Evaluation of the Use of CHA_2DS_2-VASc Scoring System to Predict Ischemic Stroke in Patients with non Valvular Atrial Fibrillation: A Single Center Experience

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ABSTRACT:

BACKGROUND:

Stroke in patients with non-valvular AF is a major cause for disability and increasing morbidity and mortality, CHA2DS2-VASc is a tool for assessing the risk of stroke in these patients

OBJECTIVE:

This study was conducted to evaluate the use of CHA_2DS_2-VASc scoring system in a sample of Iraqi patients with embolic stroke and non valvular atrial fibrillation

PATIENTS AND METHODS:

A cross-sectional study was done in Baghdad Teaching Hospital that enrolled 60 patients with non-valvular atrial fibrillation who presented with a first-time ischemic stroke. Data was collected using a questionnaire, CHA2DS2-VASc score was calculated (excluding 2 points of stroke for all patients), and also HAS-BLED score was calculated.

RESULTS:

In this study, there was a statistically significant association between age groups and CHA_2DS_2-VASc scores, as most patients with low scores were in younger age groups and most of patients with higher scores were in older age groups. The same association was found between sex and CHA_2DS_2-VASc scores, noting that the majority of the study group were females (70.0%). The most frequent risk factor was hypertension which was diagnosed in (85.0%) of the study group, followed by heart failure (51.7%), and diabetes mellitus (40.0%), while the presence of vascular diseases was the least common (26.7%). Warfarin use was recorded in only 7(11.7%) patients. There was no statistically significant association between CHA_2DS_2-VASc and HAS-BLED scores.

CONCLUSION:

CHA_2DS_2-VASc was a valuable tool for assessing risk of embolic stroke, yet, there was a low frequency of anticoagulation use which was not explained by HAS-BLED scores. Hypertension and heart failure were the most common among study group, followed by diabetes mellitus.

KEYWORDS: CHA_2DS_2-VASc score – ischemic Stroke – non valvular atrial fibrillation

INTRODUCTION:

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. Atrial fibrillation confers a 5-fold risk of stroke, and one in five of all strokes is attributed to this arrhythmia[1].

Ischaemic strokes in association with AF are often fatal, and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. [1]

Atrial fibrillation is associated with a variety of clinical conditions.

Aging increases the risk for developing AF. Hypertension is a risk for AF.[2] Symptomatic heart failure is found in 30% of AF patients, and AF is found in up to 30–40% of heart failure patients. [2]

Cardiomyopathies carry an increased risk for AF, especially in young patients.[3] Atrial septal defect is associated with AF in 10–15% of patients in older surveys.[1] Coronary artery disease is present in ≥20% of the AF population.[4] Overt thyroid dysfunction can be the sole cause of AF and may predispose to AF-related complications.[5] Obesity is found in 25% of AF patients.[6]

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Diabetes mellitus requiring medical treatment is found in 20% of AF patients. Chronic obstructive pulmonary disease (COPD) is found in 10–15% of AF patients. Sleep apnoea, especially in association with hypertension, diabetes mellitus, and structural heart disease, may be a pathophysiological factor for AF. Chronic renal disease is present in 10–15% of AF patients.[1]

Risk stratification for stroke and thromboembolism

The identification of various stroke clinical risk factors has led to the publication of various stroke risk schemes. Most have (artificially) categorized stroke risk into 'high', 'moderate', and 'low' risk strata. The simplest risk assessment scheme is the $CHADS_2$ score [7].

The $CHADS_2$ [cardiac failure, hypertension, age, diabetes, stroke (doubled)] risk index evolved from the AF Investigators and Stroke Prevention in Atrial Fibrillation (SPAF) investigators criteria, and is based on a point system in which 2 points are assigned for a history of stroke or transient ischemic attack (TIA) and 1 point each is assigned for age >75 years, a history of hypertension, diabetes, or recent cardiac failure.[8]

The $CHADS_2$ stroke risk stratification scheme should be used as a simple initial (and easily remembered) means of assessing stroke risk, particularly suited to primary care doctors and non-specialists. In patients with a CHADS2 score of ≥2, chronic oral anticoagulant therapy is indicated.

This risk factor-based approach for patients with non-valvular AF can also be expressed as an acronym, CHA_2DS_2-VASc.[9] Thus, this acronym extends the $CHADS_2$ scheme by considering additional stroke risk factors that may influence a decision whether or not to anticoagulate.

Risk of bleeding

An assessment of bleeding risk should be part of the patient assessment before starting anticoagulation. Despite the increasing use of anticoagulation for more elderly patients with AF, rates of intracerebral haemorrhage are considerably lower than in the past, typically ranging between 0.1 and 0.6% in contemporary reports. This may reflect lower anticoagulation intensity, more careful dose regulation, or better control of hypertension.

Intracranial bleeding increases with INR values > 3.5–4.0, and there is no increment in bleeding risk with INR values between 2.0 and 3.0 compared with lower INR levels. Various bleeding risk scores have been validated for bleeding risk in anticoagulated patients[10]

Using a new simple bleeding risk score, HAS-BLED score to assess bleeding risk in AF patients, a score of ≥3 indicates 'high risk', and some caution and regular review of the patient is needed following the initiation of antithrombotic therapy, whether with vitamin K antagonist (VKA) or aspirin. [11]

PATIENTS AND METHODS:

In this cross-sectional study, data was collected for a period of 10 months, extending from the first of June 2017 to the first of March 2018, at Baghdad Teaching Hospital, and a total of 60 patients were enrolled with the following criteria:

Inclusion Criteria:

First time ischaemic stroke in presence of non-valvular atrial fibrillation.

Exclusion Criteria:

1. History of stroke or TIA.
2. Valvular AF.

Data was collected using a questionnaire, which incorporated demographic data, and elements of CHA_2DS_2-VASc scoring system[congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and sex category (female)]. [24] This scheme is based on a point system in which 2 points are assigned for a history of stroke or TIA, or age ≥75; and 1 point each is assigned for age 65–74 years, a history of hypertension, diabetes, recent cardiac failure, vascular disease (myocardial infarction, complex aortic plaque, and peripheral arterial disease (PAD) including prior revascularization, amputation due to PAD, or angiographic evidence of PAD, etc.), and female sex.

Elements of HAS-BLED scoring system included hypertension, abnormal renal/ liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/ alcohol concomitantly).

Statistical Analysis

Data input, tabulation, and coding was done by use of IBM© SPSS© (Statistical Package for the Social Sciences)Statistics Version 22. Chi-square test was used to find any association between categorical data, and Univariate ANOVA was used for comparison between more than two numerical variables. P-value less than 0.05 was considered significant throughout data analysis.

RESULTS:

There was statistically significant association between age groups and CHA_2DS_2-VASc scores, as most patients with score of 1-2 were in age group < 65 years (70%), most patients with 3-4 scores were in the 65-74 years age group (46.4%), while among patients with scores from 5 to 6, the age group ≥75 years had the highest percentage of patients (45.0%) as shown in table (1).

Table (1): relationship between age groups and CHA_2DS_2-VASc score

Age groups	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
<65	7(70.0)	5(17.9)	1(4.5)	13(21.7)	**0.000**
65-74	2(20.0)	13(46.4)	5(22.7)	20(33.3)	
≥75	1(10.0)	10(35.7)	16(72.7)	27(45.0)	
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was statistically significant association between sex and CHA_2DS_2-VASc scores as the most of patients with CHA_2DS_2-VASc score ≥ 3 were females while most patients with CHA_2DS_2-VASc < 3 were males (P value= 0.002) as shown in table (2).

Table (2): relationship between sex and CHA_2DS_2-VASc score

Sex	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
Male	7(70.0)	9(32.1)	2(9.1)	18(30.0)	**0.002**
Female	3(30.0)	19(67.9)	20(90.9)	42(70.0)	
Total	10(100.0)	28(100.0)	22(100.0)	60(100.0)	

Chi-square test

The study group had patients with one or more chronic diseases, the most frequent was hypertension which was present in 51(85.0%) patients, followed by heart failure 31(51.7%), diabetes mellitus 24(40.0%); vascular diseases were the least common with only 16(26.7%) patients. Warfarin use was recorded in only 7(11.7%) patients as shown in table (3).

Table (3): frequencies of chronic diseases in the study group

Variables	Frequency	Percentage
Heart failure	31/60	51.7
Hypertension	5/60	85.0
Diabetes mellitus	24/60	40.0
Vascular disease	16/60	26.7
Warfarin use	7/60	11.7

There was no statistically significant association between heart failure and CHA_2DS_2-VASc scores, as in scores 1-2 there was only 3(30.0%) patients with heart failure but in score 3-4 and 5-6 scores there were 14 (50%) and 14 (63.6%) patients respectively as shown in table (4).

Table (4): relationship between heart failure and CHA_2DS_2-VASc score

Heart Failure	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
No	7(70.0)	14(50.0)	8(36.4)	29(48.3)	**0.205**
Yes	3(30.0)	14(50.0)	14(63.6)	31(51.7)	
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was statistically significant association between hypertension and CHA_2DS_2-VASc score, as all cases with high scores of 5-6 had hypertension, and 20 (71.4%) from patients with scores 3-4 as shown in table(5).

Table (5): relationship between hypertension and CHA_2DS_2-VASc score

Hypertension	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
No	1(10.0)	8(28.6)	0(0.0)	9(15.0)	**0.017**
Yes	9(90.0)	20(71.4)	22(100.0)	51(85.0)	
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was statistically significant association between diabetes mellitus and CHA_2DS_2-VASc, as 13(59.1%) patients had high scores of 5-6, decrease to 10(35.7%) in 3-4 group, and only one patient in 1-2 group as shown in table (6).

Table (6): relationship between diabetes mellitus and CHA_2DS_2-VASc score

Diabetes Mellitus	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
No	9(90.0)	18(64.3)	9(40.9)	36(60.0)	**0.026**
Yes	1(10.0)	10(35.7)	13(59.1)	24(40.0)	
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was statistically significant association between vascular disease and CHA_2DS_2-VASc scores, as there were 12(54.5%) patients with scores of 5-6, and the remaining 4 (14.3%) had scores of 3-4, and none had scores of 1-2 as shown in table (7).

Table (7): relationship between vascular diseases and CHA_2DS_2-VASc score

Vascular diseases	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
No	10(100.0)	24(85.7)	10(45.5)	44(73.3)	
Yes	0(0.0)	4(14.3)	12(54.5)	16(26.7)	**0.001**
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was no statistically significant association between warfarin use and CHA2DS2-VASc scores, as 3(10.7%) had scores of 3-4, and 4(18.2%) had scores of 5-6 as shown in table (8).

Table (8): relationship between warfarin use and CHA_2DS_2-VASc score

Warfarin use	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
	No (%)	No (%)	No (%)	No (%)	
No	10(100.0)	25(89.3)	18(81.8)	53(88.3)	
Yes	0(0.0)	3(10.7)	4(18.2)	7(11.7)	**0.324**
Total	**10(100.0)**	**28(100.0)**	**22(100.0)**	**60(100.0)**	

Chi-square test

There was no association between CHA_2DS_2-VASc score and HAS-BLED, as from the total 30 patients with lowest bleeding risk by HAS-BLED, which was <2%/year, 18(60.0%) had scores of 3-4, 7 (23.3%) had scores of 5-6, and 5 (16.7%) had scores of 1-2, and for the higher risks of bleeding, the mean values for HAS-BLED showed no statistically significant difference between the three groups, and HAS-BLED was 5.49±3.92 in with CHA_2DS_2-VASc scores of 1-2, 5.22±2.40 with scores of 3-4, and 5.06±2.27 with scores of 5-6. The total HAS-BLED mean for the study sample was 5.19±2.53 as shown in table (9).

Table (9): Relationship between HAS-BLED and CHA_2DS_2-VASc scores

HAS-BLED	CHA_2DS_2-VASc				P-value
	1-2	3-4	5-6	Total	
<2% /year No (%)	5 (16.7)	18 (60.0)	7 (23.3)	30 (100.0)	-
Mean ±SD	5.49±3.92	5.22±2.40	5.06±2.27	5.19±2.53	**0.950**

One way ANOVA

DISCUSSION:

This cross sectional study for patients who suffered from a stroke in the presence of non-valvular atrial fibrillation, showed that the risk of stroke increased with increasing age, as there were 13 (21.7%) patients <65 years, 20 (33.3%) patients from 65-74 years, and 27 (45.0%) in patients 75 years and older. In addition, older age groups had higher CHA_2DS_2-VASc scores. This finding was in agreement with Van Walraven C, et al (2009) [12], Kooistra HAM, et al (2016) [13], and Ansell j (2017) [14], who showed that although the risk of stroke increased with age, there was a paradoxical reduction in prescribing anticoagulants for them, probably due to concerns about complications, namely bleeding.

In the current study, females were predominant forming 42(70.0%) of total study group, and males 18(30.0%). Males had lower CHA_2DS_2-VASc scores than their female counterparts. A study done in South Korea, Son MK, et al (2017) [15], showed that from the total 10654 patients enrolled in their study, men formed (53.6%), and there was no statistically significant difference between the two genders in developing stroke after follow up. However, female sex is a recognized risk factor that increase the risk of stroke as stated by the guidelines published by the American Academy of Neurology (2014)[16]. In spite of men having a higher incidence of atrial fibrillation[17], women suffering from non-valvular atrial fibrillation have twice the risk of stroke compared to men with similar condition [18].

In the current study, CHA_2DS_2-VASc components were examined. Heart failure was observed among 31 (51.7%) of patients, which indicated that it was a risk factor for developing stroke, but the AF Working Group (2007) [19], and Friberg L, et al (2012) [20], had shown that heart failure did not increase the risk of stroke, rather it is the impairment in systolic function that increased stroke risk in patients with AF[21]. Supporting that, European Society of Cardiology guidelines focused on systolic heart failure as a risk factor for stroke. Also, many patients might have history of heart failure, but do not in fact have systolic impairment [22].

Hypertension in this study was the most predominant risk factor, with 51(85.0%) patients suffering from it. This was very similar to the results of Son MK, et al (2017)[23], as hypertension was found in (86.0%) among patients with stroke, and they showed that hypertension was the strongest risk factor for ischaemic stroke, also Kakkar AK, et al (2013) [24] showed that the prevalence of hypertension was (77.8%), as 8,249 patients out of 10,614 total study group had hypertension. Control of blood pressure can reduce ischemic strokes incidence [25]. So, better control may contribute to lower stroke incidence rates [9].

Diabetes mellitus was observed in 24 (40.0%) patients. This was very close to the results of Son MK, et al (2017) [15], with 472 (46.2%) of their study group had diabetes, with a statistically significant increased risk for developing stroke, but Suzuki S, et al (2015)[26], in their pooled analysis in Japan, showed lower rate of diabetes mellitus ranging from (9.2%) to (21.0%). Diabetes mellitus is a recognized risk factor of stroke, as it causes dysfunction of vascular endothelial, arterial stiffness at early-age, systemic inflammation and capillary basal membrane thickening [27].

Vascular diseases were observed in 16 (26.7%) of study sample, Son MK, et al (2017) [15] had shown lower rate of vascular diseases of (10.8%), also Suzuki S, et al (2015) [26] showed that its' rates ranged from (5.6%) to (15.4%), while Olesen JB, et al (2012) [28], in a nationwide study in USA, for patients diagnosed with non-valvular atrial fibrillation from 1997-2008, showed that vascular disease whether peripheral arterial disease or myocardial infarction, or both were present in (17.4%) of the total study sample, and reported that vascular diseases were independent risk factors for thromboembolism, and addition of it to the previous $CHADS_2$ score had increased the predictive value significantly in CHA_2DS_2-VAS_c. Thrombosis prophylaxis should be given to patients with AF patients who have myocardial infarction or peripheral vascular disease, so it is crucial to identify these risk factors [1].

In the current study, the rate of anticoagulation use was very low as only 7 (11.7%) patients were on warfarin, and all of them had their INR below the therapeutic level of (2-3) [(1)] with a range and ranged from (1.1-1.8). Kakkar AK, et al (2013) [(24)], had reported higher rates of using vitamin K antagonists of (58.2%), which was regarded by them as low, but after dividing them according the $CHADS_2$ risk score, it was evident that there was an overuse of anticoagulants in low risk $CHADS_2$ (0-1), and an underuse in high risk $CHADS_2$ (2-6), and they tried to identify causes for not providing anticoagulant therapy, and showed that high risk of bleeding, frequent falling, drug interactions, allergy, and in approximately half of these cases was doctor's choice rather than patients' refusal.

50/60 of patients in our study group had CHA_2DS_2-VASc ≥3, which is a very important predictor of new embolic stroke in our patient group calling for precise follow-up and optimal anticoagulation profile for these patients to reduce the high risk of recurrent embolization.

Patients with high risk for stroke have multiple comorbidities, and with these comes the concerns of physicians for the complications of anticoagulants. With the advent of novel types of anticoagulants there might be a shift towards using these medications as they probably have less side effects, more predictable dose-effect, and less drug interactions [(29)].

The balance between anticoagulation, and the risk of bleeding is challenging. In a trial to standardize that risk, HAS-BLED bleeding score was created, and it is currently recommended by the European Society of Cardiology [(1)]. In the current study, patients with risk of bleeding <2.0%/year by HAS-BLED score were 30 (50.0%) of the total 60 study sample, from them there was 18 (60%) with CHA_2DS_2-VASc of (3-4), but the remaining half of this study patients have high HAS-BLED scores, with a mean of 5.19% ± 2.53% /year risk of bleeding, and the European Society of Cardiology guidelines recommends that in patients with HAS-BLED scores ≥3 %/year; caution and/or regular visits and reviews are required in order to decrease risk of bleeding[(1)], and detect risk factors like uncontrolled hypertension, labile international normalized ratios, and aspirin use[(30)].

CONCLUSION:

CHA_2DS_2-VASc was a valuable tool for assessing risk of embolic stroke in patients with non valvular atrial fibrillations. Yet, there was low frequency of anticoagulation use, not explained by HAS-BLED scores.

Hypertension and heart failure were the two most common comorbidities among the study group, followed by diabetes mellitus.

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