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THE IMPACT OF ANTICOAGULANTS IN ATRIAL FIBRILLATION IN VIEW OF CHA2DS2VASC SCORE

Hind Saeed Hasan[1], Mousa Qasim Hussein[*2]

[1] Intervention cardiologist, Ibn Al-Bitar Cardiology Centre. Baghdad-Iraq.
[2] Department of Medicine, Al Kindy College of Medicine -University of Baghdad, Baghdad, Iraq.

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*Corresponding Author: Mousa Qasim Hussein
Email: mousaqasim@kmc.uobaghdad.edu.iq

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Abstract

Atrial fibrillation (AF) is the most common and clinically relevant form of cardiac arrhythmia, which is deemed an epidemic of cardiovascular diseases in the 21st century. This arrhythmia is related to high levels of morbidity and mortality, causing a significant strain on the healthcare system.

Thus, stratification of the patients into different categories of risk according to CHA2DS2Vasc scale is an essential step for developing treatment strategies. Nevertheless, insufficient data exists about the frequency of application of the risk scale and anticoagulation therapy in clinical practice.

The purpose of this research is the assessment of the compliance with the guidelines related to the calculation of CHA2DS2Vasc index and anticoagulant therapy of AF patients.

This was a multi-center cross-sectional study which included the patients with AF admitted to the hospitals from January 2021 to January 2022. Patient characteristics such as age, presence of comorbidity, and time of having AF were taken into account. Patients' initial hematological and biochemical parameters were included. Calculation of CHA2DS2Vasc index by the treating team and their therapy were recorded.

This study consisted of 70 subjects, 51.42% of which were female, with the mean age being 65.37 ± 13.79 years. 71% of the patients had hypertension, whereas 44.28% of the patients had heart failure. 21.42% of the patients were hospitalized in the past due to atrial fibrillation, and 20% of the patients were diagnosed with stroke in their past medical history. CHA2DS2Vasc score was calculated in 2.85% of the patients, and oral anticoagulants were used in only 18.57% of the patients. Oral anticoagulants were used only in 21.42% of the patients with past history of stroke. Underuse of oral anticoagulants in patients with atrial fibrillation was significantly influenced by female gender, hypertension, diabetes mellitus, stroke, smoking, and heart failure (all $p < 0.05$).

CHA2DS2Vasc score underuse is significant in the current practices in Iraq. More studies need to be conducted to validate the findings of the study and to discover the reasons behind non-compliance with treatment guidelines.

Keywords: Anticoagulants, Atrial fibrillation, CHA2DS2VASC Score.

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Introduction

Atrial fibrillation (AF) is the most common clinically significant cardiac rhythm disorder and is considered a 21st century cardiovascular disease epidemic. AF is associated with increased morbidity and mortality resulting in high burden of healthcare system. The Global Burden of Disease (GBD) 2019 study demonstrated that more than 59 million individuals lived with AF in 2019. Projection studies show that the prevalence of AF will rise to 15.9 million in 2050 in America and 17.9 million in 2060 in Europe (1).

It is well established that AF increases the risk of mortality, and is associated with significant morbidity. Patients with AF have an increased risk of life-threatening complications and other diseases as AF also increases the risk for heart failure 5.0-fold, stroke 2.4-fold, and mortality 2.0-fold.1 Furthermore, AF worsens quality of life (QoL) for patients and caregivers, increasingly places a critical financial burden on healthcare systems, and is rapidly becoming one of the world's most significant health issues (2).

Atrial fibrillation increases the risk for ischemic stroke and other arterial thromboembolic events. It can lead to thrombus development within the atria, particularly the left atrial appendage, which can cause thromboembolic events (3).

AF is categorised into several types. Patients are categorised on their most frequent pattern of AF and may have episodes of AF that fall into one or more of the following categories: paroxysmal (occasional AF that stops ≤7 days), early persistent (AF that lasts 7 days to 3 months), persistent (continuous AF for >7 days), longstanding persistent (episodes occur for >12 months), or permanent (episodes continue and attempts to restore sinus rhythm are ceased) (2).

The 2023 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) guidelines observe that CHA2DS2-VASc is considered the most validated score and is generally preferred, although it has shown suboptimal performance in selected populations, such as patients with kidney disease. The AHA/ACC/HRS guidelines advise that when uncertainty exists, a different score, such as GARFIELD-AF, can add additional variables to consider (4).

A Norwegian study reported that in patients with a non-sex a non-sex CHA2DS2-VASc risk score of 1, Oral Anti Coagulants use was associated with an increased risk of major bleeding (adjusted hazard ratio [aHR] 1.37) but lower risk of the combined outcome of ischemic stroke, major bleeding, and mortality (aHR 0.57). Patients with AF who did receive anticoagulation had higher risk of ischemic stroke compared to non-AF individuals with the same risk profile (aHR 2.47) (4).
Independent of AF, use of the CHA2DS2-VASc score to determine stroke risk in patients having cardiac surgery has been advocated (4).
The rates of stroke and thrombo-embolism vary considerably in patients with CHA2DS2-VASc scores of 1 or 2 due to differences in outcomes, populations, and anticoagulation status. OAC should be considered for men with a CHA2DS2VASc score of 1 and women with a score of 2, balancing the expected stroke reduction, bleeding risk, and patient preference. Importantly, age (65 years and older) conveys a relatively high and continuously increasing stroke risk that also potentiates other risk factors (such as heart failure and sex). Hence, an individualized weighing of risk, as well as patient

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preferences, should inform the decision to anticoagulate patients with only one CHA2DS2-VASc risk factor, apart from female sex. Female sex does not appear to increase stroke risk in the absence of other stroke risk factors (5).

OAC underuse may be related to an erroneous estimation of bleeding risk. Indeed, it has been recently shown that bleeding risk scores overemphasizing modifiable risk factors perform sub optimally compared with HAS-BLED [hypertension, abnormal renal/liver function (1 point each), stroke, bleeding history or predisposition, labile INR, elderly (>65 years), drugs/alcohol concomitantly (1 point each)]and, thus, may lead to OAC withholding based on only a temporary increased bleeding risk.26 On the other hand, OAC underuse in patients with AF may be related to an underestimation of its benefits (i.e., reduction of stroke risk) and an overestimation of its complications risk (i.e., bleeding). So, underestimation of thrombotic risk and overestimation of bleeding risk are major determinants of OAC under-treatment (6,7).

Many factors can be implicated for underuse of anticoagulants like older age, frailty, paroxysmal AF type and inappropriate use of platelet inhibitors in lieu of OAC; with lower socioeconomic class and lower use of specialty care and other cardiovascular medications 12. Also, it has been suggested that OAC underuse seen in patients with AF and, in particular, in concomitant HF despite being independent risk of stroke in AF. It is also reported that patients' perception and preferences have an important role in underuse of anticoagulants in AF despite indication (8).

Interestingly, gender can predict under-coagulation in AF as women with atrial fibrillation are at higher risk of stroke than men with atrial fibrillation. The reasons for this elevated risk remain unclear, but they may include older age of women, use of hormone replacement therapy, undertreatment or suboptimal management with a vitamin K antagonist, and poor anticoagulation control. Women are treated no differently to men in terms of anticoagulant therapy for stroke prevention, thromboprophylaxis was however, suboptimal in substantial proportions of women, with underuse in those at moderate-to-high risk of stroke (9).

This study sought to investigate physicians' adherence to guideline regarding calculation of CHA2DS2Vasc score in practice and use of anticoagulants in patients with Atrial Fibrillation.

Material and Methods:

Study design: a cross-sectional, multicenter study.

Study Setting: This study was conducted in Al-Kindy Teaching Hospital and Baghdad Teaching Hospital, Baghdad, Iraq. The study started from January 2021 to January 2022.

Inclusion criteria: Recruited patients in this study should fulfil the following

1. Patients with atrial fibrillation.
2. Age more than 18 years.
3. No history of malignancy and sepsis.

Exclusion Criteria:

1. patients with cardiac arrythmias other than A.F.
2. history of contraindication to use of oral anticoagulants.

Data Collection:

Participants' ages, comorbidities, duration of atrial fibrillation, and pre-study medication were recorded, along with the results of tests such as biochemical analyses (blood urea and serum creatinine) and hematological tests (hemoglobin). Information on medications prescribed

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during hospitalization, including the type and dosage of anticoagulants, was also recorded. The status of CHA2DS2-VASc score calculation was noted, indicating whether the treating physician calculated the score for each patient as part of the decision-making process regarding the initiation of anticoagulant therapy when needed. The researcher calculated and documented the CHA2DS2-VASc score for each patient.

Statistical Analysis:

The collected data were coded and analyzed using Excel 2016 software. Numerical variables were presented as mean ± standard deviation, while categorical variables were presented as percentages. Statistical analysis of numerical variables was performed using the t-test, whereas categorical variables were analyzed using the chi-square test. Differences were considered statistically significant if the p-value was less than 0.05.

Results:

This study included 70 patients hospitalized for atrial fibrillation, 34 males (48.57%) and 36 females (51.42%). Their mean age was 65.37 ± 13.79 years. Hypertension, diabetes, and ischemic heart disease were present in 85.71%, 58.57%, and 50% of patients, respectively, while heart failure, stroke, and smoking were present in 44.28%, 20%, and 37.14% of patients, respectively. Chronic kidney disease was reported in 20% of patients. 21.42% of patients reported a previous hospitalization for atrial fibrillation. Furthermore, the study showed that females were older than males and more likely to have hypertension and diabetes, as well as more likely to have ischemic heart disease, heart failure, and chronic kidney disease. In contrast, males were more likely to smoke and have a history of percutaneous coronary intervention. Females were also more likely to have been previously hospitalized for atrial fibrillation. These findings are summarized in Table 1.

Table 1: Demographic Characteristics of Patients with AF According to Gender.

Characteristic	Total	Males 34 (48.57%)	Females 36 (51.42%)	P-Value
Age (mean ± SD)	65.37±13.79	62.35±14.37	68.2±12.7	0.07
Hypertension	60 (85.71%)	27 (45%)	33 (55%)	< 0.05
Diabetes	41 (58.57%)	17 (41.46%)	24 (58.53%)	< 0.05
IHD	35 (50%)	16 (45.71%)	19 (54.28%)	< 0.05
Heart Failure	31 (44.28%)	15 (48.38%)	16 (51.61%)	< 0.05
Stroke	14 (20%)	7 (50%)	7 (50%)	< 0.05
Smoking	26 (37.14%)	23 (88.46%)	3 (11.53%)	< 0.05
Peptic Ulcer	2 (2.85%)	-	2 (100%)	N/A
Thyroid Disease	3 (4.28%)	1 (33.33%)	2 (66.66%)	0.2
CKD	14 (20%)	6 (42.85%)	8 (57.14%)	< 0.05
Prior admission	15 (21.42%)	4 (26.66%)	11 (73.33%)	< 0.05
History of PCI	7 (10%)	5 (71.42%)	2 (28.57%)	< 0.05

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This study evaluated various parameters in patients with atrial fibrillation, revealing a mean ejection fraction (EF) of 45.71 ± 12.17; lower values were recorded in males compared to females, whereas mean blood urea and serum creatinine levels were higher in female patients—though these differences were not statistically significant. The mean hemoglobin level across all patients was 12.52 ± 1.13, with significantly lower levels observed in female patients.

Table 2: Investigational Parameters of Patients with AF According to Gender

Parameter	Total Mean ± SD	Males	Females	P Value
Ejection Fraction	45.71±12.17	42.56±13.47	48.87±10.17	0.14
Urea	65.37±38.14	58.05±31.94	72.27±42.48	0.11
Creatinine	1.56±1.47	1.5±1.52	1.62±1.43	0.7
Hemoglobin	12.52±1.13	13.22±2.46	11.86±1.53	0.006

This study evaluated the actual adherence to practices for calculating the CHA2DS2-VASc score in patients with atrial fibrillation during their hospital stay—a step intended to guide the decision on whether to initiate oral anticoagulant therapy. The results showed that the treating medical team calculated this score for only two patients (2.85%), as illustrated in Figure 1.

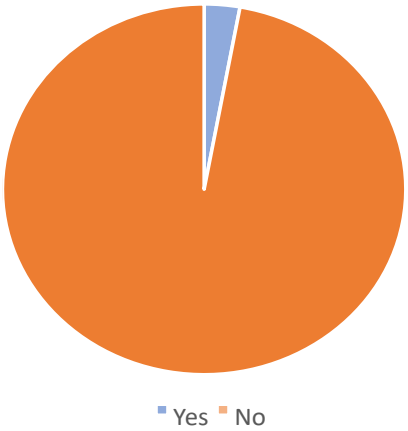

Figure 1: Calculation Status of CHA2DS2-VASc score in Hospitalized AF Patients

This study also assessed use of oral anticoagulants in patients with AF by dividing them into those with CHA2DS2VASc score≥2 and those with score ≤1 and it revealed that 62(88.57%) patients had score ≥2 versus 8 (11.42%) patients with score ≤1.Among those with high score, 13 patients (18.57%) had put on oral anticoagulant therapy, while none of those with low score had started on anticoagulant medication. These results are clarified in figure (2).

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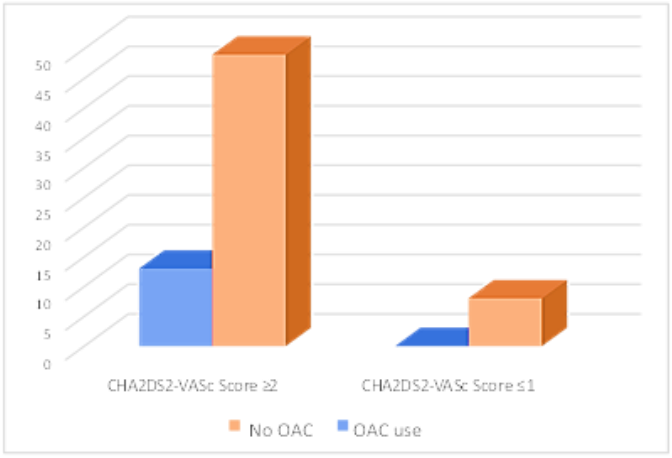

Figure 2: Use of Oral Anticoagulation in Patients According to their CHA2DS2-VASc Score

This study also assessed factors that might predict using or denying OAC therapy in patients with AF and it was shown that patients who were initiated OAC were older than who did not, however, this did not reach level of statistical significance.

Female gender predicts denying OAC in AF patients in this study, as 77.77% of females were not on OAC (P <0.05). OAC therapy was used less in hypertension, diabetes and heart failure in 18.33%,24.39% and 19.35% respectively. Among patients with stroke 21.42% were on OAC. Smokers were more to be on no OAC. This study also revealed underuse of OAC in CKD patients.

Renal indices including blood urea and serum creatinine were higher in patients who were initiated on OAC therapy while lower hemoglobin level was recorded in those on no OAC, however, these changes did not reach level of statistical significance. These results can be seen in table (3).

Table 3: Factors That Predict Use of Oral Anticoagulation in AF Patients

Factor	OAC Use	No OAC	P value
Age Mean ± SD	71.3±13.36	64.01±3.64	0.08
Female Gender	8 (22.22%)	28 (77.77%)	< 0.05
Hypertension	11 (18.33%)	49 (81.66%)	< 0.05
Diabetes	10 (24.39%)	31 (75.6%)	< 0.05
Stroke	3 (21.42%)	11 (78.57%)	< 0.05
CKD	4 (28.57%)	10 (71.42%)	< 0.05
Smoking	4 (15.38%)	22(84.61%)	< 0.05
Heart Failure	6 (19.35%)	25 (80.64%)	< 0.05
Blood Urea	73±36.01	63.63±38.7	0.4
Serum Creatinine Mean ± SD	1.77±1.14	1.52±1.54	0.5
Hemoglobin Mean ± SD	12.74±2.53	12.47±2.05	0.6

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This study assessed types of anticoagulants and antiplatelet used in patients with AF and it showed that heparin was initiated in 59 (84.28%) of patients on admission, yet, only 13 (18.57%) of patients were started OAC during hospitalization and on discharge.

Most used OAC in this study was warfarin which was used in 69.23% of orally anticoagulated patients. Most common antiplatelet used in patients was aspirin which was used in 20 (28.57%) patients. These results were illustrated in figure (3).

This study also evaluated treatment strategy in patients with AF i.e. whether rhythm control or rate control strategy was adopted by treating physicians, in 34.28% of patients rhythm control strategy was adopted. These findings can be shown in figure (4).

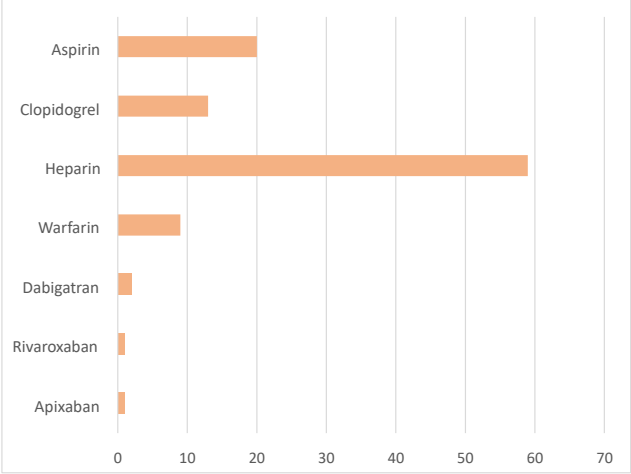

Figure 3: Distribution of Use of Anticoagulants and Antiplatelet in Hospitalized AF Patients

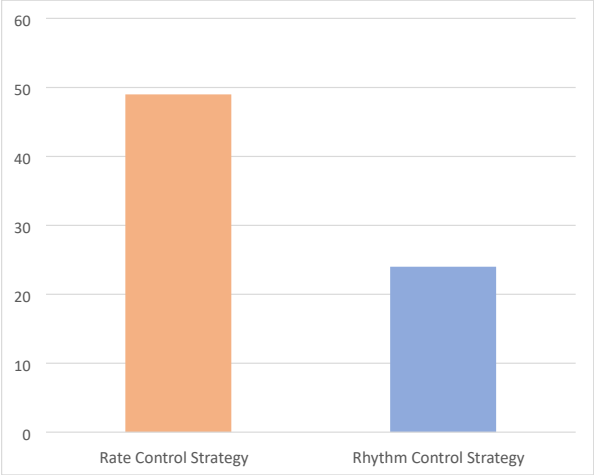

Figure 4: Management Strategy of Hospitalized AF Patients

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Discussion

This study evaluated adherence to international standards regarding the use of the CHA2DS2-VASc score and the subsequent use of anticoagulants in patients with atrial fibrillation.

It highlights a gap in clinical practice characterized by the underutilization of the CHA2DS2-VASc score for risk stratification in atrial fibrillation patients, resulting in the suboptimal use of oral anticoagulants in cases where they are indicated.

The study also found that the mean age of patients with atrial fibrillation was 65.37 years; the prevalence of the disorder increases with age, reaching 5% among individuals over 55 and 18% among those over 85 (specifically within the 80–89 age group (10,11).

It was hypothesized that the electrophysiological changes and the elevated resting membrane potential are the main pathophysiological mechanisms driving the abnormal intracellular calcium handling and the subsequent development of arrhythmia can explain the association of aging with AF (12).

This study found a higher prevalence of AF in females compared to males, consistent with other researchers. Another study suggested that Male gender is associated with a 1.5-fold increased risk of developing AF (13).

Hormonal factors were proposed to play a major role in AF in female patients. The estrogen–progesterone fluctuation throughout the menstrual cycle was shown to have an impact on QT intervals. Females with AF have been reported to have more complications (especially cerebrovascular stroke and bleeding risk) and poorer outcomes than males (14,15).

Diabetes was evident in 58.57% of patients with AF, which can be explained by impaired insulin and glucose control. This directly affects the myocardium in both the atria and ventricles. The underlying mechanism of atrial fibrillation may be related to inflammation, as atrial biopsies show elevated C-reactive protein levels. Diabetes is also associated with the formation of inflammatory mediators, and atrial fibrosis is commonly observed in atrial fibrillation. Left ventricular hypertrophy is a common complication of hypertension and a known risk factor for atrial fibrillation. Several studies have indicated an association between left ventricular hypertrophy and impaired glucose tolerance and insulin resistance. The duration of diabetes and elevated glycated hemoglobin (HbA1c) levels are also associated with an increased risk of AF (16,17).

Heart failure was observed in 44.28% of patients with atrial fibrillation in this study. The global prevalence of atrial fibrillation and heart failure is known to be increasing. Population studies have observed that atrial fibrillation and heart failure often co-occur, increase the likelihood of developing each other, and share common risk factors (18).

Stroke was reported in the history of 20% of AF patients in this study. Consistent with other researchers who suggested that AF not only confers a 3- to 5-fold increased risk of stroke at all ages, but AF-associated strokes are also more severe, resulting in greater disability, institutionalization, and healthcare cost (19)
The current study also highlights the high prevalence of CKD in the AF population 20% which was comparable to other studies (20), as AF and chronic kidney disease (CKD) often coexist as

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they share multiple risk factors, including hypertension, diabetes mellitus, and coronary artery disease (21).

This study revealed a 21.42% rate of repeated hospital admissions due to atrial fibrillation. Readmission rates for atrial fibrillation have been a subject of considerable interest, and previous researchers have reported a lower rate of repeated admissions of 14.5%, which is lower than the rate found in our study (22).

In addition, this study compared the baseline characteristics of atrial fibrillation patients according to their sex and revealed that females are more likely to have other comorbidities associated with atrial fibrillation than males, such as diabetes, hypertension, ischemic heart disease, heart failure, and chronic kidney disease. However, this finding was not supported by other studies that showed higher rates of comorbidities in male patients with atrial fibrillation (23).

Furthermore, this study also assessed kidney function indices in patients with atrial fibrillation, which were significantly elevated. Atrial fibrillation is the most common cardiac arrhythmia and is frequently observed in patients with chronic kidney disease, who are at high risk of cardiovascular complications. The presence of AF also worsens prognosis. Atrial fibrillation and chronic kidney disease often coexist and have a strong bidirectional relationship (24).

Furthermore, this study revealed a significant underutilization of the CHA2DS2 VASC score in our practice. It also showed that oral anticoagulants were used in only 18.57% of patients with a score ≥2, representing the lowest adherence rate among international studies of anticoagulant use in patients with indicated oral anticoagulant therapy, compared to other studies (25,26).

In addition, this study discussed the main factors explaining the low use of oral anticoagulants in patients with AF. It was observed that females were more likely to receive anticoagulants, while patients with comorbidities such as hypertension, diabetes, heart failure, ischemic heart disease, and chronic kidney disease were less likely to receive them. These findings are consistent with other studies that have indicated a decrease in the prescription of oral anticoagulants for patients with chronic kidney disease (27). Conversely, these results contradict those of other researchers who suggested that the presence of these comorbidities increases the use of oral anticoagulants in patients with atrial fibrillation, which seems logical given the association of these comorbidities with higher indications for oral anticoagulant use (28,29).

Furthermore, this study evaluated the use of antiplatelet agents and anticoagulants in patients with atrial fibrillation, yielding notable results: 47.14% of patients were treated with antiplatelet agents. This finding aligns with other studies indicating that a significant proportion of patients with atrial fibrillation receive antiplatelet therapy instead of oral anticoagulants (OACs), despite the high efficacy of OACs in reducing the burden of stroke associated with this disorder (26).

The current study also revealed that warfarin is the most commonly used oral anticoagulant (OAC) among patients with AF—despite its association with higher rates of bleeding complications—a finding that can be attributed to the fact that most patients struggle to afford newer oral anticoagulants (NOACs); this contrasts with the results of other researchers who

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reported higher usage rates for NOACs compared to warfarin (30).

Additionally, this study also evaluated adopted strategy in managing AF patients and rate control strategy was most common adopted strategy in management the better strategy is still a matter of debate, however, In the largest of studies that discuss both strategies, the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) study, there was a trend for increased mortality in the rhythm control arm and hospitalization rates were higher in the rhythm control group (in part due to recurrent AF), and the groups did not differ with respect to any of the other prespecified outcomes, including stroke, major bleeding, cognitive function, and quality of life; the consensus explanation for these somewhat unexpected findings was that antiarrhythmic drug toxicity was the likely culprit, and that if only we could develop better drugs or nondrug therapies, surely the rhythm control strategy would prevail (31).

Conclusion:

There is a notable shortcoming in the use of the "CHA2DS2-VASc" score in current medical practice in Iraq; therefore, further studies are needed to validate the findings and to explore the factors contributing to non-adherence to clinical guidelines and the impact thereof on patient health outcomes.

Ethical Approvals: Ethical approvals were taken from Iraqi Board for Medical Specializations. Oral and written consent to be recruited in the study was obtained from each patient. The researcher and her supervisor were passively auditing management of each case according to international guidelines.

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Conflict of interest: The authors declare that they have no conflict of interest.

Author contributions: All authors contributed to the preparation, writing, and revision of this article and approved the final version of the manuscript.

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