


# Management and 1-Year Outcomes of Patients With Atrial Fibrillation in the Middle East: Gulf Survey of Atrial Fibrillation Events

Angiology  
2015, Vol. 66(5) 464-471  
© The Author(s) 2014  
Reprints and permission:  
sagepub.com/journalsPermissions.nav  
DOI: 10.1177/0003319714536980  
ang.sagepub.com  


Mohammad Zubaid, FRCPC<sup>1</sup>, Wafa A. Rashed, FRCP<sup>2</sup>,  
Alawi A. Alsheikh-Ali, MD, MS<sup>3,4</sup>, Ibrahim Al-Zakwani, PhD<sup>5,6</sup>,  
Wael AlMahmeed, FRCPC<sup>7</sup>, Abdullah Shehab, MD, FRCP, FACC, FESC<sup>8</sup>,  
Kadhim Sulaiman, FRCPI, FESC<sup>9</sup>, Ahmed Al Qudaimi, MSc, MD, FAHA<sup>10</sup>,  
Nidal Asaad, FRCPC<sup>11</sup>, and Haitham Amin, FRCPC<sup>12</sup>; on behalf of the  
Gulf Survey of Atrial Fibrillation Events (Gulf SAFE) Investigators

## Abstract

We describe management and outcomes of patients with nonvalvular atrial fibrillation (AF) in the Middle East. Consecutive patients with AF presenting to emergency departments (EDs) were prospectively enrolled. Among 1721 patients with nonvalvular AF, mean age was  $59 \pm 16$  years and 44% were women. Comorbidities were common such as hypertension (59%), diabetes (33%), and coronary artery disease (33%). Warfarin was not prescribed to 40% of patients with Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke/TIA<sub>2</sub> score of  $\geq 2$ . One-year rates of stroke/transient ischemic attack (TIA) and all-cause mortality were 4.2% and 15.3%, respectively. Warfarin use at hospital–ED discharge was independently associated with lower 1-year rate of stroke/TIA (odds ratio [OR], 0.38; 95% confidence interval [CI], 0.17-0.85;  $P = .015$ ) and all-cause mortality (OR, 0.51; 95% CI, 0.32-0.83;  $P = .006$ ). Prior history of heart failure and peripheral vascular disease was independent mortality predictors. Our patients are relatively young with significant cardiovascular risk. Their anticoagulation treatment is suboptimal, and 1-year all-cause mortality and stroke/TIA event rates are relatively high.

## Keywords

atrial fibrillation, stroke, anticoagulation, risk assessment, Middle East

## Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia associated with significant mortality and morbidity, most notably stroke, transient ischemic attack (TIA), and heart failure.<sup>1-3</sup> Moreover, management of this common arrhythmia comes at a significant economic cost predominantly driven by in-hospital care.<sup>4</sup>

Evidence from large randomized clinical trials has shaped the current guidelines for AF management (eg, rate vs rhythm control and stroke prevention).<sup>5-8</sup> In addition, several observational registries studied management and outcomes of patients with AF in the uncontrolled setting of daily practice.<sup>9-14</sup> Most of these trials and registries were conducted in Europe and North America, where the majority of patients are caucasians, typically older, and often treated in health care settings that are different from other regions of the world.<sup>15,16</sup> This limitation is also apparent in 2 large contemporary, ongoing AF registries, in which patients from the Middle East are not included.<sup>17,18</sup> Management and outcomes of patients with AF in the Middle East may differ from other parts of the world, given the different demographics, health care settings, and risk factor profile.

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Safat, Kuwait

<sup>2</sup>Department of Medicine, Mubarak Al-Kabeer Hospital, Ministry of Health, Jabriya, Kuwait

<sup>3</sup>Heart and Vascular Institute, Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates

<sup>4</sup>Department of Medicine, Tufts Clinical and Translational Science Institute, Tufts Medical Center and Tufts University School of Medicine, Boston, MA, USA

<sup>5</sup>Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman

<sup>6</sup>Gulf Health Research, Muscat, Oman

<sup>7</sup>Heart and Vascular Institute, Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates

<sup>8</sup>Department of Medicine, Faculty of Medicine, UAE University, Al-Ain, United Arab Emirates

<sup>9</sup>Department of Medicine, Royal Hospital, Muscat, Oman

<sup>10</sup>Department of Medicine, Al Thawra Hospital, Sana'a, Yemen

<sup>11</sup>Department of Cardiology and Cardiovascular Surgery, Hamad Medical Corporation, Doha, Qatar

<sup>12</sup>Department of Cardiology, Mohammed Bin Khalifa Cardiac Centre, Manama, Bahrain

## Corresponding Author:

Mohammad Zubaid, Department of Medicine, Faculty of Medicine, Kuwait University, PO Box 24923, Safat 13110, Kuwait.

Email: zubaid@hsc.edu.kw

We conducted a prospective registry of patients with AF presenting to emergency departments (EDs) in 6 countries in the Gulf region of the Middle East. In this report, we describe characteristics, management practices, and outcomes of patients with nonvalvular AF in this part of the world, where no such studies have been previously carried out.

## Methods

Gulf Survey of Atrial Fibrillation Events (Gulf SAFE) is a prospective, observational study of consecutive patients with AF recruited between October 2009 and June 2010 from EDs of 23 hospitals in 6 countries of the Gulf region of the Middle East. Patients were followed for 1 year after enrollment. Full details of the methods have been previously published.<sup>19</sup> Briefly, patients were eligible if they were  $\geq 18$  years, found to have AF  $>30$  seconds on a 12-lead electrocardiogram or rhythm strip while in ED, and provided informed consent. Patients were enrolled regardless of the primary reason for their ED visit. Patient management was at the discretion of the treating physician. Follow-up by clinic visit or telephone interview was planned at 1, 6, and 12 months from the time of enrollment. For the purpose of this report, we analyzed data for patients with AF who do not have rheumatic mitral stenosis or a prosthetic heart valve (ie, nonvalvular AF).

## Ethics

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by internal review bodies/ethics committees of each institution/country. All patients provided informed consent prior to their enrollment in the study.

Data were collected on a standardized case report form (CRF) and entered online. Data included patient baseline characteristics, AF type and history, ED, and hospital management and outcomes. Variable definitions were in accordance with American College of Cardiology/American Heart Association key data elements and definitions for AF.<sup>20</sup> At the time of study design and conduct, Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke/TIA<sub>2</sub> (CHADS<sub>2</sub>) score was recommended by AF guidelines for estimating the risk of stroke and thromboembolism in patients with nonvalvular AF.<sup>21</sup> Therefore, variables required for calculating CHADS<sub>2</sub> score were included in the CRF. The Congestive heart failure, Hypertension, Age  $\geq 75$  years, Diabetes mellitus, Stroke/TIA<sub>2</sub>, vascular disease, age 65-74 years, sex category (CHA<sub>2</sub>DS<sub>2</sub>-VASc) score was later introduced by the European Society of Cardiology for risk stratification of patients with AF.<sup>22</sup> Therefore, in this article, we refer to the CHADS<sub>2</sub> score when we report on practice pattern and refer to both CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores when we report on patients' outcomes.

Data source verification was performed by a clinical research associate who conducted site visits in 35% of participating hospitals. Key data variables like age, gender, and comorbidities were 100% complete. Key outcome data such

as mortality, stroke, and bleeding were known for all patients who completed 1-year follow-up (96%).

## Statistical Analysis

Patient characteristics were summarized using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. We used medians and interquartile range (IQR) for continuous variables that were not normally distributed. Group comparisons for categorical variables were performed using Pearson chi-square test. Multivariate logistic regression models were constructed to identify factors independently associated with the outcomes of stroke/TIA and all-cause mortality during 1 year of follow-up. For the outcome stroke/TIA, we adjusted for age, gender, stroke risk score, and other baseline characteristics not accounted for in the risk score but associated with stroke/TIA in univariate analyses. We considered 2 risk scores (the CHADS<sub>2</sub> and the CHA<sub>2</sub>DS<sub>2</sub>-VASc) and constructed 2 separate multivariate logistic models with each score. For the outcome of all-cause mortality, we adjusted for age, gender, and other baseline characteristics associated with all-cause mortality in univariate analyses. Model fit of the regressions was analyzed using Hosmer and Lemeshow statistics and area under the receiving-operating curve, also known as c-statistics. A *P* value  $< .05$  was considered statistically significant. Analyses were performed using STATA version 12.1 (STATA Corporation, College Station, Texas).

## Results

### Baseline Characteristics

Of 2043 patients with AF recruited, 1721 (84%) had nonvalvular AF (Table 1). The mean age was  $59 \pm 16$  years, 60% were younger than 65 years and 44% were women. The most common baseline comorbid conditions were hypertension (59%), diabetes mellitus (33%), coronary artery disease (32%), and history of heart failure (27%). Prior stroke/TIA was reported in 13% of patients. About half (52%) of the patients presented to ED for a reason/symptoms other than AF (26% for cardiac and 26% for noncardiac reasons). The most common cardiac reasons for ED presentation were heart failure (9%), acute coronary syndrome (5%), and chest pain (4%). The most common noncardiac reasons for ED presentation were stroke/TIA (6%), infection/fever (4%), and respiratory disease (3%).

### Management

Rhythm management in ED is shown in Figure 1. A small (10%) proportion of patients spontaneously cardioverted to sinus rhythm. Almost three-quarters were managed with rate control strategy. When rhythm control strategy was selected, cardioversion was attempted using amiodarone in the majority of patients. Sinus rhythm was achieved in 76% of patients when electrical cardioversion was attempted and 43% of patients when pharmacological cardioversion was attempted. Overall,

**Table 1.** Baseline Characteristics of 1721 Patients With Nonvalvular Atrial Fibrillation.

Characteristic	No. (%), n = 1721
Age, mean $\pm$ SD, years	59.1 $\pm$ 15.8
Age $\geq$ 65 years	686 (39.9)
Female gender	764 (44.4)
Comorbid conditions and risk factors	
Hypertension	1019 (59.2)
Diabetes	563 (32.7)
Smoking	409 (23.8)
CAD	553 (32.1)
Heart failure	461 (26.8)
LV systolic dysfunction	337 (19.6)
Valvular heart disease (moderate to severe)	
Mitral regurgitation	147 (8.5)
Aortic regurgitation	30 (1.7)
Aortic stenosis	22 (1.2)
Tricuspid regurgitation	73 (4.2)
COPD	95 (5.5)
Thyroid disease	100 (5.8)
Stroke	159 (9.2)
TIA	65 (3.8)
Major bleeding	35 (2.0)
Alcohol use	33 (1.9)
Body mass index <sup>a</sup> , kg/m <sup>2</sup>	
Underweight, <18.5	22 (1.4)
Normal weight, 18.5-24.9	462 (28.6)
Overweight, 25-30	597 (37.0)
Obese, >30	534 (33.1)
LA diameter, <sup>b</sup> mean $\pm$ SD, mm	42.7 $\pm$ 8.1
First heart rate, mean $\pm$ SD, bpm	120 $\pm$ 33
First SBP, mean $\pm$ SD, mm Hg	133 $\pm$ 26
Serum creatinine, mean $\pm$ SD, $\mu$ mol/L	110 $\pm$ 92
Type of AF	
First attack ever	720 (41.8)
Paroxysmal AF	328 (19.1)
Permanent AF	458 (26.6)
Persistent AF	155 (9.0)
Unknown	60 (3.5)
Reason for ED visit	
Atrial fibrillation	827 (48.1)
Cardiac	450 (26.2)
Heart failure	157 (34.9)
ACS	87 (19.3)
Chest pain	64 (14.2)
Noncardiac	444 (25.8)
Stroke/TIA	97 (21.9)
Infection/fever	65 (14.6)
Respiratory disease	47 (10.6)
CHADS <sub>2</sub> score	
Mean $\pm$ SD	1.6 $\pm$ 1.4
0	430 (25.0)
1	467 (27.1)
$\geq$ 2	824 (47.9)

Abbreviations: SD, standard deviation; CAD, coronary artery disease; LV, left ventricular; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; LA, left atrial; SBP, systolic blood pressure; ED, emergency department; ACS, acute coronary syndrome; CHADS<sub>2</sub>, Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke/TIA<sub>2</sub>.

<sup>a</sup> Data on body mass index was missing in 106 patients (n = 1615).

<sup>b</sup> Data on LA diameter was missing in 481 patients (n = 1240).

1388 (81%) patients were admitted to hospital. The median length of hospital stay was 3 days (IQR 1-6 days).

Warfarin prescription at hospital discharge increased with increasing CHADS<sub>2</sub> score (28% in score 0, 43% in score 1 and 60% in score  $\geq$ 2,  $P < .001$ ; Table 2), whereas 28% of CHADS<sub>2</sub> score 0 received warfarin at discharge, 40% of patients with CHADS<sub>2</sub> score  $\geq$ 2 were not on warfarin at discharge. There were 608 patients who were discharged in AF rhythm, 62% of whom were prescribed warfarin at the time of discharge. Reasons for not prescribing warfarin to the rest of them were due to physician preference/decision (48%), high bleeding risks (28%), anticipated noncompliance (18%), and other reasons. Of 1209 available international normalized ratios (INRs) for 621 patients at 1-, 6-, and 12-month follow-up, 28% were  $<$ 2, 56% were between 2 and 3, and 16% were  $>$ 3.

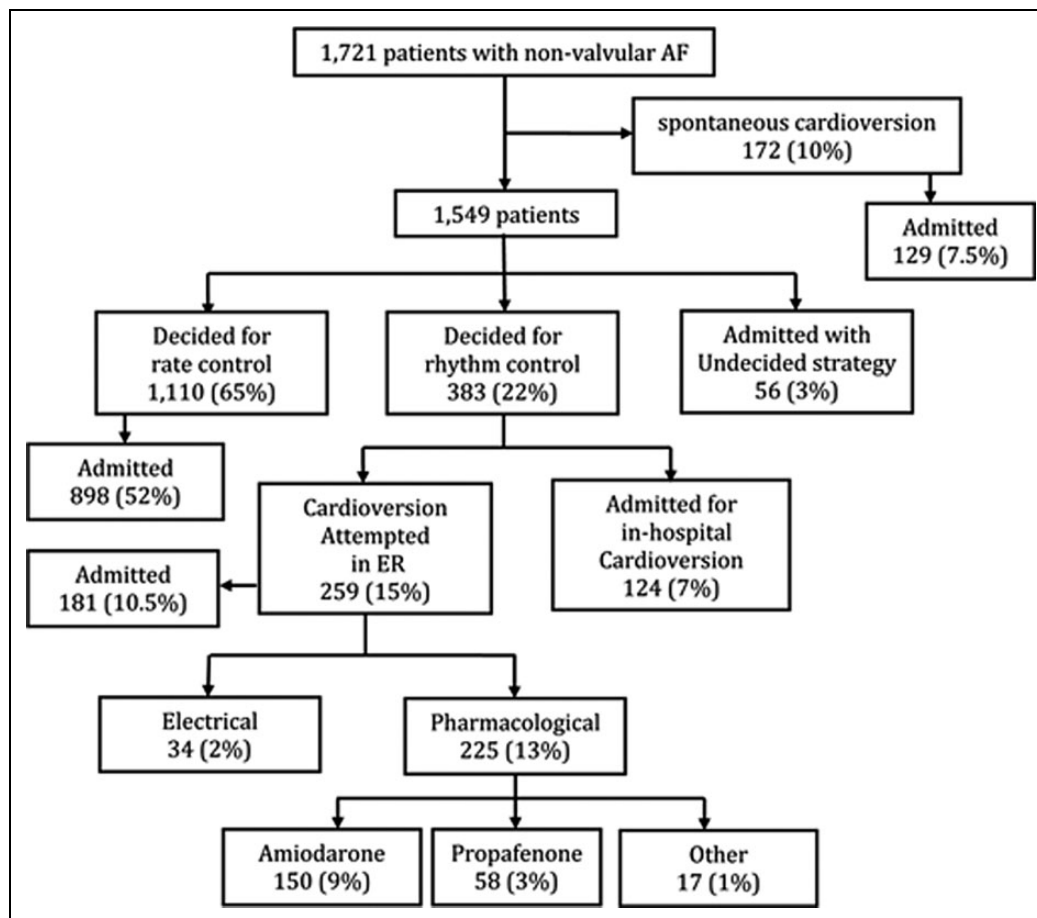
## Outcomes

One-year follow-up was completed in 1654 (96%) patients. One-year mortality rate was 15.3% while that for stroke/TIA was 4.2%. Mortality and stroke/TIA rates differed according to the reason for ED visit (Table 3). Patients whose primary reason for ED visit was noncardiac had the highest mortality rate (31%), while those with cardiac reason had the highest stroke/TIA rate (7.8%). In patients with AF as the primary reason for ED visit, mortality and stroke/TIA rates were 4.2% and 2.2%, respectively.

In multivariate models, smoking, cardiac, and noncardiac reasons for ED visit, CHADS<sub>2</sub> score  $\geq$ 2, and CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq$ 2 were independently associated with higher odds of stroke/TIA during 1-year follow-up (Table 4). The odds of developing stroke/TIA were approximately 60% lower for patients who were discharged on warfarin compared to patients who were not (odds ratio [OR], 0.38; 95% confidence interval [CI], 0.17-0.83;  $P = .015$ ). The strongest independent predictors of mortality were reason for ED visit (specifically cardiac and noncardiac reasons), congestive heart failure, peripheral vascular disease, and lack of warfarin use (Table 5). Older age, higher serum creatinine, lower body mass index, and absence of a past history of hypertension were also associated with higher odds of death at 1 year.

## CHA<sub>2</sub>DS<sub>2</sub>-VASc Score in Low-Risk Patients

Stroke/TIA rate at 1-year follow-up was 1.9% for CHADS<sub>2</sub> score 0, 3.9% for score 1, and 5.7% for score  $\geq$ 2 ( $P = .005$ ). Patients with a CHADS<sub>2</sub> score of 0/1 did not appear to be homogeneously low risk when reclassified by the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. Of 897 patients with a CHADS<sub>2</sub> score of 0 or 1, approximately 40% had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq$ 2. Adjusting for antithrombotic therapy, these patients had nearly 3-fold higher risk of stroke/TIA compared to patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 0 (adjusted OR, 2.94; 95% CI, 1.03-8.41).



**Figure 1.** Rhythm management in emergency department (ED) of 1721 patients with nonvalvular AF.

**Table 2.** Warfarin and Antiplatelet Therapy at Discharge From Hospital Based on the CHADS<sub>2</sub> Score in Patients Discharged Alive.<sup>a</sup>

Warfarin and Antiplatelet Therapy	CHADS <sub>2</sub> Score			P Value
	0, No. (%), n = 423	1, No. (%), n = 452	≥2, No. (%), n = 779	
Warfarin	117 (27.7)	196 (43.4)	465 (59.7)	<.001
Warfarin alone	87 (74)	119 (61)	230 (49)	.003
Dual therapy	28 (24)	72 (37)	207 (45)	<.001
Triple therapy	2 (2)	5 (3)	28 (6)	<.001
Antiplatelet	234 (55.3)	217 (48.0)	266 (34.1)	<.001
None	72 (17.0)	39 (8.6)	48 (6.2)	<.001

Abbreviations: CHADS<sub>2</sub>, Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke/TIA<sub>2</sub>; TIA, transient ischemic attack.

<sup>a</sup> Dual therapy, warfarin, and either of the 2 antiplatelets (aspirin or clopidogrel); triple therapy, warfarin plus aspirin plus clopidogrel; antiplatelet, aspirin or clopidogrel or both; none, neither warfarin, nor antiplatelet (n = 1654).

## Discussion

This is the first multicenter, multinational, prospective, and observational study from Middle Eastern Arab countries examining the characteristics, management, and 1-year outcomes of patients with AF. Patients with AF in Arab countries of the Middle East were relatively young but possess significant cardiovascular risk profile including high prevalence of hypertension, diabetes mellitus, obesity, smoking, and concomitant cardiac disease. A large number of patients, including

many with high stroke risk score, did not receive oral anticoagulation; and in those who received it, a significant proportion did not achieve optimal anticoagulation level. Relatively high rates of stroke/TIA and all-cause mortality were observed over the 1 year of follow-up.

Compared to randomized trials, registries have fewer exclusion criteria and consequently include a wider range of patients. Since patient management is not dictated by the registry protocol, registries provide details on how and who receives a particular treatment. Well-conducted registries, therefore, have the

**Table 3.** Outcome Events at 12-Month Follow-Up in the Entire Cohort and According to Reason for Emergency Department Visit.<sup>a</sup>

Event	Entire Cohort, No. (%), N = 1721	Reason for ED Visit		
		AF	Cardiac	Noncardiac
		No. (%), n = 827	No. (%), n = 450	No. (%), n = 444
All-cause death	263 (15.3)	35 (4.2)	90 (20)	138 (31.1)
Stroke/TIA	73 (4.2)	18 (2.2)	35 (7.8)	20 (4.5)
PE	3 (0.2)	0	0	3 (0.7)
Major bleed	20 (1.2)	2 (0.2)	7 (1.6)	11 (2.7)
Gastrointestinal	11	2	3	6
Intracerebral	3	0	2	1
Subdural	2	0	1	1
Other	4	0	1	3
Recurrent ED visit for AF	232 (14.0)	139 (16.9)	61 (14.3)	32 (7.9)
Recurrent hospital admission for AF	183 (11.1)	101 (12.2)	54 (12.7)	28 (6.9)
Recurrent hospital admission for HF	175 (10.6)	44 (5.3)	92 (21.6)	39 (9.7)

Abbreviations: AF, atrial fibrillation; ED, emergency department; TIA, transient ischemic attack; PE, peripheral embolization; HF, heart failure.

<sup>a</sup> Apart from all-cause mortality and stroke/TIA, all other outcome events were captured after hospital discharge. Hence, column percentages may not add up to 100% on the events captured after hospital discharge.

**Table 4.** Factors Independently Associated With Risk of Stroke/TIA in 2 Logistic Models for 1712 Patients With Nonvalvular AF.

Predictor	OR	95% CI	P Value	Predictor	OR	95% CI	P Value
Male	1.10	0.64-1.87	.735	Male	1.23	0.72-2.13	.449
Smoking	1.94	1.12-3.36	.017	Smoking	2.01	1.16-3.47	.013
Reason for ED visit				Reason for ED visit			
AF	Ref	Ref	Ref	AF	Ref	Ref	Ref
Cardiac	3.01	1.64-5.53	<.001	Cardiac	2.89	1.56-5.32	.001
Noncardiac	1.97	1.01-3.86	.048	Noncardiac	1.90	0.97-3.71	.061
CHADS <sub>2</sub> score				CHA <sub>2</sub> DS <sub>2</sub> -VASc score			
0	Ref	Ref	Ref	0	Ref	Ref	Ref
1	2.18	0.92-5.18	.078	1	1.60	0.48-5.38	.448
2+	3.01	1.34-6.76	.008	2+	3.47	1.29-9.35	.014
Antithrombotic therapy at discharge				Antithrombotic therapy at discharge			
None	Ref	Ref	Ref	None	Ref	Ref	Ref
Aspirin/clopidogrel	1.04	0.59-1.83	.903	Aspirin/clopidogrel	1.03	0.59-1.82	.907
Warfarin	0.38	0.17-0.83	.015	Warfarin	0.39	0.18-0.84	.016

Abbreviations: TIA, transient ischemic attack; AF, atrial Fibrillation; ED, emergency department; OR, odds ratio; CI, confidence interval; Ref, reference; CHADS<sub>2</sub>, Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke/TIA<sub>2</sub>.

benefit of providing a representative “real-world” view of both clinical practice and patient outcomes.<sup>23</sup> Such studies are needed to understand how we are really doing, to develop targets for interventions, and to provide benchmarks for evaluating future improvements in practice. Gulf SAFE is one of the few prospective registries evaluating AF in non-Western populations.<sup>15</sup> The mean age of 59 years in our patients is 7 years younger than in other multinational AF registries.<sup>11,12</sup> This may reflect the population demographics in the region, where only 2% to 5% of the general population of Gulf SAFE participating countries are older than the age of 60.<sup>24</sup> Alternatively, the younger age of our patients may reflect a predisposition to AF driven by prevalent comorbid conditions including hypertension, obesity, diabetes mellitus, cigarette smoking, and prior cardiac disease. The high prevalence of risk factors in the AF population is probably a reflection of the high incidence in

the general population in this part of the world.<sup>25</sup> A recent report from the Atherosclerosis Risk in Communities (ARIC) study showed that 57% of incident AF could be attributed to potentially modifiable risk factors.<sup>26</sup> Additionally, there may be other unmeasured genetic or environmental factors that predispose our populations to AF, a possibility that should stimulate future research.<sup>27,28</sup>

The management strategy of choice while in ED was rate control for most of our patients. It is uncertain why a relatively low proportion of physicians opted for a rhythm control strategy in the present study. This may reflect limited availability of antiarrhythmic drugs other than amiodarone, concerns over long-term adverse events and proarrhythmia, low familiarity with clinical indications for antiarrhythmics, or broad conviction among practicing physicians in the region that rate control is universally a noninferior strategy in all patients. The

**Table 5.** Factors Independently Associated With Risk of Death in Patients With Nonvalvular AF in Gulf SAFE.

Predictor	Adjusted OR	95% CI	P Value
Age	1.04	1.03-1.05	<.001
Male	0.83	0.59-1.18	.302
Reason for ED visit			
AF	Ref	Ref	Ref
Cardiac	2.46	1.51-4.02	<.001
Noncardiac	5.99	3.74-9.61	<.001
Hypertension	0.64	0.43-0.95	.026
Diabetes mellitus	1.34	0.92-1.93	.123
CAD	1.12	0.77-1.64	.550
CHF	2.64	1.79-3.89	<.001
COPD	1.49	0.84-2.62	.172
Prior stroke/TIA	1.41	0.91-2.19	.126
PVD	2.26	1.01-5.08	.048
BMI	0.96	0.93-0.99	.012
Serum creatinine	1.01	1.01-1.01	<.001
AF type			
First attack ever	Ref	Ref	Ref
Paroxysmal	1.01	0.60-1.73	.959
Permanent	0.86	0.55-1.34	.499
Persistent	1.44	0.78-2.67	.241
Antithrombotic therapy at discharge			
None	Ref	Ref	Ref
Aspirin/clopidogrel	0.55	0.35-0.87	.010
Warfarin	0.51	0.32-0.83	.006

Abbreviations: AF, atrial fibrillation; TIA, transient ischemic attack; OR, odds ratio; CI, confidence interval; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; BMI, body mass index; ED, emergency department; SAFE, Survey of Atrial Fibrillation Events.

great majority (81%) of patients were admitted to hospital regardless of the management strategy used. This high rate of hospital admission has important economic implications. Half of the financial costs of AF management relates to hospital admissions.<sup>4,29</sup> Possible reasons for the high admission rate in our population include tendency of ED physicians to defer decisions regarding management strategy to admitting doctors, preference to cardiovert patients while in-hospital, unavailability of urgent transesophageal echocardiography service to guide immediate cardioversion, anticipated poor follow-up in primary care clinics, and limited availability of anticoagulation clinics.

We observed higher rate of stroke/TIA (4.2%) at 1-year follow-up in our relatively young patients compared to rates (0.5%-2%) reported by most AF registries conducted in the West.<sup>9-14</sup> This may be explained by the lack of anticoagulation in 40% of the patients with CHADS<sub>2</sub> score  $\geq 2$  and the suboptimal levels of INRs achieved in almost half of those who received warfarin. This deficiency in anticoagulation was also observed in patients who were in AF rhythm at the time of hospital discharge, where only 62% of patients were placed on anticoagulation. When physicians were asked about the reason why the rest of this group of patients was not anticoagulated, 48% cited "physician preference/decision." This hesitancy on the part of physicians needs to be explored and whether the

new novel oral anticoagulants would reduce this hesitancy remains to be seen. We observed that warfarin prescription at discharge was independently associated with  $\sim 60\%$  lower risk of stroke/TIA at 1 year. This magnitude of risk reduction is similar to that observed in clinical trials comparing warfarin to placebo for stroke prevention in AF and suggests that better adherence to evidence-based guidelines of stroke prevention with oral anticoagulation should improve outcomes in our patients.<sup>30</sup> At the time our registry was designed and conducted, CHADS<sub>2</sub> score was the only risk stratification score for guiding anticoagulation treatment. Since then, CHA<sub>2</sub>DS<sub>2</sub>-VASc score was developed and is currently used in patients with CHADS<sub>2</sub> score of 0/1 to improve risk stratification.<sup>31</sup> We found that patients with a CHADS<sub>2</sub> score of 0/1 were not uniformly low risk. Among them, those who were reclassified with CHADS<sub>2</sub>-VASc score of  $\geq 2$  had nearly 3-fold greater risk of stroke/TIA compared to the subgroup with CHADS<sub>2</sub>-VASc score of 0.

We observed high mortality rates (15%) at 1-year follow-up in our patients. The mortality rate was lowest in patients presenting mainly with AF (4.2%) and highest (31%) in patients presenting with noncardiac reasons (eg, stroke, infection, or respiratory disease). The high mortality rate could be related to the comorbidity associated with AF in these patients.

Our study presents data on patients with AF from the region, making it possible to validate the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores in Middle Eastern populations. Training and educating ED physicians, internists, and cardiologists managing AF are likely to improve adherence to treatment guidelines. Additional reduction to the cost of AF management can be achieved by revising our admission policy to reduce the rate of admission of patients with AF at low risk of short-term complications. Finally, the high prevalence of atherosclerotic risk factors in our patients highlights the need to focus on primary prevention programs aimed at smoking cessation, a healthier diet, and a more active lifestyle. Such programs will be expected to decrease the burden of AF, coronary artery disease, and stroke.

### Strengths and Limitations

This study's strengths include its prospective design and high completed follow-up rate (96%), lending validity to our results. The near equal representation of both genders and recruitment from a wide range of hospitals make our findings representative of the region.<sup>19</sup> Future work should overcome some of the limitations of the current study including more information on interim medication use, adequacy of anticoagulation levels, and longer follow-up. Although we believe that we enrolled all consecutive patients with AF who presented to the EDs of participating hospitals, we did not use log-books to document the number of patients who were not enrolled and the reasons for not enrolling them.

### Conclusion

Patients with AF in the Middle East are relatively young with high burden of atherosclerotic risk factors that may play a

major role in the onset of AF at this young age. Their anticoagulation treatment is suboptimal, and mortality and stroke/TIA events at 1 year are high. Emergency department management revealed high use of rate control strategy and high rate of hospital admissions, which would contribute to the increased cost of management.

## Appendix

### Gulf SAFE Administrative Organization

#### Steering Committee

Mohammad Zubaid (chair and principal investigator), Wafa Rashed (registry coordinator), Wael AlMahmeed and Abdulla Shehab (UAE), Kadhim Sulaiman (Oman), Nidal Asaad (Qatar), Haitham Amin (Bahrain), Ahmed Al-Qudaimi (Yemen), Alawi A. Alsheikh-Ali (UAE), Ibrahim Al-Zakwani (biostatistician).

#### National Coordinators (NC) and Investigators

**Bahrain:** Haitham Amin (NC); Adel K. Hamad\*, Rajesh Jayakumar, Babu Thevan, Devashish Sheel, Manal Matar, Hugmi B. Jain, Fawaz Bardooli, Wala Mattar.

**Kuwait:** Wafa Rashed (NC); Adan Hospital: Mustafa M. Ridha\*, Amin S. Amin, Bobby Cherian; Mubarak AlKabeer Hospital: Hisham Saad\*, Ashraf Hamad, Hani Abdul Salam, Maged Yousef, Ihab Awwad, Gladis Hefny, Nabil Ragab, Mohammad Abdul Moneim, Sameh El Masry, Mohammad Samir; Farwaniyah Hospital: Fahad Al-Enezi\*, Ashraf Abdelwahed, Mahmoud Abdultawab, Musaad Elbanna, Ayman Abdulmogoud.

**Oman:** Kadhim Sulaiman (NC); Sohar Hospital: Marei Aysha\*, Ali Alkhafaji, Mohammad Agar, Hamada M. Amin, Hatem H. Mohammed, Abu Baker, Nashat Abdulhalim, Pasupathy Seshadri, Sohail Shahzad; Sultan Qaboos Hospital: Prit P. Singh\*, S. Wettewe; Royal Hospital: Najeeb Al-Rawahi\*, Hood Al-Abri; Nizwa Hospital: Faisal Al Tamimi\*, Dilip Kumar, Saquib Ahmed, Refaat Abdulla, Ahmed Hagazy, Abdulslam Abdulrahman, M.R. Shajee, Abu Baker Elsadiq, Ahmed Moawed, Wael Mohammed, Abdulwaheed Baig; Ibri Hospital: Sharat K. 23 Samantray\*, Mohammed N. El-Nour, Waseem Mohammad; Ibra Hospital: Narayan A. Narayan\*, Elmutaz Elamin, Addulnasser Awadh, Sharath Ali.

**Qatar:** Nidal Assad(NC), Soaly E\*, Ahmad Shaaban, Esam Eljerjawy, R.F. Al-Aqeedi, Gomaa M. Maauf.

**United Arab Emirates:** Abdulla Shehab (NC); Al-Noor hospital (Al-Ain): Jasim AlHayali\*, Eman Mohammed; Dubai Hospital: Dr Afzalhussein Yusufali\*, Ambreen F. Tariq; Fujairah Hospital: Amrisha Agrawal\*, Abdulrahman Aboobaker; Ras Al Khaima Hospital: Adel Wassef\*, Ajaz alhaq; Rashed Hospital (Dubai): Fahad Baslaib\*, Ali Raza, Sameera Ali, Kabad Rao; Shaikh Khalif Medical City (Abu Dhabi): Wael AlMahmeed\*, Irfan Maqsood, Amer Sana; Zayed Military Hospital (Abu Dhabi): Salim AlKaabi\*, Waheed Murad.

**Yemen:** Ahmed Al-Qudaimi (NC); Al-Thawra Hospital (Sana'a): Abdulwahab Almatry\*, Sameera Al-Ragwi\*, Ali Othman, Afrah Almulsi, Mohammed Alshami; Al Jamhuri Teaching Hospital (Sana'a): Abdu Hamod\*; Modern Medical Center (Aldalee): Motea Alawlaqi\*, Moaeen Hussein; Al-Wehdah Teaching Hospital: Fuad Ali\*; Al-Jamhuria Hospital (Aden): Salem Almehdar\*.

\*Chief site officer.

### Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Drs Zubaid and Alsheikh-Ali received speaker honoraria from Sanofi and Boehringer Ingelheim. Dr AlMahmeed received speaking honoraria from Sanofi and Boehringer Ingelheim. Dr Al-Zakwani received workshop honoraria from Sanofi.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Gulf SAFE is an investigator-initiated study under the auspices of the Gulf Heart Association and was financially supported by Sanofi-Aventis. The sponsor had no role in study design, data collection, data analysis, or writing of the manuscript.

### References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke*. 1991;22(8):983-988.
2. Vidaillet H, Granada JF, Chyou PH, et al. A population-based study of mortality among patients with atrial fibrillation or flutter. *Am J Med*. 2002;113(5):365-370.
3. Cha YM, Redfield MM, Shen WK, Gersh BJ. Atrial fibrillation and ventricular dysfunction: a vicious electromechanical cycle. *Circulation*. 2004;109(23):2839-2843.
4. Stewart S, Murphy NF, Walker A, McGuire A, McMurray JJ. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart*. 2004;90(3):286-292.
5. de Denus S, Sanoski CA, Carlsson J, Opolski G, Spinler SA. Rate vs. rhythm control in patients with atrial fibrillation: a meta-analysis. *Arch Intern Med*. 2005;165(3):258-262.
6. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have non-valvular atrial fibrillation. *Ann Intern Med*. 2007;146(12):857-867.
7. Connolly SJ, Ezekowitz MD, Yusuf S, et al. RE-LY steering committee and investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361(12):1139-1151.
8. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31(19):2369-2429.
9. Kerr CR, Boone J, Connolly SJ, et al. The Canadian registry of atrial fibrillation: a noninterventional follow-up of patients after the first diagnosis of atrial fibrillation. *Am J Cardiol*. 1998;82(8A):82N-85N.

10. Friberg L, Niklas H, Hans P, Marten R. Increased mortality in paroxysmal atrial fibrillation: report from the Stockholm Cohort-Study of Atrial Fibrillation (SCAF). *Eur Heart J*. 2007;28(19):2346-2353.
11. Nieuwlaat R, Capucci A, Camm AJ, et al. European heart survey investigators. Atrial fibrillation management: a prospective survey in ESC member countries. The Euro heart survey. *Eur Heart J*. 2005;26(22):2422-2434.
12. Camm AJ, Breithardt G, Crijns H, et al. Real-life observations of clinical outcomes with rhythm- and rate-control therapies for atrial fibrillation RECORDAF (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation). *J Am Coll Cardiol*. 2011;58(5):493-501.
13. Potpara TS, Vasiljevic ZM, Vujisic-Tesic BD, et al. Mitral annular calcification predicts cardiovascular morbidity and mortality in middle-aged patients with atrial fibrillation: the Belgrade atrial fibrillation study. *Chest*. 2011;140(4):902-910.
14. Reiffel JA, Kowey PR, Myerburg R, et al. Practice patterns among United States cardiologists for managing adults with atrial fibrillation. (AFFECTS). *Am J Cardiol*. 2010;105(8):1122-1129.
15. Hersi A, Alsheikh-Ali AA, Zubaid M, Al Suwaidi J. Prospective observational studies of the management and outcomes in patients with atrial fibrillation: a systematic review. *J Saudi Heart Assoc*. 2012;24(4):243-252.
16. Lip GY, Brechin CM, Lane DA. The global burden of atrial fibrillation and stroke: a systematic review of the epidemiology of atrial fibrillation in regions outside North America and Europe. *Chest*. 2012;142(6):1489-1498.
17. Piccini JP, Fraulo ES, Ansell JE, et al. Outcomes registry for better informed treatment of atrial fibrillation: rationale and design of ORBIT-AF. *Am Heart J*. 2011;162(4):606-612.
18. Kakkar AK, Mueller I, Bassand JP, et al. International longitudinal registry of patients with atrial fibrillation at risk of stroke: Global Anticoagulant Registry in the FIELD (GARFIELD). *Am Heart J*. 2012;163(1):13-19.
19. Zubaid M, Rashed WA, Alsheikh-Ali AA, et al. Gulf Survey of Atrial Fibrillation Events (Gulf SAFE) Investigators. Gulf Survey of Atrial Fibrillation Events (Gulf SAFE): design and baseline characteristics of patients with atrial fibrillation in the Arab Middle East. *Circ Cardiovasc Qual Outcomes*. 2011;4(4):477-482.
20. McNamara RL, Brass LM, Drozda JP Jr, et al. ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with atrial fibrillation: a report of the American college of cardiology/American heart association task force on clinical data standards (writing committee to develop data standards on atrial fibrillation). *Circulation*. 2004;109(25):3223-3243.
21. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the national registry of atrial fibrillation. *JAMA*. 2001;285(22):2864-2870.
22. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137(2):263-272.
23. Gliklich RE, Dreyer NA, eds. *Registries for Evaluating Patient Outcomes: A User's Guide*. 2nd ed. (Prepared by Outcome DEcIDE Center [Outcomes Sciences, Inc d/b/a Outcome] under contract No. HHS290200500351T03.) AHRQ publication No. 10-EHC049. Rockville, MD: Agency for Healthcare Research and Quality; 2010.
24. United Nations. World Population Prospects: The 2008 Revision; Vol. II: Sex and Age Distribution of Populations. United Nations Publication, ST/ESA/SER.A/291. New York: United Nations; 2008.
25. Al Rashdan I, Al Nesef Y. Prevalence of overweight, obesity, and metabolic syndrome among adult Kuwaitis: results from community-based national survey. *Angiology*. 2010;61(1):42-48.
26. Huxley RR, Lopez FL, Folsom AR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the atherosclerosis risk in communities (ARIC) study. *Circulation*. 2011;123(14):1501-1508.
27. Lubitz SA, Yin X, Fontes JD, et al. Association between familial atrial fibrillation and risk of new-onset atrial fibrillation. *JAMA*. 2010;304(20):2263-2269.
28. Rich DQ, Mittleman MA, Link MS, et al. Increased risk of paroxysmal atrial fibrillation episodes associated with acute increases in ambient air pollution. *Environ Health Perspect*. 2006;114(1):1120-1123.
29. Ringborg A, Nieuwlaat R, Lindgren P, et al. Costs of atrial fibrillation in five European countries: results from the Euro Heart Survey on atrial fibrillation. *Europace*. 2008;10(4):403-411.
30. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146(12):857-867.
31. Olesen JB, Torp-Pedersen C, Hansen ML, Lip GY. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: a nationwide cohort study. *Thromb Haemost*. 2012;107(6):1172-1179.