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Cohort Study

Impact of thyroid disease in patients with atrial fibrillation: Analysis from the JoFib registry

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ABSTRACT

Background: Thyroid disease is a well-established risk factor for atrial fibrillation (AF). However, only a handful of studies examined its impact on treatment. This study aims to report the prevalence rate of thyroid disease in patients with AF and to demonstrate the effect of thyroid disease on AF treatment.

Materials and methods: We retrospectively analyzed the Jordanian Atrial Fibrillation Study (JoFib). Among Jordan and Palestine, patients with AF were evaluated for their sociodemographic, clinical, and pharmacological characteristics.

Results: A total of 2000 patients with AF (53.3% males, mean age 67.6 ± 13.1 years) were enrolled in the JoFib registry from May 2019 to November 2020. Thyroid disease was present in 210 (10.5%) patients. Hypertension, diabetes mellitus, and dyslipidemia were the most common comorbidities among patients with thyroid history (75.2%, 51.0%, and 45.7%, respectively). Diabetes mellitus ($p = .04$), pulmonary hypertension ($p = .01$), and chronic kidney disease ($p = .01$) were significantly higher in this particular subgroup. Patients with thyroid disease demonstrated significantly higher usage of anticoagulants ($p = .02$).

Conclusion: Despite having similar stroke and bleeding risks, patients with thyroid disease demonstrated meaningful differences in their baseline characteristics. Prospective studies are required to assess the influence of thyroid hormone fluctuations on the progression of AF.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide, affecting more than 30 million persons all over the globe [1]. Characterized by ever increasing prevalence and incidence rates, AF contributes significantly to morbidity and mortality through increased risk of stroke, heart failure and hospitalizations [2]. In particular, AF increases the risk of stroke by 5 folds; these strokes are of greater severity and lethality than those of their non-AF counterparts [2]. Despite its slightly increased prevalence in men, AF's adverse complications are more pronounced in women [3]. A multitude of clinical conditions predispose to AF including but not limited to hypertension, obesity, metabolic syndrome, diabetes, obstructive sleep apnea, ischemic heart disease, congestive heart failure, and thyroid disease [1–4].

Overt and occult hyperthyroidism is a documented risk factor of AF [1,2,4,5]. The prevalence rate of AF in patients with hyperthyroidism is 10–15%, while its incidence is 1.41 per 1,000 patients [5,6]. On the other end of the spectrum, hypothyroidism is associated with an increased risk of cardiovascular events, even though its direct association with AF is still conflicting [1]. Data from large cohorts suggest that variations in thyroid hormones within their normal reference range is associated with cardiac complications. In particular, higher free thyroxine (T4) is associated with higher risk of heart failure, sudden cardiac death, and AF [7–9]. Nevertheless, the impact of thyroid hormone imbalance on risk of AF is still underestimated [6,9].

The burden of thyroid disease on patients with AF could be anticipated from the systematic effects of thyroid hormone as it contributes to increased vascular resistance, cardiac contractility, heart rate and left ventricular mass [1]. In addition, high levels of thyroid hormones lead to increased rates of arrythmia, increased frequency of atrial premature beats, and are prothrombotic [1,4]. These mechanisms may clarify the

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impact of hyperthyroidism but not that of hypothyroidism, despite the overlapping risk factors for both disease entities [4]. Furthermore, since thyroid dysfunction impacts response to anticoagulants, the safety and efficacy of traditional anticoagulation regimens in AF patients with thyroid disease are yet to be elucidated [4,10]. Such observations imply risk-assessment and therapeutic concerns about the feasibility of including T4 as part of thyroid screening for patients with AF, and the risks associated with thyroid replacement therapy.

While AF is on a rising trend in Asia, epidemiological data on Middle Eastern patients with AF are severely lacking, which leads to ambiguous treatment regimens in terms of safety and efficacy [11]. Furthermore, global reviews and local registries fail to account for thyroid disease as a risk factor for patients with AF [12–15]. Therefore, this paper aims to determine the prevalence of thyroid disorders in patients with AF among a Middle Eastern cohort and predict the cardiovascular-oriented characteristics and risk factors associated with the development of thyroid disease in AF patients.

2. Materials and Methods

2.1. Study population

We performed a retrospective analysis on AF patients recruited as part of the Jordanian Atrial Fibrillation Study (JoFib) (NCT03917992) [16]. JoFib is a prospective, observational, multi-center study registry aimed to explore the characteristics, treatment patterns and outcomes of patients with AF recruited from 19 Jordanian hospitals, 30 out-patient clinics and one hospital in the Palestinian territories from May 2019 to November 2020. The registry enrolled 2000 patients who were either newly diagnosed with AF or have existing AF, and are older than 18 years of age. The manuscript fully complies with the STROCSS criteria for reporting [17].

2.2. Data collection

We collected patients' data through standardized forms at time of enrollment, and at 1, 6, and 12 months of follow up. Baseline data, with which this study was conducted, were sociodemographic characteristics, baseline clinical features, co-morbidities, and medication history. The CHA_2DS_2-VASc [18] and HAS-BLED [19] scores, which estimate the risk of stroke and major bleeding in patients with non-rheumatic AF, were calculated for all patients. In addition, patients' echocardiographic data were extracted when applicable and/or available.

Demographic data included age (in years), gender, and BMI (kg/cm^2). Baseline clinical characteristics included presence of comorbidities, smoking status, AF characteristics (symptoms, frequency, type), history of AF complications (frequency of cerebrovascular strokes in the past year, type of old strokes, stroke recurrence rate and presence, site and recurrence rate of systemic embolization), and history of procedures (ablation, presence of occluder device, electric cardioversion, permanent pacemaker implantation). In addition, the study extracted medications history (e.g., anticoagulants, anti-platelets, anti-arrhythmics).

Presence or absence of thyroid disease was determined based on (1) prior diagnosis made by a physician or (2) prescription of thyroid replacement therapy. Diagnosis of AF is confirmed by (1) 12-lead EKG, (2) rhythm strip, lasting >30 seconds, (3) one or more episodes of AF on Holter monitor, or (4) a diagnosis by a treating cardiologist. The definitions of AF types, namely first attack of AF, paroxysmal AF, persistent AF, and permanent AF, were based according to the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) 2019 Guidelines for the Treatment of patients with AF [20].

2.3. Statistical analysis

All statistical analysis was conducted on the statistical package for social sciences (SPSS) version 23.0 (SPSS Inc., Chicago, IL, USA). Frequencies were reported for categorical data [n (%)] while continuous data were reported as means ± standard deviation (n ± SD). Associations between presence of thyroid disease and various categorical variables were evaluated through Chi-Square testing. ANOVA and student's *t*-test were utilized to detect significant mean differences between categories of thyroid disease and age and left ventricular ejection fraction. A *p*-value equal or less than 0.05 is considered statistically significant.

2.4. Ethical approval

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional/regional/national ethics/committee/ethics board of the University of Jordan (NO.: 10/2021/416) and individual consent for this retrospective analysis was waived.

3. Results

3.1. Baseline characteristics

Among the 2000 AF patients included in the study, the mean age of participants was 67.6 ± 13.1 with 1067 (53.3%) being males. Thyroid disease was present in 210 (10.5%) patients. Of those with thyroid disease, 20.4% had normal weight, 30.6% were overweight, and 49.0% were obese. In terms of comorbidities, hypertension, diabetes mellitus, and dyslipidemia were present in 75.2%, 51.0%, and 45.7% in AF patients with thyroid disease, respectively. In addition, about 8% of those patients were active smokers. However, active smokers with more likely not to have thyroid disease ($p = .025$).

The most common type of AF in patients with thyroid disease was non-paroxysmal AF (65.2%). In addition, the most prevalent etiology of AF in this group was non-valvular AF (89.0%). Associated symptoms included palpitations (42.4%), shortness of breath (41.0%), fatigue (28.6%), dizziness (15.2%), syncope (3.8%), and chest pain (1.9%), of which only fatigue ($p = .005$) and shortness of breath ($p = .020$) were significantly different in comparison to their non-thyroid counterparts. Out of the recorded comorbidities, pulmonary hypertension ($p = .017$) and chronic kidney disease ($p = .015$) were significantly higher in patients with thyroid disorders, while the prevalence of coronary artery disease was significantly higher in their non-thyroid counterparts ($p = .028$). Risks of stroke and of major bleeding were not significantly different between groups with or without thyroid disease as evident from the relative distributions of the CHA_2DS_2-VASc ($p = .179$) and HAS-BLED ($p = .731$) scores (see Table 1).

Patients' pharmacological characteristics are reported in Table 2. With respect to the patients' pharmacological history, AF patients with thyroid disorders were significantly more likely to use anticoagulants ($p = .027$), whether in the form of vitamin K antagonists (33.8%) or oral anticoagulants (54.3%). On the other hand, AF patients without thyroid disease had significantly higher usage of antiplatelets ($p = .019$). The most prevalent types of antiarrhythmics within both groups of patients were beta blockers (80.0%) and amiodarone (20.0%). The sociodemographic characteristics, clinical features and pharmacologic histories of patients with specific thyroid statuses (hyper-, eu-, or hypothyroidism) are reported in Table 3.

4. Discussion

We performed a retrospective analysis of the latest Jordanian multicentric registry for patients with AF. Our analysis demonstrated a thyroid disease prevalence rate of 10.5% among patients with AF. This rate is almost twice of that reported in the Gulf Survey of Atrial Fibrillation Events (GULF SAFE) registry, which prospectively observed the

Table 1
Demographic and clinical characteristics of AF patients with/out thyroid disorders.

Clinical feature		Total n (%)	AF/ Thyroid disease n (%)	AF/no Thyroid disease n (%)	*p*-value
Age in years (mean ± SD)		67.6 ± 13.1	69.9 ± 11.0	67.4 ± 13.3	**.007**
Gender					**<.01**
	Male	933 (46.7%)	54 (25.7%)	879 (49.1%)	
	Female	1067 (53.3%)	156 (74.3%)	911 (50.9%)	
Medical History					
	Hypertension	1486 (74.3%)	158 (75.2%)	1328 (74.2%)	.802
	Diabetes Mellitus	882 (44.1%)	107 (51%)	775 (43.3%)	**.040**
	Dyslipidemia	878 (43.9%)	96 (45.7%)	782 (43.7%)	.607
	Currently smokers	273 (13.7%)	16 (7.6%)	257 (14.4%)	**.025**
BMI					.071
	X ≥ 24.9	409 (22.8%)	38 (20.4%)	371 (23.0%)	
	25 > X > 29.9	649 (36.1%)	57 (30.6%)	592 (36.7%)	
	X ≥ 30	739 (41.1%)	91 (49.0%)	648 (40.2%)	
	Total	1797 (100%)	186 (10.4%)	1611 (89.6%)	
Type of AF					.649
	Paroxysmal	727 (36.4%)	73 (34.8%)	654 (36.5%)	
	Non-paroxysmal	1273 (63.6%)	137 (65.2%)	1136 (63.5%)	
	Total	2000 (100%)	210 (10.5%)	1790 (89.5%)	
Etiology of AF					.735
	Valvular	177 (8.8%)	23 (21.0%)	154 (8.5%)	
	Non-valvular	1823 (91.2%)	187 (89.0%)	1636 (91.4%)	
		2000 (100%)	210 (10.5%)	1790 (89.5%)	
AF symptoms					
	Palpitations	859 (43.0%)	89 (42.4%)	770 (43%)	.883
	SOB	673 (33.7%)	86 (41.0%)	587 (32.8%)	**.020**
	Fatigue	420 (21.0%)	60 (28.6%)	360 (20.1%)	**.005**
	Dizziness	226 (11.3%)	32 (15.2%)	194 (10.8%)	.065
	Syncope	45 (2.3%)	8 (3.8%)	37 (2.1%)	.133
	Chest pain	34 (1.7%)	4 (1.9%)	30 (1.7%)	.776
	Asymptomatic	591 (29.5%)	59 (28.1%)	532 (29.7%)	.689
Comorbid diseases					
	Stroke or systemic embolization	319 (15.9%)	35 (16.6%)	284 (15.8%)	.907
	Heart failure	467 (23.3%)	47 (22.3%)	420 (23.4%)	.796
	Left ventricular hypertrophy	707 (39.1%)	71 (37.4%)	636 (39.3%)	.638
	Coronary artery disease	225 (11.2%)	14 (6.6%)	211 (11.7%)	**.028**
	Congenital heart disease	11 (0.5%)	1 (0.4%)	10 (0.5%)	.999
	Pulmonary hypertension	543 (27.2%)	72 (34.3%)	471 (26.3%)	**.017**
	Sleep apnea	76 (3.8%)	10 (4.8%)	66 (3.7%)	.444
	Chronic kidney disease	181 (9.0%)	29 (13.8%)	152 (8.5%)	**.015**
	Active malignancy	117 (5.8%)	10 (4.8%)	107 (5.9%)	.995
CHA_2DS_2-VASc score					.179
	Score 1 in women and 0 in men (1)	173 (8.6%)	12 (5.7%)	161 (8.9%)	
	Score 2 in women and 1 in men (2)	251 (12.5%)	23 (10.9%)	228 (12.7%)	
	Score ≥ 3 in women and ≥ 2 in men (3)	1575 (78.7%)	175 (83.3%)	1400 (78.2%)	
HAS-BLED score					.731
	0	266 (13.3%)	27 (12.9%)	239 (13.4%)	
	1	728 (36.4%)	72 (34.3%)	656 (36.6%)	
	2	623 (31.1%)	69 (32.9%)	554 (30.9%)	
	≥ 3	384 (19.2%)	42 (20%)	341 (19.1%)	
Echocardiography findings					
	LVEF (mean ± SD)	53.6 ± 12.4	54.6 ± 12.8	53.5 ± 12.3	.261
	Moderate to severe rhematic mitral stenosis	66 (3.3%)	9 (4.3%)	57 (3.2%)	.411
	Metallic prosthetic valve	111 (5.5%)	14 (6.7%)	97 (5.4%)	.427

baseline characteristics and clinical outcomes of more than 2000 patients with AF [21]. In addition, our detected thyroid disease prevalence is similar to that of global and European AF registries such as the Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation (RecordAF) and the German Competence Network on Atrial Fibrillation (AFNET), both of which report a prevalence rate of 9.0% in enrolled patients with AF [22,23].

Our analysis showed significant differences in baseline characteristics between AF patients with thyroid disease and their non-thyroid counterparts. Notably, significantly higher rates of diabetes mellitus, chronic kidney disease, and pulmonary hypertension were observed in AF patients with thyroid disease. Although the exact mechanisms are not elucidated, thyroid disease is highly prevalent in patients with pulmonary hypertension and chronic kidney disease [24,25]. The prevalence of diabetes mellitus in such patients can be either due to its observed high rates in Jordanians with thyroid dysfunction [26], or a manifestation of diabetes mellitus as a surrogate marker for metabolic syndrome, which is already associated with higher risk of AF [15]. Furthermore, it hypothesized that pulmonary hypertension and thyroid disease may share a common autoimmune etiology [24,27]; on the other hand, chronic kidney disease, which can be theoretically accelerated by hyperthyroidism, impacts the pituitary-thyroid axis and peripheral thyroid hormone metabolism resulting in a hypothyroid state [25].

Assessment tools of risk of stroke or major bleeding such as the CHA_2DS_2-VASc or HAS-BLED score categories did not significantly change in relation to the presence of thyroid disease. Such results were surprising as the effect of altered thyroid function on higher stroke and bleeding risks is well documented in the literature [1,4,10]. In fact,

Table 2
Pharmacological history of AF patients with/out thyroid disorders.

Variables		Total n (%)	AF/ Thyroid disease n (%)	AF/no Thyroid disease n (%)	*p*-value
Anticoagulants					.027
	Use of anticoagulants	1625 (81.3%)	185 (88.1%)	1440 (80.4%)	
	Vitamin K antagonist	632 (31.6%)	71 (33.8%)	561 (31.3%)	
	Oral anticoagulants	993 (49.7%)	114 (54.3%)	879 (49.1%)	
Antiplatelets					
	Use of antiplatelets	925 (46.3%)	81 (38.6%)	844 (47.2%)	**.019**
Antiarrhythmics					
	Beta blockers	1603 (80.2%)	168 (80%)	1435 (80.2%)	.927
	Amiodarone	403 (20.2%)	43 (20.5%)	360 (20.1%)	.928
	Calcium Channel Blockers	199 (10.0%)	23 (11.0%)	176 (9.8%)	.626
	Digoxin	299 (15.0%)	32 (15.2%)	267 (14.9%)	.919
Others					
	RAAS	746 (37.3%)	85 (40.5%)	661 (36.9%)	.327
	Diuretics	759 (38.0%)	77 (36.7%)	666 (37.2%)	.051
	Statins	727 (36.4%)	93 (44.3%)	650 (36.3%)	.940

hyperthyroidism have been shown to increase the risk of thrombotic episodes in AF patients independently of CHA_2DS_2-VASc score [28]. Yet, the impact of thyroid disease on thrombosis risk could have been underestimated in our population due to inherit concerns towards the validity of such predictive models in a Middle Eastern population, which is a concern that was previously raised by the GULF SAFE study [21]. Interestingly, AF patients with thyroid disease were more likely to complain of shortness of breath and fatigue despite having similar rates of left ventricular hypertrophy and ejection fraction to their non-thyroid counterparts, which could be attributed to the effect of thyroid hormone dysfunction on the cardiovascular system.

Management of AF with anticoagulants is a class Ia as recommended by the ACC/AHA/ESC 2019 guidelines [20]. In comparison with vitamin K antagonists, non-vitamin K oral anticoagulants (NOAC) display non-inferiority in terms of efficacy with even higher safety, and are now the preferred method of anticoagulation in patients with non-valvular AF [12]. Nonetheless, the optimal use of anticoagulants represents a therapeutic dilemma due to the increased risk of bleeding [29]. Thyroid disorders impact the hemostatic balance, therefore affecting the efficacy of anticoagulant use in patients with AF. While hyperthyroidism increases the risk of strokes through establishing a prothrombotic state [1], hypothyroidism aggravates bleeding complications by shifting the hemostatic balance towards a hypocoagulable and hyperfibrinolytic state [10]. Nonetheless, a secondary analysis from the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial recommended similar oral anticoagulants management protocols for AF patients with thyroid disease as it demonstrated comparable efficacy and safety outcomes in such population in comparison to their non-thyroid counterparts [4]. Among our cohort, the use of anticoagulation was significantly higher in AF patients with thyroid disease. This is mostly owed to physician concerns over the pharmacodynamic interactions between altered thyroid hormone balance and anticoagulants, and the inherently increased risk of stroke in AF patients with both clinical and subclinical thyroid disease [1,2,30].

Hyperthyroidism is associated with higher risk of AF incidence, prevalence, recurrence, and complications [1,2,4,5]. Higher levels of free thyroxine and low levels of thyroid stimulating hormone are proportionally associated with higher risk of AF [4]. Moreover, a Danish observational cohort of more than 500,000 participants and subsequent studies demonstrated increased AF risk with subclinical hyperthyroidism [6,28]. Despite being associated with a multitude of cardiovascular risk factors and diseases, the relationship between hypothyroidism and AF is still controversial as one secondary analysis of the Framingham study failed to demonstrate increased 10-year risk of AF with hypothyroidism while a Danish cohort reported protective effects of subclinical hypothyroidism on patients with AF [6,31]. This warrants further investigation due to the overlap of risk factors and high density of hypothyroid patients in published AF registries [4,21–23].

A secondary analysis of the ARISTOTLE trial conducted on a randomized cohort of 18,021 AF participants with and without thyroid disease is the only scholarly work investigating distinct clinical findings in between those two groups while also assessing the effectiveness of oral anticoagulants in AF patients with thyroid disease [4]. Their analysis found that AF patients with and without thyroid disease history are similar in terms of rates of systemic strokes/embolization, all-cause mortality, and major bleeding due to oral anticoagulants. Moreover, they demonstrated the superiority of NOACs (apixaban) over warfarin, and the appropriateness of oral anticoagulation management in AF patients with thyroid disease. In contrast to this secondary analysis, we demonstrated no significant differences in terms of type of AF, CHA_2DS_2-VASc score categories, and pharmacological agents with the exception of anticoagulants, while similarly finding significantly comparable rates of stroke/embolization between AF patients with and without thyroid disease, and significantly higher rates of AF with concomitant thyroid disease in older individuals and females.

As far as is known, this is the earliest and largest study examining the epidemiological characteristics among AF patients with a history of thyroid disease throughout the entire Middle Eastern region. AF treatment recommendations for this important and vulnerable population, as set by the ACC/AHA, are scarce and inconclusive. Therefore, this preliminary analysis could act as a starting point for future researchers to advance our understanding of the clinical differences, epidemiological characteristics, and therapy recommendations among AF patients with thyroid disease. However, our analysis is not devoid of limitations. Firstly, the retrospective nature of the study subjected it to various biases including recall bias and selection bias. Secondly, the criteria for diagnosing thyroid disease were not based on laboratory values. Thirdly, the study conducted its analysis on a baseline thyroid disease history, of which thyroid-related treatment data were not available. Finally, the study's sampling protocol (i.e., recruiting patients from specialized cardiology centers) may have affected the generalizability of our results and conclusions.

5. Conclusions

Our analysis demonstrated a thyroid disease prevalence rate of 10.5% in patients with AF, of which 90.0% were hypothyroid, 6.1% were hyperthyroid, and 3.3% were euthyroid. Despite having similar risks of stroke and major bleeding, patients with thyroid disease had significantly higher rates of comorbidities and usage of anticoagulants. Further prospective studies should be conducted in order to assess the impact of thyroid disease on treatment outcomes. Due to the high prevalence of hypothyroidism within AF registries, a better understanding of its course in AF would aid in tailoring screening and treatment protocols for such a vulnerable population.

Reporting checklist

The authors have completed the STROBE reporting checklist.

Table 3
Demographic and clinical characteristics of 210 AF patients with thyroid disorders with reference to thyroid status.

Clinical feature		AF/Hypothyroidism n (%)	AF/Hyperthyroidism n (%)	AF/Euthyroid n (%)	*p*-value
Age in years (mean ± SD)		70.0 ± 11.0	70.5 ± 11.6	67.1 ± 9.0	.779
Gender					**.029**
	Male	44 (20.9%)	7 (3.3%)	3 (1.4%)	
	Female	146 (69.5%)	6 (2.8%)	4 (1.9%)	
Medical History					
	Hypertension	145 (69.0%)	10 (4.7%)	3 (1.4%)	.130
	Diabetes Mellitus	95 (45.2%)	8 (3.8%)	4 (1.9%)	.684
	Dyslipidemia	85 (40.4%)	9 (4.2%)	2 (0.9%)	.150
	Currently smokers	12 (5.7%)	3 (1.4%)	1 (0.4%)	.070
BMI					.132
	X ≥ 24.9	32 (15.2%)	4 (1.9%)	2 (0.9%)	
	25 > X > 29.9	48 (22.8%)	5 (2.3%)	4 (1.9%)	
	X ≥ 30	87 (41.4%)	3 (1.4%)	1 (0.4%)	
Type of AF					.593
	Paroxysmal	64 (30.4%)	6 (2.8%)	3 (1.4%)	
	Non-paroxysmal	126 (60.0%)	7 (3.3%)	4 (1.9%)	
Etiology of AF					.277
	Valvular	19 (9.0%)	3 (1.4%)	1 (0.4%)	
	Non-valvular	171 (81.4%)	10 (3.3%)	6 (2.8%)	
AF symptoms					
	Palpitations	80 (38.0%)	7 (3.3%)	2 (0.9%)	.535
	SOB	77 (36.6%)	7 (3.3%)	2 (0.9%)	.509
	Fatigue	54 (25.7%)	4 (1.9%)	2 (0.9%)	.984
	Dizziness	29 (13.8%)	3 (1.4%)	0 (0.0%)	.391
	Syncope	7 (3.3%)	1 (0.4%)	0 (0.0%)	.664
	Chest pain	2 (0.9%)	1 (0.4%)	1 (0.4%)	**.012**
	Asymptomatic	52 (24.7%)	4 (1.9%)	3 (1.4%)	.645
Comorbid diseases					
	Stroke or systemic embolization	31 (16.6%)	2 (0.9%)	2 (0.9%)	.539
	Heart failure	41 (19.5%)	4 (1.9%)	2 (0.9%)	.687
	Left ventricular hypertrophy	65 (30.9%)	3 (1.4%)	3 (1.4%)	.850
	Coronary artery disease	11 (5.2%)	1 (0.4%)	2 (0.9%)	.059
	Congenital heart disease	1 (0.4%)	0 (0.0%)	0 (0.0%)	.948
	Pulmonary hypertension	68 (32.3%)	2 (0.9%)	2 (0.9%)	.308
	Sleep apnea	10 (4.7%)	0 (0.0%)	0 (0.0%)	.575
	Chronic kidney disease	27 (12.8%)	1 (0.4%)	1 (0.4%)	.804
	Active malignancy	10 (4.7%)	0 (0.0%)	0 (0.0%)	.575
CHA_2DS_2-VASc score					.387
	Score 1 in women and 0 in men (1)	11 (5.2%)	1 (0.4%)	0 (0.0%)	
	Score 2 in women and 1 in men (2)	21 (10.0%)	0 (0.0%)	2 (0.9%)	
	Score ≥ 3 in women and ≥ 2 in men (3)	158 (75.2%)	12 (5.7%)	5 (2.3%)	
HAS-BLED score					.693
	0	25 (11.9%)	2 (0.9%)	0 (0.0%)	
	1	68 (32.3%)	2 (0.9%)	2 (0.9%)	
	2	60 28.5%)	6 (2.8%)	3 (1.4%)	
	≥ 3	37 (17.6%)	3 (1.4%)	2 (0.9%)	
Echocardiography findings					
	LVEF (mean ± SD)	54.8 ± 12.3	53.8 ± 19.6	49.1 ± 14.0	.503
	Moderate to severe rhematic mitral stenosis	7 (3.3%)	2 (0.9%)	0 (0.0%)	.112
	Metallic prosthetic valve	12 (5.7%)	1 (0.4%)	1 (0.4%)	.700

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical approval

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional/regional/national ethics/committee/ethics board of the University of Jordan (NO.: 10/2021/416) and individual consent for this retrospective analysis was waived.

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Author contribution

Conceptualization, H.A, and A.H; Data curation, R.A, D.A, L.S and Y. A; Formal analysis, A.A, and N.S; Methodology, A.A; Project administration, H.A, and A.H Supervision, H.A, and A.H; Writing – original draft, All authors; Writing – review & editing, all authors. H.A: Hanna Al-Makhamreh, A.H: Ayman Hammoudeh, R.A: Rusul Almarayaty, D.A: Dana Alkhulaifat, L.S: Liza Shaban, Y.A: Yazan Alhuneidy, A.A: Abdallah Al-Ani, N.S: Neveen Salah.

Consent

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Registration of research studies

•Name of the registry: Clinicaltrials.gov; Research Registry
•Unique Identifying number or registration ID: NCT03917992; researchregistry (UIN:7578)
•Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/ct2/show/NCT03917992; https://www.researchregistry.com/register-now#user-researchregistry/registerresearchdetails/61ebc6a40c2646001ef56d26/

Guarantor

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Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103325.

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