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Comparison between $CHADS_2$ and CHA_2DS_2-VASc score in a stroke cohort with atrial fibrillation

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Background and purpose: In patients with atrial fibrillation (AF), stroke risk stratification schemes have been developed to optimize antithrombotic treatment. The $CHADS_2$ score is frequently used but has limitations. The CHA_2DS_2-VASc score improves risk prediction. Our objectives are to describe $CHADS_2$ and CHA_2DS_2-VASc score distribution in a cohort of patients with AF and first-ever ischaemic stroke (FIS) and to identify differences in embolic risk stratification.

Methods: Our cohort included 589 patients with FIS, previous modified Rankin score ≤ 3, and non-valvular AF. We recorded demographic data, vascular risk factors, and antithrombotic pre-treatment. The $CHADS_2$ and CHA_2DS_2-VASc scores were calculated according to clinical status before stroke onset.

Results: In 186 (31.6%) patients, AF was previously unknown. Of patients with known AF and $CHADS_2 \geq 2$ ($n = 320$), only 103 (32.2%) were taking anticoagulants; more than half of these patients had an INR <2. The $CHADS_2$ score placed 142 (24.1%) patients in the low–intermediate risk (score ≤ 1) category compared with 21 (3.6%) with CHA_2DS_2-VASc, $P < 0.001$. Applying CHA_2DS_2-VASc reclassified 121 (85.2%) subjects in the $CHADS_2$ low–intermediate risk category as high risk (≥ 2), an indication for anticoagulants. Of the 21 patients who suffered a stroke despite their low CHA_2DS_2-VASc score (≤ 1), seven (33.3%) reported alcohol overuse, and six (28.5%) had a concomitant stroke etiology.

Conclusions: About 25% of FIS patients with AF had a $CHADS_2$ score ≤ 1. Despite the high $CHADS_2$ score of our population, few patients received the recommended antithrombotic treatment according to their thromboembolic risk. Using the CHA_2DS_2-VASc schema significantly increased the percentage of patients indicated for anticoagulation.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia and is associated with a five-fold increase in risk of stroke [1]. In the elderly, this cardiac rhythm disorder represents the most important single cause of ischaemic stroke (IS). In addition, these IS cases are more severe, with a high mortality rate [2]. The absolute stroke risk in patients with AF is extremely heterogeneous. Multiple risk stratification schemes have been developed in recent years with the aim of identifying the best antithrombotic treatment. Despite high variability between the scores, all guidelines recommend that patients in the high-risk category should be treated with anticoagulation. Several studies have shown large relative IS risk reductions in patients treated with adjusted-dose warfarin (62%) over aspirin (22%) [3]. Beyond its well-established benefit for stroke prevention [4], effective oral anticoagulation (OAC) therapy markedly reduces stroke severity and short-term mortality [4,5]. Despite the efficacy of OAC in stroke prevention, at-risk patients are still clearly undertreated [6].

The $CHADS_2$ score is probably the most often used stratification scheme because of its simplicity [7]. Unfortunately, a large proportion of patients [8] are

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classified as having intermediate risk, for which either antiplatelet or anticoagulation treatment could be recommended, which generates uncertainty for their physicians.

The CHA_2DS_2-VASc score improves risk prediction [9] and is also a useful prognostic tool in stroke patients [10]. This new score includes more variables (i.e. sex) and gives a double score for advanced age or previous transient ischaemic attack (TIA) or IS (Table 1).

The objectives of our study are to describe the $CHADS_2$ and CHA_2DS_2-VASc score distribution of a large cohort of first-ever ischaemic stroke (FIS) patients with non-valvular AF and their antithrombotic pre-treatment, looking for changes in treatment recommendation if the new schema had been applied. Second, we focused on those patients who suffered a stroke despite a previous determination of low or intermediate thromboembolic risk.

Methods

From January 2003 through October 2011, 2437 consecutive patients with a diagnosis of IS or TIA, assessed by a neurologist and fulfilling World Health Organization criteria [11], were registered in Basic-Mar, an ongoing prospective registry of IS/TIA at the IMIM-Hospital del Mar [12].

Of these, 771 had AF but we restricted our analysis to 589 patients presenting with a first IS/TIA and non-valvular AF (previously known or newly diagnosed during admission). We excluded patients with prior IS/TIA ($n = 85$) and those who were highly dependent for activities of daily living (modified Rankin score > 3), with the aim of avoiding bias related to antithrombotic prophylaxis ($n = 54$).

Furthermore, we did not include patients with concomitant valvular disease, defined as previous diagnoses of severe mitral or aortic valve diseases or heart-valve repair or replacement ($n = 33$). Finally, we excluded patients with a prior thromboembolism other than IS, such as peripheral artery embolism or pulmonary embolism ($n = 10$).

Following CC/AHA/ESC clinical guidelines, AF was defined as the absence of P waves in the electrocardiogram (EKG), with the isoelectric line being replaced by irregular high-frequency oscillations (f waves), and wholly irregular ventricular response; this was based on EKG results during admission or in previous medical reports. In addition, echocardiographic data were available for 304 patients (51.6%). All patients had a complete neurovascular study that included at least one of the following explorations: a continuous extracranial or pulsate intracranial Doppler study, carotid duplex, CT angiography, and/or MRI-angiography. Stroke subtypes were categorized using the Trial of ORG 10171 in Acute Stroke Treatment (TOAST) classification [13].

Demographic data (age, sex, current smoking, and consumption of > 40 g alcohol/day) and information

Table 1 Details of $CHADS_2$ and CHA_2DS_2-VASc scores

$CHADS_2$ acronym	Score	CHA_2DS_2-VASc acronym	Score
Congestive heart failure	1	Congestive heart failure/LV dysfunction (EF < 35%)	1
Hypertension	1	Hypertension	1
Age ≥ 75 years	1	Age ≥ 75 years	2
Diabetes mellitus	1	Diabetes mellitus	1
Stroke/TIA	2	Stroke/TIA/ thromboembolism	2
		Vascular disease[a]	1
		Age 65–74	1
		Sex (female)	1
Maximum score	6	Maximum score	9
Total score	Recommended treatment [7]	Total score	Recommended treatment [15]
0 Low risk	Aspirin	0 Low risk	None
1 Intermediate risk	Aspirin or warfarin	1 Intermediate risk	Warfarin rather than aspirin
>1 High risk	Warfarin	>1 High risk	Warfarin

LV, left ventricle; EF, ejection fraction; TIA, transient ischaemic attack. [a]Defined as prior myocardial infarction, complex aortic plaque, or peripheral artery disease.

on vascular risk factors and antithrombotic treatment before admission were obtained from patients, their caregivers, or previous medical records using a standardized data collection methodology. Risk factor assessment included arterial hypertension (evidence of at least two elevated blood pressure measurements, systolic > 140 mmHg or diastolic > 90 mmHg, recorded on different days before stroke onset, a physician's diagnosis, or use of medication); diabetes (diagnosis or medication); hyperlipidemia (diagnosis, medication, serum cholesterol concentration >220 mg/dl, LDL cholesterol >130 mg/dl, or serum triglyceride concentration >150 mg/dl); current smoking habits; coronary artery disease (CAD), that is, prior myocardial infarction, angina pectoris, percutaneous coronary intervention, or coronary artery bypass surgery; previous history of congestive heart failure (CHF) or left ventricular ejection fraction <35%; and peripheral arterial disease (PAD), which includes previous history of intermittent claudication, arterial thrombosis, and percutaneous or surgical intervention in the thoracic, abdominal aorta, or lower extremity vessels. A vascular disease variable was created according to the CHA_2DS_2-VASc author's definition, and scored as one point in patients with CAD and/or PAD.

We recorded antithrombotic treatment before admission, categorized into four groups: none, antiplatelets, subtherapeutic anticoagulation if initial INR <2, and INR ≥2. One patient taking both OAC and antiplatelet therapy was assigned to the anticoagulation group. The $CHADS_2$ and CHA_2DS_2-VASc score were calculated for each patient according to clinical status before stroke onset.

Statistical analysis was performed with the SPSS software package 19.0 (IMIM-Hospital del Mar, Barcelona, Spain). Continuous variables were expressed as mean and standard deviation, and categorical data as real numbers and percentages. Univariate analysis compared patients with previously known and unknown AF. Differences in proportions were analyzed with the chi-squared test. We used the *t*-test for continuous variables or Mann–Whitney *U*-test when normal distribution was difficult to assume. Significance was set at $P < 0.05$ (two-tailed test). Written informed consent was obtained from each study participant.

Results

The final cohort was 589 patients, 374 (63.5%) of whom were women. The mean age was 79.06 (SD 8.89), with 439 (74.5%) patients aged 75 years or older. Hypertension was the most frequently reported thromboembolic risk factor in our cohort (78.4%). The AF was previously unknown in 186 (31.6%). The demographic data and vascular risk factors distribution are presented as a comparison between patients with known AF and those who were unaware of their diagnosis (Table 2). Patients with a silent arrhythmia were significantly younger ($P = 0.006$). The only other significant difference was a higher prevalence of CHF and

Table 2 Demographic data and vascular risk factors comparing patients with known and unknown AF

Demographic data and vascular risk factors	Total cohort $n = 589$	Known AF $n = 403$	Unknown AF $n = 186$	*P*
Median age, years	79.06 [8.887]	79.74 [8.827]	77.58 [8.86]	0.006
Female sex	374 (63.5)	255 (63.3)	119 (64)	0.927
Current smoking	65 (11)	44 (10.9)	21 (11.3)	0.888
Alcohol overuse	52 (8.8)	38 (9.4)	14 (7.5)	0.533
Hypertension	462 (78.4)	321 (79.74)	141 (75.8)	0.332
Diabetes	192 (32.6)	128 (31.8)	64 (34.4)	0.571
Hyperlipidemia	236 (40.1)	162 (40.2)	74 (39.8)	1
CHF	161 (27.3)	133 (33)	28 (15.1)	<0.001
CAD	136 (23.1)	114 (28.3)	22 (11.8)	<0.001
PAD	52 (9)	40 (9.9)	13 (7)	0.281
$CHADS_2$[a]	2 (2–3)	2 (2–3)	2 (1–3)	0.002
CHA_2DS_2-VASc[a]	4 (3–5)	4 (3–5)	4 (3–5)	<0.001
Antithrombotic pretreatment				
None	239 (40.6)	96 (23.8)	143 (76.9)	<0.001
Antiplatelets	230 (39)	187 (46.4)	43 (23.1)	
OAC	120 (20.4)	120 (29.8)	0 (0)	

CHF, congestive heart failure; PAD, peripheral arterial disease; CAD, coronary artery disease; OAC, oral anticoagulants; AF, atrial fibrillation. Figures in brackets represent standard deviation; values in parentheses are percentages. [a]$CHADS_2$ and CHA_2DS_2-VASc as median values and quartile values q1–q3 in parentheses.

CAD in the known AF group. Using the $CHADS_2$ scheme, the most frequent score was 2 (41.3%), and the most frequent CHA_2DS_2-VASc score was 4 (32.4%).

In relation to antithrombotic treatment in the 403 patients with previously diagnosed AF, we would highlight that 96 (23.8%) patients received no antithrombotic treatment before admission, 187 (46.4%) were taking antiplatelet drugs, and only 120 (29.8%) of those with known AF were receiving anticoagulants, but 68 (56.7%) of them had an INR <2. Considering only those 320 patients with a previously known AF and $CHADS_2$ ≥2, 103 (32.2%) received anticoagulation therapy, but 52 (53.4%) patients were not achieving an INR within the therapeutic range (≥2). We reviewed the medical charts of the remaining 217 patients with a known arrhythmia and $CHADS_2$ ≥2, high-risk patients who should have started OAC but had not received adequate antithrombotic treatment. Only 34 (15.7%) had any formal contraindication for OAC, such as cancer, predisposition to falls, previous intracranial hemorrhage, gastrointestinal bleeding, or history of peptic ulcer, severe liver or kidney disease, anemia, alcohol overuse (>40 g alcohol/day), or very recent severe head trauma. In 16 (7.3%) patients, acenocoumarol had been prescribed, but was stopped because of compliance problems, perceived difficulty in monitoring anticoagulation levels, or a patient's personal decision. Two patients had stopped OAC therapy after a cardioversion. In the remaining 167 (77%), no explanation was found for the lack of anticoagulation.

The $CHADS_2$ score placed 142 (24.1%) patients in the low–intermediate risk (score ≤ 1) category compared with 21 (3.6%) with CHA_2DS_2-VASc, $P < 0.001$. Applying CHA_2DS_2-VASc reclassified 121 (85.2%) subjects in the $CHADS_2$ low–intermediate risk category as high risk (≥2), an indication for anticoagulants. Using CHA_2DS_2-VASc, only four (0.7%) patients remain in the lowest risk category (score = 0), and 17 (2.9%) in the intermediate risk category (score = 1). Table 3 presents the score distribution for each instrument.

Of the 21 patients in the low–intermediate CHA_2DS_2-VASc risk category (score ≤ 1), 11 patients had previously known AF, but only one patient was taking anticoagulants. A high incidence of alcohol overuse was found in this group (33.3%). In six (28.5%) patients, a second concomitant stroke etiology was found. Table 4 summarizes patient characteristics.

Table 3 Distribution of the $CHADS_2$ and CHA_2DS_2-VASc scores

$CHADS_2$ score	*n* (%)	$CHADS_2$ redistribution to CHA_2DS_2-VASc score	CHA_2DS_2-VASc	*n* (%)
0	29 (4.9)	→**0** 4 (13.8) →**1** 13 (44.8) →**2** 12 (41.4)	**0**	4 (0.7)
1	113 (19.2)	→**1** 4 (3.5) →**2** 43 (38.1) →**3** 59 (52.2) →**4** 7 (6.2)	**1**	17 (2.9)
2	243 (41.3)	→**2** 3 (1.2) →**3** 48 (19.8) →**4** 155 (63.8) →**5** 37 (15.2)	**2**	58 (9.8)
3	161 (27.3)	→**3** 2 (1.2) →**4** 29 (18) →**5** 101 (62.7) →**6** 29 (18.1	**3**	109 (18.5)
4	43 (7.3)	→**5** 5 (11.6) →**6** 26 (60.5) →**7** 12 (27.9)	**4**	191 (32.4)
			5	143 (24.3)
			6	55 (9.3)
			7	12 (2.0)

Bold values represent the $CHADS_2$ score redistribution applying the CHA_2DS_2-VASc score.

Discussion

In a high proportion of our patients, silent AF was first diagnosed owing to an IS. Therefore, we would emphasize the need to improve AF detection in the general population, because of the severity and mortality of this stroke subtype [4,5].

Previous studies have shown that in daily clinical practice anticoagulation has been substantially underused in eligible patients with AF, particularly amongst the elderly [6]. Although the 2001 ACC/AHA/ESC guidelines recommend the use of anticoagulation in high-risk patients ($CHADS_2$ ≥2), only 103 (32.2%) of the 320 patients with previously known AF and high thromboembolic risk were taking an anticoagulant, and less than half of this subgroup had an appropriately controlled INR. Furthermore, of the remaining 217 in this high-risk category only 34 (15.7%) had a major contraindication for OAC. The vast majority simply had not received the recommended antithrombotic treatment.

Moreover, about 25% of our patients with IS with AF have a low–intermediate risk according to the $CHADS_2$ score. Although the $CHADS_2$ score distribution in our total AF population is unknown, a previous population study of a single-center Mediterranean cohort [14] reported that 50.7% of patients with AF had a $CHADS_2$ score of 0–1. This points out the importance of accurate stroke risk calculation in this category, which includes half of the AF population and a significant proportion of patients with IS. Therefore, using the CHA_2DS_2-VASc

Table 4 Characteristics of stroke patients with a previous CHA_2DS_2-VASc 0–1

CHA_2DS_2-VASc	Known atrial fibrillation	Age/sex	Risk factor	Other pathologies	Antithrombotic pretreatment	TOAST
0	Yes	57/male	None	Alcohol overuse	None	C
0	Yes	53/male	None	Alcohol overuse	None	C
0	Yes	63/male	None	None	Antiplatelets	C
0	No	53/male	None	HIV+ HTP	Antiplatelets	C
1	Yes	71/male	Age	Alcohol overuse and bladder tumor	Antiplatelets	U: C + S
1	Yes	69/male	Age	Alcohol overuse	None	U: C + L
1	Yes	57/female	Sex	Alcohol overuse and HCV	None	C
1	Yes	66/male	Age	Hypertrophic myocardiopathy	Anticoagulants	C
1	Yes	61/male	HTA	Alcohol overuse	Antiplatelets	C
1	Yes	60/male	HTA	None	Antiplatelets	U: C + S
1	Yes	63/male	CHF	Lymphoma, chemotherapy	None	U: C + O
1	No	65/male	Age	None	None	C
1	No	73/male	Age	None	None	U: C + S
1	No	73/male	Age	None	None	C
1	No	64/female	Sex	None	None	C
1	No	62/female	Sex	Hypothyroidism and obesity	None	C
1	No	58/female	Sex	None	None	C
1	No	60/male	HTA	Alcohol overuse	None	C
1	No	63/female	Sex	None	None	C
1	No	65/male	Age	None	None	C
1	No	53/male	PAD	None	None	U: C + L

C, cardioembolism; S, small-artery occlusion; L, large-artery atherosclerosis; O, stroke of other determined etiology; U, stroke of undetermined etiology because two or more causes were identified; HIV, human immunodeficiency virus; HTP, pulmonary hypertension; HCV, hepatitis C virus; HTA, hypertension; CHF, congestive heart failure; PAD, peripheral artery disease.

score would increase the recommended anticoagulation from 75.9% to 96.4% of this population.

We would emphasize that 121 subjects (85.2%) stratified as low–intermediate risk (score ≤ 1) using the $CHADS_2$ scheme were reclassified by CHA_2DS_2-VASc into its high-risk category, leaving only four (0.7%) patients in its low-risk group (score = 0), in which patients could be managed with antiplatelet agents or preferably without antithrombotic therapy. In the validation study, this category did not report any thromboembolic events [9]. The number of patients in the intermediate risk category (CHA_2DS_2-VASc = 1) was dramatically reduced, from 19.2% using $CHADS_2$ to just 2.9%. Moreover, the new schema recommends anticoagulation over antiplatelet agents in the intermediate risk group [15]. A question arises about this category, in which being women is the only non-major risk factor. The need to start anticoagulation treatment in this group is still being debated. As some authors suggest, another risk factor is probably necessary to begin therapy [15]. It is well established that not all risk factors were equally associated with thromboembolic risk [16].

Moreover, the high presence of alcohol overuse is particularly important in the 21 patients with a CHA_2DS_2-VASc score ≤ 1, most of them without any other risk factor. This supports previous observations that long-term high alcohol consumption may increase AF risk [17,18]. We want to emphasize that six cases with IS had undetermined etiology because, following the TOAST stroke classification, two or more causes coexisted. In these six patients, we cannot be sure that AF was the main cause of stroke.

Our study has some limitations. First, the score distribution in our AF population is unknown. Therefore, the score distribution once the stroke has occurred is not equivalent to the proportion of patients at risk in each category. Second, we included patients with concomitant stroke etiologies (i.e. atherothrombotic). However, this better approximates our total population and, furthermore, in validation studies of thromboembolic risk schemes other stroke etiologies were not ruled out.

In conclusion, a significant number of stroke patients with AF are at low–intermediate thromboembolic risk using the $CHADS_2$ score, a proportion that decreases drastically when the CHA_2DS_2-VASc score is used. In addition, despite a high $CHADS_2$ score, only a small number of patients in our cohort were anticoagulated prior to suffering a stroke. The CHA_2DS_2-VASc score might have a great impact in cardioembolic stroke prevention not only by improving risk stratification but also by increasing the number of patients with AF in whom anticoagulation is appropriately recommended.

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Disclosure of conflicts of interest

The authors declare no financial or other conflict of interests.

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