those who survived STEMI and who experienced chest pain and/or ischemia inducible on treadmill testing. Patients were excluded from study if they had previously documented AF prior to the index MI, a positive exercise stress test suggestive of residual myocardial ischemia, New York Heart Association (NYHA) functional class IV, and/or other terminal illness. Informed consent was obtained from all patients. The final analysis included 607 patients who were categorized according to the $CHADS_2$ and CHA_2DS_2-VASc scores.

Study design

This was a single center, prospective observational study, approved by the local Research Ethics Committee. Following recruitment to the Cardiac Rehabilitation Program, data pertaining to the index MI, demographics, cardiovascular risk factors, and medications were entered into the Tung Wah Hospital Cardiac Rehabilitation Program Database. All patients underwent baseline exercise stress tests and echocardiography, and were prospectively followed up in our cardiac outpatient clinic. All patients were also followed up in the Cardiac Rehabilitation Program once every 3 months. The presence of AF was defined as the presence of fibrillatory P waves with irregular R-R intervals for > 5 beats at rest or on 24 h electrocardiogram (ECG) recording. The occurrence of new-onset AF and/or ischemic stroke within the follow-up period was retrieved from the medical records and discharge summaries from the territory wide information network of all public hospitals in Hong Kong. The primary endpoint of new occurrence of clinical AF was defined as the presence of AF documented by resting 12-lead ECG. The secondary endpoint was ischemic stroke during the follow-up period. Ischemic stroke was defined as a neurological deficit of sudden onset that persisted for more than 24 h and corresponded to a vascular territory in the absence of primary hemorrhage, and that could not be explained by other causes (trauma, infection, vasculitis). Stroke was confirmed by computerized axial tomography or magnetic resonance imaging of the brain [15, 16].

Statistical analysis

Continuous and discrete variables are expressed as mean ± standard derivation and percentages, respectively. Statistical comparisons of the baseline clinical characteristics were performed using Student's t-test, one-way ANOVA or Fisher's exact test, as appropriate. Kaplan-Meier survival analyses with the log-rank test were carried out and the Cox proportional hazards regression model was used to calculate the hazard ratios (HRs) of some predictive factors and their 95% confidence intervals (CIs) for the incidence of new AF and ischemic stroke.

For descriptive purposes, patients were classified into strata according to the $CHADS_2$ ($CHADS_2 = 0$, $CHADS_2 = 1$, $CHADS_2 = 2$, and $CHADS_2 \geq 3$) and CHA_2DS_2-VASc scores (CHA_2DS_2-VASc ≥ 1, CHA_2DS_2-VASc = 2, CHA_2DS_2-VASc = 3, CHA_2DS_2-VASc ≥ 4). The prognostic performance of the $CHADS_2$ and the CHA_2DS_2-VASc scores with regard to AF and ischemic stroke was assessed

Table 1. Baseline characteristics of patients stratified according to the $CHADS_2$ score.

	$CHADS_2$ score				
	0 (n = 155)	1 (n = 203)	2 (n = 181)	≥ 3 (n = 68)	P
Age [years]	58.1 ± 10.6	64.2 ± 10.8	66.7 ± 10.4	76.0 ± 6.8	< 0.001*
Female gender	15 (9.7%)	47 (23.2%)	62 (34.3%)	27 (39.7%)	< 0.001*
Hypertension	0 (0%)	101 (49.8%)	156 (86.2%)	60 (88.2%)	< 0.001*
Diabetes mellitus	0 (0%)	55 (27.1%)	127 (70.2%)	54 (79.4%)	< 0.001*
Heart failure	0 (0%)	13 (6.4%)	35 (19.3%)	41 (60.3%)	< 0.001*
Hypercholesterolemia	71 (45.8%)	92 (45.3%)	75 (41.4%)	29 (42.6%)	0.83
Lung disease	17 (11.0%)	22 (10.8%)	14 (7.7%)	5 (7.4%)	0.61
Significant renal impairment	4 (2.6%)	19 (9.4%)	17 (9.4%)	11 (16.2%)	< 0.01*
Left ventricular ejection fraction [%]	47.0 ± 9.6	46.4 ± 10.1	44.8 ±10.4	42.3 ± 10.8	< 0.01*
Revascularization:					
PCI	25 (16.1%)	33 (16.3%)	30 (16.6%)	12 (17.6%)	0.99
CABG	1 (0.6%)	2 (1.0%)	2 (1.1%)	0 (0%)	0.83
Medications:					
Aspirin	150 (96.8%)	189 (93.1%)	167 (92.3%)	63 (92.6%)	0.34
ACEI	119 (76.8%)	164 (80.8%)	145 (80.1%)	52 (76.5%)	0.74
Beta-blockers	109 (70.3%)	154 (75.9%)	135 (74.6%)	44 (64.7%)	0.26
Statin	5 (3.2%)	14 (6.9%)	20 (11.0%)	10 (14.7%)	< 0.01*
Calcium channel blocker	119 (76.8%)	146 (71.9%)	141 (77.9%)	44 (64.7%)	0.13

*p < 0.05; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting; ACEI — angiotensin-converting-enzyme inhibitor; $CHADS_2$ score — Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, previous Stroke score

using area under the curve (C-statistic) for receiver operating characteristic curve calculated using Analyze-It for Excel with Delong-Delong comparison for C-statistic. The C-statistic integrates measures of sensitivity and specificity of the range of a variable. Ideal prediction yields a C-statistic of 1.00, whereas a value of < 0.5 reflects a prediction ability no better than chance. Calculations were performed using SPSS software (version 12.0) and MedCalc software. All tests were two-sided, and p-values were considered significant if < 0.05.

Results

A total of 607 post-MI patients with no previously documented AF were recruited. Tables 1 and 2 summarize the clinical characteristics across the strata of $CHADS_2$ and CHA_2DS_2-VASc scores, respectively. As expected, the $CHADS_2$ and CHA_2DS_2VASc scores were strongly associated with each of the components constituting the scores. Specifically, compared with patients with low $CHADS_2$ score, the group of patients with a high score was older ($p < 0.01$), and had a higher proportion of females ($p < 0.001$), hypertension ($p < 0.001$) and diabetes mellitus ($p < 0.001$). In addition, these patients were more likely to have renal impairment ($p < 0.01$) and a lower left ventricular ejection fraction (LVEF; $p < 0.01$), and be prescribed statin therapy ($p < 0.01$). Similar trends were also observed in the CHA_2DS_2-VASc group (Table 2).

New-onset atrial fibrillation

After a mean follow-up of 63 ± 44 months (3,184 patient-years), new-onset clinical AF was detected in 83 patients (13.7%, 2.80 per 100 patient-years). Patients with new-onset AF were older (70.2 ± 7.8 vs. 63.8 ± 11.7 years, $p < 0.001$), were more likely to be female (39.5% vs. 22.5%, $p = 0.001$), and had a higher prevalence of heart failure (31.3% vs. 12.0%, $p < 0.001$), but lower prevalence of hypercholesterolemia (43.4% vs. 58.0%, $p = 0.01$), and a lower LVEF (42.0 ± 9.6% vs. 46.2 ± 10.2%, $p = 0.001$; Table 3). In addition, patients with new-onset AF were less likely to be prescribed beta-blocker therapy (53.0% vs. 76.0%, $p < 0.001$) or statins (59.0% vs. 76.5%, $p = 0.001$). Patients with new-onset AF also had a significantly higher mean $CHADS_2$ score (1.71 ± 1.04 vs. 1.21 ± 0.98, $p < 0.0001$) and mean CHA_2DS_2-VASc score (3.90 ± 1.34 vs. 2.97 ± 1.40, $p < 0.001$) than those without AF (Table 3).

Table 4 summarizes the baseline demographic factors, the $CHADS_2$ and CHA_2DS_2-VASc scores; and

Table 2. Baseline characteristics of patients stratified according to the CHA_2DS_2-VASc score.

	CHA_2D_2-VASc score				
	1 (n = 90)	2 (n = 141)	3 (n = 142)	≥ 4 (n = 234)	P
Age [years]	51.0 ± 7.3	59.8 ± 9.2	64.3 ± 9.8	73.2 ± 7.2	< 0.001*
Female gender	0 (0%)	6 (4.3%)	21 (14.8%)	124 (53.0%)	< 0.001*
Hypertension	0 (0%)	52 (36.9%)	85 (59.9%)	180 (76.9%)	< 0.001*
Diabetes mellitus	0 (0%)	25 (17.7%)	65 (45.8%)	146 (62.4%)	< 0.001*
Heart failure	0 (0%)	8 (5.7%)	15 (10.6%)	66 (28.2%)	< 0.001*
Hypercholesterolemia	35 (38.9%)	62 (44.0%)	62 (43.7%)	108 (46.2%)	0.71
Lung disease	83 (15.1%)	130 (92.2%)	121 (85.2%)	215 (91.9%)	0.12
Significant renal impairment	2 (2.2%)	7 (5.0%)	16 (11.3%)	26 (11.1%)	0.02*
Left ventricular ejection fraction [%]	47.1 ± 9.3	47.0 ± 10.2	45.5 ± 10.8	44.2 ± 10.1	0.03*
Revascularization:					
PCI	19 (21.1%)	21 (14.9%)	21 (14.8%)	39 (16.7%)	0.58
CABG	1 (1.1%)	1 (0.7%)	1 (0.7%)	2 (0.9%)	0.99
Medications:					
Aspirin	88 (97.8%)	132 (93.6%)	135 (95.1%)	214 (91.5%)	0.17
ACEI	74 (82.2%)	113 (80.1%)	108 (76.1%)	185 (79.1%)	0.70
Beta-blockers	68 (75.6%)	108 (76.6%)	103 (72.5%)	163 (69.7%)	0.47
Statin	2 (2.2%)	6 (4.3%)	14 (9.9%)	27 (11.5%)	0.01*
Calcium channel blocker	74 (82.2%)	105 (74.5%)	100 (70.4%)	171 (73.1%)	0.24

*$p < 0.05$; CHA_2DS_2-VASc score — CHA_2D_2-Vascular disease, Age 65–74 years, Sex category score; rest abbreviations as in Table 1

their corresponding HRs and 95% CIs that were associated with new-onset AF based on a Cox proportional hazards model. Amongst these parameters, age ≥ 65, age ≥ 75, female gender, hypertension, diabetes mellitus, heart failure, previous stroke, as well as the $CHADS_2$ and CHA_2DS_2-VASc scores were strongly associated with new-onset AF (Table 4). Kaplan-Meier analysis revealed a significantly higher incidence of new-onset AF in patients with higher $CHADS_2$ score (Log-rank: 21.5, $p < 0.0001$, Fig. 1A) and higher CHA_2DS_2-VASc score (Log-rank: 31.4, $p < 0.0001$, Fig. 1B). Patients with a higher $CHADS_2$ or CHA_2DS_2-VASc score were much more likely to develop new-onset AF than those with a lower score. The corresponding incidence of new-onset AF was 1.18 per 100 patient-years in patients with $CHADS_2 = 0$; 2.10 per 100 patient-years in patients with $CHADS_2 = 1$; and 4.52 per 100 patient-years in those with $CHADS_2 = 2$; 7.03 per 100 patient-years in those with $CHADS_2 \geq 3$. The incidence of new-onset AF also increased with the CHA_2DS_2-VASc score: CHA_2DS_2-VASc = 1: 0.39 per 100 patient-years; CHA_2DS_2-VASc = 2: 1.72 per 100 patient-years; CHA_2DS_2-VASc = 3: 1.83 per 100 patient-years; and CHA_2DS_2-VASc ≥ 4: 5.83 per 100 patient-years.

To compare the prognostic performance of these parameters, within the $CHADS_2$ and CHA_2DS_2-VASc scores, in predicting new-onset AF, the sensitivity, specificity and C-statistic for the $CHADS_2$ and CHA_2DS_2-VASc scores in relation to new-onset AF were determined (Table 5). Among all these factors, test discrimination of the CHA_2DS_2-VASc score (C-statistic = 0.676) was superior to the $CHADS_2$ (C-statistic = 0.632) and age ≥ 65 (C-statistic = 0.632).

Ischemic stroke

There were 29 ischemic strokes during the follow-up period. Table 6 summarizes the baseline characteristics of patients with and without ischemic stroke. Apart from a higher proportion of females among patients with ischemic stroke (44.8% vs. 23.9%, $p = 0.01$), there were no statistically significant differences between patients with and without stroke (Table 6). In the Cox proportional hazards model, female gender, hypertension, previous stroke, as well as the $CHADS_2$ and CHA_2DS_2-VASc scores were strongly associated with stroke (Table 4). Kaplan-Meier analysis revealed a significantly higher incidence of ischemic stroke in patients with higher $CHADS_2$ score (Log-rank: 6.0, $p = 0.014$, Fig. 2A) and higher CHA_2DS_2-VASc score (Log-rank: 7.1, $p = 0.002$, Fig. 2B). The incidence of stroke was 0.41 per 100 patient-years in patients with $CHADS_2 = 0$; 1.02 per 100 patient-years in

Table 3. Baseline characteristics of patients with or without new onset atrial fibrillation (AF).

	AF (n = 83)	No AF (n = 524)	P
Age [years]	70.2 ± 7.8	63.8 ± 11.7	< 0.001*
Female gender	33 (39.8%)	118 (22.5%)	0.001*
Diabetes mellitus	39 (47.0%)	197 (37.6%)	0.10
Hypertension	47 (56.6%)	270 (51.5%)	0.39
Heart failure	26 (31.3%)	63 (12.0%)	< 0.001*
Hypercholesterolemia	36 (43.4%)	304 (58.0%)	0.01*
Lung disease	7 (8.4%)	51 (9.7%)	0.71
Significant renal impairment	11 (13.3%)	41 (7.8%)	0.10
Left ventricular ejection fraction [%]	42.0 ± 9.6	46.2 ± 10.2	0.001*
Revascularization:			
PCI	12 (14.5%)	88 (16.8%)	0.59
CABG	0 (0%)	5 (1.0%)	0.37
Mean $CHADS_2$ score	1.71 ± 1.04	1.21 ± 0.98	< 0.001*
$CHADS_2$ score:			0.001*
0	11 (13.3%)	144 (27.5%)	
1	22 (26.5%)	181 (34.5%)	
2	34 (41.0%)	147 (28.1%)	
≥ 3	16 (19.3%)	52 (9.9%)	
Mean CHA_2DS_2-VASc score	3.90 ± 1.34	2.97 ± 1.40	< 0.001*
CHA_2DS_2-VASc score:			< 0.001*
1	2 (2.4%)	88 (16.8%)	
2	13 (15.7%)	128 (24.4%)	
3	14 (16.9%)	128 (24.4%)	
≥ 4	54 (65.1%)	180 (34.4%)	
Medications:			
Aspirin	75 (90.4%)	494 (94.3%)	0.17
ACEI	67 (80.7%)	413 (78.8%)	0.69
Beta-blockers	44 (53.0%)	398 (76.0%)	< 0.001*
Statin	49 (59.0%)	401 (76.5%)	0.001*
Calcium channel blocker	9 (10.8%)	40 (7.6%)	0.32

*p < 0.05; abbreviations as in Tables 1 and 2

patients with $CHADS_2$ = 1; 1.11 per 100 patient-years in patients with $CHADS_2$ = 2; and 1.95 per 100 patient-years in patients with $CHADS_2$ ≥ 3; p-value for trend < 0.0001. In a similar fashion, the incidence of stroke also increased with the CHA_2DS_2-VASc score (CHA_2DS_2-VASc = 1: 0.39 per 100 patient-years; CHA_2DS_2-VASc = 2: 0.49 per 100 patient-years; CHA_2DS_2-VASc = 3: 1.02 per 100 patient-years; and CHA_2DS_2-VASc ≥ 4: 1.48 per 100 patient-years; p-value for trend < 0.0001). The C-statistic of the CHA_2DS_2-VASc score as a predictor of ischemic stroke was 0.601, superior to that of $CHADS_2$ score (0.573) (Table 5). The cut-off value of the CHA_2DS_2-VASc for ischemic stroke was 3 (sensitivity: 79.3%; specificity: 38.9%).

Discussion

We have demonstrated that post-MI patients are at high risk of developing AF (2.8% per year) as well as ischemic stroke (0.9% per year). The $CHADS_2$ and CHA_2DS_2-VASc scores, originally designed for stroke risk stratification in AF patients, have been shown to be predictive of the occurrence of both new AF and ischemic stroke in these patients. The test discrimination of the CHA_2DS_2-VASc score appears to be superior to the $CHADS_2$ for both new AF and ischemic stroke. Such scores may thus be used in post-MI patients to identify those at risk of developing new AF and ischemic stroke in order to institute close clinical surveillance and early intervention.

Traditional risk factors that contribute to AF include increasing age [17, 18], male gender [19], hypertension [19], diabetes mellitus [19], obesity [19, 20], hyperthyroidism [16, 21, 22], congestive heart failure, and other structural heart diseases [19, 23, 24]. In addition, in the recent ECHOES study of a non-selected cohort of 3,960 individuals

Table 4. Association between baseline factors, $CHADS_2$, and CHA_2DS_2-VASc scores and new atrial fibrillation (AF) and ischemic stroke (n = 607).

	New AF			Ischemic stroke		
	HR	95% CI	P	HR	95% CI	P
Age > 65	2.77	1.77–4.33	0.0001	0.96	0.46–2.01	0.92
Age > 75	2.34	1.33–4.13	0.02	2.06	0.78–5.42	0.14
Female	2.32	1.39–3.87	0.002	3.11	1.33–7.28	0.009*
Hypertension	1.36	0.87–2.12	0.59	2.15	1.03–4.49	0.04
Diabetes mellitus	1.69	1.06–2.70	0.03	1.23	0.56–2.67	0.60
Heart failure	7.58	3.82–15.02	< 0.0001	1.82	0.57–5.77	0.31
Stroke	40.55	1.96–839.5	0.005	328.6	1.98–54521	0.03*
$CHADS_2$						
0	Reference	Reference		Reference	Reference	
1	2.29	1.40–3.75	0.007*	2.39	1.09–5.23	0.03*
2	3.15	1.84–5.39	0.0005*	3.02	1.12–7.76	0.02*
≥ 3	7.30	2.92–18.26	0.0001*	11.6	2.12–63.45	0.005*
CHA_2DS_2-VASc						
1	Reference	Reference		Reference	Reference	
2	2.93	1.60–5.36	0.004*	2.04	0.78–5.40	0.15
3	3.23	1.78–5.84	0.001*	2.32	0.91–5.93	0.08
≥ 4	4.19	2.30–7.61	0.0001	3.26	1.19–8.94	0.02*

*p < 0.05; HR — hazard ratio; CI — confidence interval; rest abbreviations as in Tables 1 and 2

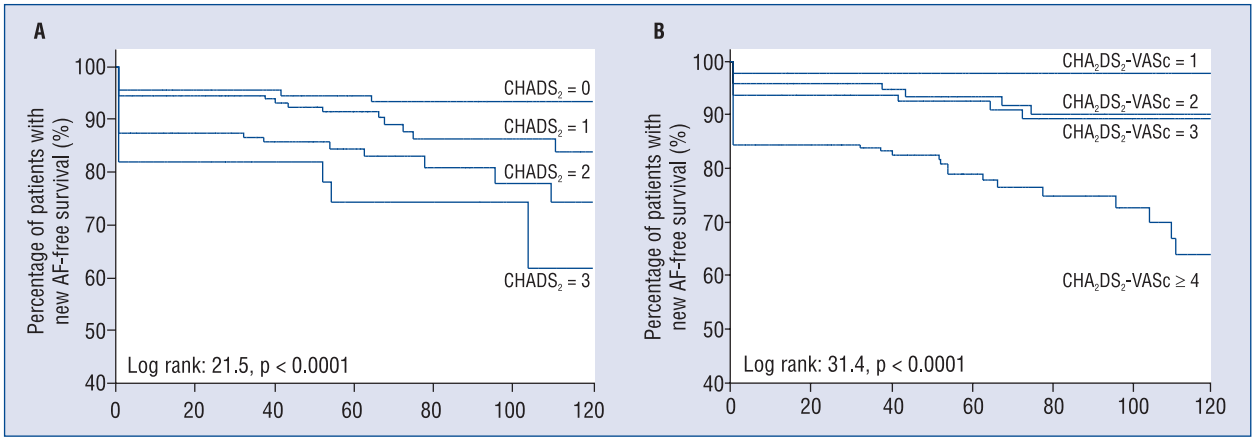

Figure 1. New atrial fibrillation (AF); **A.** Kaplan-Meier estimate of percentage of new AF stratified by the $CHADS_2$ score; **B.** Kaplan-Meier estimate of percentage of new AF stratified by the CHA_2DS_2-VASc score; $CHADS_2$ score: Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, previous Stroke score; CHA_2DS_2-VASc score: CHA_2DS_2-Vascular disease, Age 65–74 years, Sex category score.

from the general population, subjects with a prior history of myocardial infarct also had a higher prevalence of AF at around 6%, nearly 3-fold higher than that of the general population [25]. Consistent with these studies, most traditional risk factors such as increasing age, diabetes mellitus, congestive heart failure, and prior stroke have been demonstrated to be associated with new AF in the present cohort of post-MI patients. Nonetheless, in our cohort, hypertension, one of the strongest risk factors of AF [9], did not appear to contribute to the subsequent development of AF. In stark contrast to previous community studies [26], female gender instead of male gender was shown to be associated with new AF in our cohort. This may be because hypertension and male gender are both

Table 5. Sensitivity, specificity, and predictive ability (C-statistics and the 95% confidence interval [CI]) for individual risk factors, $CHADS_2$ score and CHA_2DS_2VASc score in relation to new atrial fibrillation (AF) and ischemic stroke.

	Sensitivity	Specificity	C-statistic (95% CI)	P
New AF				
Age > 75	31.3	80.5	0.559 (0.52–0.60)	0.03*
Hypertension	56.6	48.5	0.525 (0.49–0.57)	0.39
Diabetes mellitus	47.0	52.4	0.547 (0.51–0.59)	0.11
Heart failure	31.3	88.0	0.597 (0.56–0.64)	0.0003*
Stroke	2.4	99.6	0.510 (0.47–0.55)	0.24
Female gender	39.8	77.5	0.586 (0.55–0.63)	0.003*
$CHADS_2$			0.632 (0.59–0.67)	< 0.0001
$CHADS_2 \geq 0$	100.0	0.0		
$CHADS_2 \geq 1$	86.8	27.5		
$CHADS_2 \geq 2$	60.2	62.0		
$CHADS_2 \geq 3$	19.3	90.1		
CHA_2DS_2VASc	100.0	0.0	0.676 (0.64–0.71)	< 0.0001
$CHA_2DS_2VASc \geq 2$	97.6	16.8		
$CHA_2DS_2VASc \geq 3$	81.9	41.2		
$CHA_2DS_2VASc \geq 4$	65.1	65.7		
Ischemic stroke				
Age > 75	27.6	79.2	0.534 (0.49–0.57)	0.43
Hypertension	65.5	48.4	0.570 (0.53–0.61)	0.13
Diabetes mellitus	62.1	38.9	0.510 (0.46–0.55)	0.92
Heart failure	17.2	85.5	0.514 (0.47–0.55)	0.71
Stroke	3.5	99.5	0.520 (0.47–0.56)	0.40
Female gender	44.8	76.1	0.61 (0.57–0.64)	0.03*
$CHADS_2$			0.573 (0.53–0.61)	0.15
$CHADS_2 \geq 0$	100.0	0.0		
$CHADS_2 \geq 1$	86.2	26.1		
$CHADS_2 \geq 2$	48.3	59.3		
$CHADS_2 \geq 3$	17.2	89.1		
CHA_2DS_2VASc			0.601 (0.56–0.64)	0.03*
$CHA_2DS_2VASc \geq 1$	100.0	0.0		
$CHA_2DS_2VASc \geq 2$	93.1	15.2		
$CHA_2DS_2VASc \geq 3$	79.3	38.9		
$CHA_2DS_2VASc \geq 4$	51.7	62.1		

*$p < 0.05$; abbreviations as in Tables 1 and 2

strong risk factors for coronary artery disease and contribute at least partly to the development of AF through myocardial ischemia. As all the subjects in the current cohort had prior MI in contrast to previous community studies in which only a minority of subjects had established coronary artery disease, the contributory effects of hypertension and male gender to AF development may thus be attenuated. Nonetheless, while these individual risk factors have been unequivocally shown to predispose to new AF, they lack sensitivity and/or specificity to identify high-risk individuals. For instance, the sensitivity of these individual components such as age of more than 75 years, diabetes mellitus, congestive heart failure and prior ischemic stroke ranges from 2.4% to 79.5%, with the corresponding C-statistic only slightly better than that of chance. Amongst patients with AF, the $CHADS_2$ and CHA_2DS_2VASc scores have been validated, most recently amongst the Chinese [27], and are currently widely used stratification tools to estimate the risk of stroke, thus guiding the decision for long-term anticoagulation. These scores, nevertheless, also represent a panel of most

Table 6. Baseline characteristics of patients with or without stroke.

	Stroke (n = 29)	No stroke (n = 578)	P
Age [years]	66.9 ± 9.7	64.6 ± 11.5	0.28
Female gender	13 (44.8%)	138 (23.9%)	0.01*
Diabetes mellitus	11 (37.9%)	225 (38.9%)	0.91
Hypertension	19 (65.5%)	298 (51.6%)	0.14
Heart failure	5 (17.2%)	84 (14.5%)	0.69
Hypercholesterolemia	13 (44.8%)	254 (43.9%)	0.93
Lung disease	1 (3.4%)	57 (9.9%)	0.25
Significant renal impairment	3 (10.3%)	49 (8.5%)	0.73
Left ventricular ejection fraction [%]	48.2 ± 8.0	45.5 ± 10.3	0.09
Revascularization:			
PCI	7 (24.1%)	93 (16.1%)	0.25
CABG	0 (0%)	5 (0.9%)	0.62
Mean $CHADS_2$ score	1.55 ± 1.02	1.27 ± 1.00	0.14
$CHADS_2$ score:			0.15
0	4 (13.9%)	151 (26.1%)	
1	11 (37.9%)	192 (33.2%)	
2	9 (31.0%)	172 (29.8%)	
≥ 3	5 (17.2%)	63 (10.9%)	
Mean CHA_2DS_2-VASc score	3.55 ± 1.37	3.07 ± 1.43	0.08
CHA_2DS_2-VASc score:			0.05
1	2 (6.9%)	88 (15.2%)	
2	4 (13.8%)	137 (23.7%)	
3	8 (27.6%)	134 (23.2%)	
≥ 4	15 (51.7%)	219 (37.9%)	
Medications:			
Aspirin	26 (89.7%)	543 (93.9%)	0.35
ACEI	24 (82.8%)	456 (78.9%)	0.62
Beta-blockers	24 (82.8%)	418 (72.3%)	0.22
Statin	19 (65.5%)	431 (74.6%)	0.28
Calcium channel blocker	3 (10.3%)	46 (8.0%)	0.65

*$p < 0.05$; abbreviations as in Tables 1 and 2

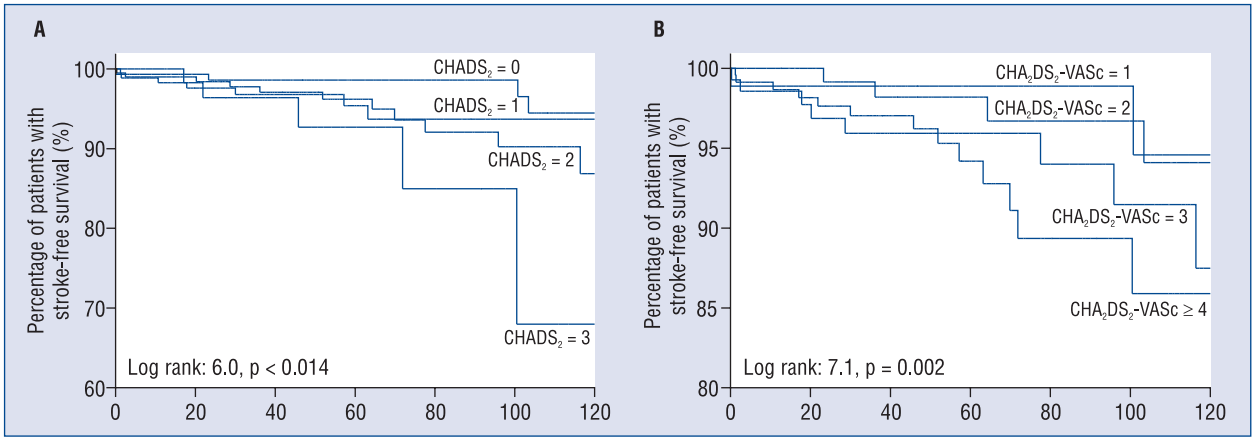

Figure 2. Ischemic stroke; **A.** Kaplan-Meier estimate of percentage of new atrial fibrillation (AF) stratified by the $CHADS_2$ score; **B.** Kaplan-Meier estimate of percentage of new AF stratified by the CHA_2DS_2-VASc score; $CHADS_2$ score: Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, previous Stroke score; CHA_2DS_2-VASc score: CHA_2DS_2-Vascular disease, Age 65–74 years, Sex category score.

common co-morbidities that predispose to AF; it is conceivable that their inclusion in these scores can collectively improve the predictive power of new onset AF and stroke.

The results of our study have several important clinical implications. First, the co-occurrence of MI and AF often represents a challenging management problem to the attending physician, particularly when coronary stenting is required. For patients with pre-existing AF who developed MI and were undergoing coronary stenting, current guidelines recommend a combination of aspirin, clopidogrel, and oral anticoagulation, the so-called triple therapy [7, 28]. This is because the dual antiplatelet therapy, (aspirin and clopidogrel) essential to prevent stent thrombosis, has been proven inferior to warfarin for the prevention of AF-related ischemic stroke [29, 30]. Nevertheless, as prolonged triple therapy (1 year) is associated with an excessive major bleeding risk [31–33], the duration of such therapy should be shortened in order to avoid/minimize bleeding complications. The use of drug-eluting stents in such patients is thus discouraged [28]. Among patients with no pre-existing AF, a drug-eluting stent is often the preferred stent of many interventional cardiologists given the advantages of a small reduction of target vessel revascularization over bare-metal stents [34, 35]. In the present study, despite the lack of previously documented AF, patients with MI and a $CHADS_2$, score of ≥ 3 had an exceedingly high risk of new AF: 7.03%, i.e., around ~1 in 14 patients per year. Similarly, the incidence of new AF in patients with a CHA_2DS_2-VASc score of ≥ 4 was as high as 5.83% per years (~1 in 17 patients per year). The occurrence of new AF, particularly during the first year after MI and drug-eluting stent implantation can be problematic. Attending physicians often face a therapeutic dilemma to either initiate a prolonged course of triple therapy that imposes an excessive bleeding risk, or to leave patients unprotected from the high ischemic stroke risk [36]. In addition to the risk factors for in-stent restenosis such as vessel size and concomitant diabetes mellitus, the choice of stents in patients with MI may also take into account the likelihood of the development of new AF according to the simple $CHADS_2$, and CHA_2DS_2-VASc scores. It would be important to evaluate the "net clinical benefit" of a drug-eluting stent with a small reduction in target vessel revascularization, balancing the excessive bleeding risk of triple therapy deemed necessary to minimize ischemic stroke risk as new AF ensues. For the longer term, in those patients with increased CHA_2DS_2 or CHA_2DS_2-VASc score, more intense follow-up, including repeated 24 h ECG monitoring or even an implantable device [13] may allow early detection of the occurrence as well as the burden of AF, and thus allow implementation of effective preventive measures including anti-coagulation in high-risk subjects.

Limitations of the study

This study had several limitations. First, asymptomatic episodes of AF were not assessed routinely by ambulatory ECG monitoring or implantable device. The lack of routine 24 h ambulatory ECG monitoring was one of the major shortcomings of this work. As all patients in the present cohort had an acute STEMI and thus represented a very special patient population, extrapolation of our results to other patient populations may be inappropriate. Nonetheless, the current study provides novel data that support the potential use of CHA_2DS_2-VASc score in post-MI patients to stratify their risk of new AF and ischemic stroke.

Conclusions

The $CHADS_2$ and CHA_2DS_2-VASc scores can identify post-STEMI patients at high risk of AF and ischemic stroke. This enables close surveillance and prompt anticoagulation for stroke prevention.

Conflict of interest: None declared

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