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RESEARCH ARTICLE

Is there a Concordance between CHA2DS2 VASc and HAS-BLED Scores in Middle Eastern Patients with Nonvalvular AF? Analysis of the Jordan Atrial Fibrillation (JoFib) Study

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Abstract:

Background:

Nonvalvular Atrial Fibrillation (NVAf) is a common arrhythmia that potentially contributes to stroke and systemic embolization. Anticoagulants may contribute to the risk of bleeding in these patients. Reports of NVAf on Middle Eastern populations are scarce and outdated. This study investigated the concordance between congestive heart failure, hypertension, ≥ 75 years of age, diabetes mellitus, stroke or transient ischemic attack, vascular disease, 65 to 74 years of age group, sex category (CHA2DS2 VASc), and Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly (HAS-BLED) scores, and the risks of stroke and bleeding in Jordanian NVAf patients.

Methods:

Results were extracted from the Jordan Atrial Fibrillation (JoFib) multicenter registry (NCT03917992). To assess the risk of stroke, a CHA2DS2 VASc score was used. The HAS-BLED score was used to assess the risk of bleeding. Subgroup analysis for males and females was carried out.

Results:

We included 1823 NVAf patients, almost equally distributed among males and females. The overall mean age was 68.2 years. Most patients had a body mass index (BMI) ≥ 25 (71.5%). Almost half of the patients were smokers, 45.5% had diabetes, and 76.3% had hypertension. Paroxysmal AF was the most common subtype (38%), followed by the permanent (28.6%), long-standing (17.3%), and persistent types (16.1%). Females had a significantly higher CHA2DS2 VASc score than males ($p=0.012$). For the risk of bleeding, 48.9% of patients had a low risk, 31.5% had intermediate risk, and 19.6% had a high risk. A correlation was found between the two scoring systems. Out of the 357 patients who had a high HAS-BLED score, 354 (99.2%) patients also had a high CHA2DS2 VASc score.

Conclusion:

In almost all NVAf patients with a high risk of bleeding (high HAS-BLED score), the use of anticoagulants is highly recommended and strongly indicated according to the CHA2DS2 VASc score stratification. Therefore, strict strategies of well-controlled administration of anticoagulants should always be considered and followed in Middle Eastern patients with NVAf and a high risk of bleeding.

Keywords: Atrial fibrillation, CHA2DS2 VASc, HAS-BLED, Concordance, Middle Eastern, Patients.

Article History

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1. INTRODUCTION

Atrial Fibrillation (AF) is the most common type of arrhythmia that increases the risk of stroke and systemic

embolization and may worsen cardiac function [1]. The prevalence of AF is age-dependent, and it is a major cause of mortality and morbidity worldwide, particularly among the elderly [2]. Electrocardiograph findings may not always be conclusive. Therefore, negative findings at hospital admission may not rule out AF, and patients suspected to have paroxysmal AF are advised to remain monitored at home [2].

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This is important when considering the increased risk of strokes by 5-fold among patients with AF, according to the Framingham study [3]. Moreover, at least 50% of strokes in patients aging 80 or older are attributed to AF [4].

AF is classified according to etiology as either valvular (VAF) or non-valvular atrial fibrillation (NVAF). VAF is related to the presence of moderate to severe rheumatic mitral stenosis or metallic prosthetic valve. In NVAF patients, AF is caused by certain structural heart diseases, such as ischemic heart disease, cardiomyopathies, non-rheumatic valvular disease, and hypertension [5]. The valvular pathologies in VAF mandate the use of vitamin K antagonists (VKA). However, in those patients with NVAF, the use of direct oral anticoagulant agents (DOACs) over VKA is recommended as a preventive measure against developing strokes and systemic embolization among those patients with high congestive heart failure, hypertension, ≥ 75 years of age, diabetes mellitus, stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, or sex category (CHA2DS2 VASc) scores. On the other hand, the use of DOACs in AF patients is associated with an increased risk of bleeding events [6]. Therefore, an accurate stratification of risks for stroke or bleeding should guide the use and dosage of antithrombotic treatments. This is critical, especially in NVAF patients where the risk-benefit equation is tightly balanced [7].

Reports about AF and its characteristics among the Middle Eastern population are scarce and outdated [8, 9]. Therefore, there is an urgent need for more investigations regarding the unique risk factors. On the other hand, the clinical management of AF patients in the Middle East necessitates clinical evidence driven by real-world registries [10]. In light of that, the Jordan AF (JoFib) Registry was established to provide more insight into the clinical characteristics and the management progress of Middle Eastern AF patients [11, 12].

The present study aimed to report if there is any concordance between the CHA2DS2 VASc score (determining the need for anticoagulants therapy) and Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly (HAS-BLED) scores (determining the risk for bleeding and the need for dose adjustment when using OACs) in Middle Eastern patients with NVAF. To achieve that, we conducted an analysis using the JoFib Registry [11, 12].

2. MATERIALS AND METHODS

Data for this study were retrospectively collected from the JoFib Registry [11, 12], a prospective multicentre non-interventional observational registry of adult patients aged ≥ 18 years and diagnosed with AF. The JoFib registry was generated from those patients who visited 18 hospitals and >30 outpatient cardiology clinics in Jordan from mid-2019 until the end of 2020 (NCT03917992) [13]. Baseline characteristics of clinical and demographic data were documented. The diagnosis of AF was confirmed by a 12-lead electrocardiogram (ECG), rhythm

strip lasting ≥ 30 sec, ≥ 1 episode of AF on ambulatory ECG monitoring, or a past diagnosis by a cardiologist. We used a standard formula to calculate the CHA2DS2-VASc and HAS-BLED scores [14, 15]. This study was approved by the institutional review board (IRB) at our institute, and informed consent was obtained from the patients.

2.1. The CHA2DS2 VASc and HAS-BLED Scores

For the evaluation of the risk of stroke, we used the CHA2DS2 VASc assessment tool, which was updated by Lip *et al.*, and replaced the CHADS₂ by adding more risk factors for ischemic stroke [13]. Scores were calculated according to congestive heart failure (1 point), hypertension (1 point), age >75 years (2 points), diabetes (1 point) and prior stroke (2 points), age >65 (1 point), female sex (1 point) and vascular disease (1 point). A high-risk CHA2DS2 VASc score is defined as ≥ 3 in women and ≥ 2 in men; the intermediate-risk score is defined as a score of 2 in women and 1 in men; a low-risk score as 1 in women and 0 in men.

To assess the risk of bleeding, we used the HAS-BLED score that relies on hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio (INR), elderly (age ≥ 65 years), and drugs/alcohol simultaneously [15]. Risk scores were stratified as either low (0 points), moderate (1-2 points), or high risk (≥ 3 points).

2.2. Statistical Analysis

Summary statistics such as means and medians were used for continuous variables, in addition to counts and percentages for categorical variables. A Student's t-test was used to compare means and a chi-square test to compare frequencies between male and female subgroups. We also generated donut charts to represent classifications of CHA2DS2 and HAS-BLED scores. All statistical analyses were carried out using R statistical language (version 4.0.5) (R Foundation for Statistical Computing, Vienna, Austria).

3. RESULTS

3.1. Demographics and Comorbidities

This study included 1823 NVAF patients, with an approximately equal distribution of males and females. Their average age was 68.2 years. Most patients had a body mass index (BMI) ≥ 25 (71.5%), the mean BMI was 29.6, and 45.5% of them had dyslipidemia. Almost half of the patients were smokers, 45.5% of them had diabetes, and 76.3% of patients had hypertension. Past history of stroke was reported by 11.1% of patients, and 22 patients reported a history of systematic embolism. There were 335 (19.5%) patients with heart failure, and 145 (8%) patients had coronary artery disease. Finally, 10.3% of patients had thyroid disease, 9.3% had chronic kidney disease, and 5.7% had an active malignancy. Patient characteristics are summarized in Table 1.

Table 1. Patient characteristics.

-	Overall (n=1823)
Age	
Mean (SD)	68.2 (13.1)
Median [Min, Max]	71.0 [18.0, 106]
Sex, n (%)	
Male	874 (47.9%)
Female	949 (52.1%)
Body Mass Index	
Mean (SD)	29.6 (5.8)
Median [Min, Max]	28.7 [15.6, 62.4]
BMI category, n (%)	
<25	363 (19.9%)
≥25	1303 (71.5%)
Hypertension, n (%)	1391 (76.3%)
Diabetes Mellitus, n (%)	827 (45.4%)
Dyslipidemia, n (%)	829 (45.5%)
Smoking, n (%)	829 (45.5%)
History of Stroke, n (%)	203 (11.1%)
History of Systemic embolization, n (%)	22 (1.2%)
Atrial fibrillation type, n (%)	
Paroxysmal	692 (38.0%)
Persistent	294 (16.1%)
Long-standing	316 (17.3%)
Permanent	521 (28.6%)
Comorbidities, n (%)	
None	1188 (65.2%)
Heart failure	355 (19.5%)
Coronary artery disease	145 (8.0%)
DVT/PE	5 (0.3%)
TGA	1 (0.1%)
Complex CHD	3 (0.2%)
Sick sinus syndrome	1 (0.1%)
Pericarditis	1 (0.1%)
Left ventricular hypertrophy, n (%)	653 (35.8%)
Pulmonary hypertension, n (%)	464 (25.5%)
Sleep apnea, n (%)	73 (4.0%)
Thyroid disease, n (%)	187 (10.3%)
Chronic kidney disease, n (%)	170 (9.3%)
Active malignancy, n (%)	104 (5.7%)
Echo cardiographic findings, n (%)	
None	1477 (81.0%)
Moderate to severe MR	186 (10.2%)
Moderate to severe aortic stenosis	41 (2.2%)
Moderate to severe aortic regurgitation	14 (0.8%)
Mild pericardial effusion	3 (0.2%)
Moderate to severe pericardial effusion	5 (0.3%)
Moderate to severe tricuspid regurgitation	76 (4.2%)
Atrial septal defect	3 (0.2%)
HCM	3 (0.2%)
Ebstein anomaly	5 (0.3%)
Complex congenital heart disease	3 (0.2%)
TAVI	0 (0%)

(Table 1) contd....

-	Overall (n=1823)
Bicuspid aortic valve	2 (0.1%)
VSD	1 (0.1%)
Subaortic membrane	1 (0.1%)
Left ventricular ejection fraction	
Mean (SD)	53.7 (12.6)

Abbreviations: DVT: Deep Vein Thrombosis, PE: Pulmonary Embolism, VD: Valve Disease, CHD: Congestive Heart Failure, TGA: Transposition of the Great Arteries, TAVI: Transcatheter Aortic Valve Implantation, MR: Mitral Valve Regurgitation, HCM: Hypertrophic Cardiomyopathy, VSD: Ventricular Septal Defect, BMI: Body Mass Index

3.2. Characteristics of Patients with NVAF

The most common NVAF type was paroxysmal AF (38%), followed by permanent type (28.6%), long-standing (17.3%), and persistent (16.1%) AF. Left ventricular hypertrophy was found in 35.8% of patients, moderate-to-severe mitral regurgitation was found in 186 patients, moderate-to-severe tricuspid regurgitation, aortic regurgitation, and aortic stenosis in 76, 14, and 41 patients, respectively, and pulmonary hypertension in 25.5% of patients. Most patients did not show any abnormal ECG findings. The mean left ventricular ejection fraction (LVEF) was 53.7% (\pm 12.6%), where most patients had a normal LVEF (59.9%), 36.8% of patients had LVEF <55%, and 3.3% of them had an LVEF >70% (Table 1).

3.3. Risk of Ischemic Stroke and Risk of Bleeding

The comparison of 949 females and 874 males showed that females had a significantly higher rate of a high CHA2DS2 VASc score than males (83.0 vs. 77.9%, $p=0.012$) and a lower rate of patients with a low score (6.7 vs. 10.1%) (Table 2).

Additionally, 105 male patients (12.0%) and 97 (10.2%) females had a moderate CHA2DS2 VASc score (Table 2).

Most patients had a HAS-BLED score of 1 and 2 (37.0 and 31.5%, respectively). Only 23 (1.3%) patients had a score of 5. Seven patients had a score of ≥ 6 (Table 3). Therefore, 48.9% of patients had a low risk of bleeding, 31.5% had intermediate risk, and 19.6% had a high risk. A notable trend was found between the two scoring systems. Out of 357 patients who had a high HAS-BLED score, 354 (99.2%) patients had a high CHA2DS2 VASc score. Conversely, out of 895 patients who had a low HAS-BLED score, 568 (63.7%) had a high CHA2DS2 VASc score (Table 4).

4. DISCUSSION

This study evaluated NVAF patients from the JoFib Registry [11, 12]. AF accounts for 15-20% of strokes in the USA and remains a major health burden due to the increased risk of stroke and hospitalization [16, 17]. Although epidemiological studies suggest that the prevalence of AF increases with aging, AF patients in the Middle East are younger and have more comorbidities than AF patients in the west [10, 18]. Nevertheless, this disease remains understudied in this region.

Table 2. Comparing CHA2DS2 VASc categories with respect to gender.

Table 2	Male (n=874)	Female (n=949)	p
CHA2DS2 VASc			
Mean (SD)	3.06 (1.81)	4.11 (1.67)	
CHA2DS2 VASc category			
Low n (%)	88 (10.1%)	64 (6.7%)	0.012
Moderate n (%)	105 (12.0%)	97 (10.2%)	
High n (%)	681 (77.9%)	788 (83.0%)	

CHA2DS2 VASc: Congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category score.

Table 3. Comparing HAS-BLED scores by categories and with respect to gender.

-	Male (n=874)	Female (n=949)	Overall (n=1823)
HAS-BLED			
0	124 (14.2%)	94 (9.9%)	218 (12.0%)
1	318 (36.4%)	356 (37.5%)	674 (37.0%)
2	257 (29.4%)	317 (33.4%)	574 (31.5%)
3	118 (13.5%)	121 (12.8%)	239 (13.1%)
4	41 (4.7%)	47 (5.0%)	88 (4.8%)
5	13 (1.5%)	10 (1.1%)	23 (1.3%)
6	2 (0.2%)	3 (0.3%)	5 (0.3%)

(Table 3) contd.....

-	Male (n=874)	Female (n=949)	Overall (n=1823)
7	1 (0.1%)	1 (0.1%)	2 (0.1%)

HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly score. Results are expressed as n (%).

Table 4. Exploring the correlation between CHA2DS2 VASc and HAS-BLED scores in NVAF patients.

-	HAS-BLED		
	Low (n=895)	Intermediate (n=574)	High (n=357)
CHA2DS2 VASc			
Low	148 (16.6%)	3 (0.5%)	1 (0.3%)
Moderate	179 (19.7%)	24 (4.2%)	2 (0.6%)
High	568 (63.7%)	547 (95.3%)	354 (99.2%)

CHA2DS2 VASc: Congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category score, HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly score. NVAF: Nonvalvular atrial fibrillation. Results are expressed as n (%).

Out of 2000 AF patients in the JoFib Registry [11, 12], we evaluated epidemiological and clinical data of 1823 (91.2%) NVAF patients. The other 177 (8.2%) patients had a valvular AF mainly related to rheumatic heart disease. Hypertension is an established risk factor for cardiovascular disease and a leading worldwide disease burden [17]. It is also known to be the most frequent comorbidity in AF patients. Studies like Framingham, Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA), and the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) reported that almost 50% of subjects had hypertension [19 - 21]. The rate of patients with hypertension is 76.3% in our study, which may suggest that epidemiological risk factors of AF are different in the Middle East than in other regions. AF drastically increases the risk of ischemic stroke, but the risk depends on each patient’s risk factors for stroke, such as congestive heart failure, hypertension, vascular disease, diabetes mellitus, previous stroke or transient ischemic attack, and age [22, 23].

The CHA2DS2 VASc score is an updated version of CHADS₂ and it aims to stratify AF patients according to their risk of developing an ischemic stroke [24]. In our study, 83.0% of females and 77.9% of males had a high risk of stroke. The female gender was found to be an independent risk factor for stroke. Meta-analyses have found that women have an increased risk of stroke compared with men, regardless of oral anticoagulation therapy [25]. This led to the evolution of risk stratification models to include the female gender as a risk score, including the CHA2DS2 VASc score, Framingham stroke risk score, and the European Society of Cardiology (ESC), the American College of Cardiology (ACC), and the American Heart Association (AHA) guidelines [4]. As for bleeding, we incorporated the HAS-BLED score to assess this risk. Although CHADS₂ and CHA2DS2 VASc scores are correlated with bleeding, a study found that in the multivariate analysis, they lose statistical significance after adjusting for HAS-BLED scores [26]. This suggests that HAS-BLED has a better predictive performance for bleeding events [27]. Almost half of the patients in our study had a low risk of bleeding, 31.5% had intermediate risk, and 19.6% had a high risk according to the HAS-BLED score. We also found that almost

all patients with a high HAS-BLED score have high CHA2DS2 VASc scores, which indicates that risks of stroke and bleeding coexist in these patients. Also, 63.7% of patients with a low risk of bleeding have a high risk of stroke, which can justify the value of using anticoagulants in this group of patients. This could be attributed to the higher specificity of HAS-BLED, but some predictability of CHA2DS2 VASc score for bleeding as well [26, 27]. In agreement with that, recent studies indicated the similarities of both scores in mortality prediction in patients with AF and the higher predictability when combined [28]. As indicated by our results, increasing the risk for bleeding in the patients (high HASBLED category) was associated with increasing the risk for complications (high CHA2DS2 VASc category) and consequently increasing the risk for death. In the Middle East, only a minimum number of studies have been carried out on AF. Thus, this study constitutes an important report regarding the NVAF subpopulation in the region.

Our study has some limitations. Although the sample size is sufficient, this study is descriptive, and our analysis does not conclude definitive answers for the validity of CHA2DS2 VASc and HAS-BLED for Middle Eastern AF patients, which still requires further investigation. We also have not investigated other viable scoring systems such as the age, biomarker, and clinical history (ABC) score [29].

CONCLUSION

In almost all NVAF patients with a high risk of bleeding (high HAS-BLED score), the use of anticoagulants is highly recommended according to the CHA2DS2 VASc score stratification. Therefore, strategies with a well-controlled administration of anticoagulants should always be considered and followed in our hospitals.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Institutional Review Board (IRB) at the Jordan University of Science and Technology (IRB-JUST) approved this study.

HUMAN AND ANIMAL RIGHTS

No animals were used that are the basis of this study.

CONSENT FOR PUBLICATION

Participants gave informed consent before they participated in the study.

AVAILABILITY OF DATA AND MATERIALS

Data will be made available upon request to the corresponding author [M.I.J] via e-mail.

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None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest, financial or otherwise.

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Declared none.

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