Heart Failure in Patients With Atrial Fibrillation Is Associated With a High Symptom and Hospitalization Burden: The RealiseAF Survey

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ABSTRACT

Background: Atrial fibrillation (AF) and heart failure (HF) often coexist; the consequences of such coexistence are unclear.

Hypothesis: HF in patients with AF is associated with poor outcomes.

Methods: This post hoc analysis of RealiseAF, a survey of AF patients, compared symptoms, hospitalizations, management, and AF control in patients with vs without HF. A total of 10,523 AF patients were analyzed according to presence/absence of HF.

Results: History of HF was present in 45.8%, and in more patients with permanent vs persistent, paroxysmal, or first-episode AF (55.6%, 44.3%, 32.9%, and 29.8%, respectively; $P < 0.0001$). Patients with vs those without history of HF, and patients with HF and reduced ejection fraction (HF-REF) vs those with HF and a preserved ejection fraction (HF-PEF), had more frequent cardiovascular (CV) risk factors and more severe symptoms. Presence vs absence of HF, and HF-REF vs HF-PEF, were associated with lower rates of AF control (54.6% vs 62.8% and 49.3% vs 60.3%, respectively; both $P < 0.0001$). The rate-control strategy was used more frequently in HF patients, particularly those with HF-REF, than the rhythm-control strategy. CV hospitalizations occurred more frequently in patients with HF than those without (41.8% vs 17.5%; $P < 0.001$) and more frequently in patients with HF-REF than in those with HF-PEF (51.6% vs 35.6%; $P < 0.0001$).

Conclusions: AF patients with HF, particularly HF-REF, experience heavy symptom and hospitalization burdens, and have relatively low rates of AF control. Further studies are needed to identify ways to improve the management and treatment outcomes of this very high-risk patient population.

The RealiseAF survey was sponsored by Sanofi, which provided assistance with data collection. The study was designed, conducted, and analyzed by an academic international steering committee, with nonvoting participation of the sponsor representatives. The sponsor had no role in submitting the article for publication. PAREXEL was funded by the sponsor.

J.S.C. has consulted and received speaker fees for Abbott, AstraZeneca Pharmaceuticals, Menarini, Merck, Merck Sharp & Dohme, Novartis, Pfizer, and Sanofi. O.J.Z. has received research grants from Sanofi. P.P. has consulted for or received speaker's fees from Abbott, Abbott Vascular, Amgen, Bayer HealthCare, Boehringer Ingelheim, MSD, Merck Serono, Novartis, Pfizer, Sanofi, Servier, and Vifor Pharma. L.N.-B. is an employee of Sanofi S.B. is an employee of Lincoln, which is under contract with Sanofi to oversee and review statistical analyses. P.G.S. has consulted for Astellas, AstraZeneca Pharmaceuticals, Bayer HealthCare, LLC, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi, Gilead Sciences, Medtronic, Merck, Otsuka Research Institute, Pfizer, Roche Diagnostics, Sanofi, and Servier.

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

Additional Supporting Information may be found in the online version of this article.

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22209

Received: March 20, 2013
Accepted with revision: August 21, 2013

Introduction

The prevalence of atrial fibrillation (AF) and heart failure (HF) are increasing steadily due to an aging population and improved management of cardiovascular (CV) disease.[1,2] These conditions coexist in >1% of the general population.[3] AF can cause or worsen pre-existing HF, and the prevalence of AF in patients with HF is high, ranging from ~15% in patients with New York Heart Association (NYHA) class II or III to approximately half of patients with NYHA class IV.[4] This dual epidemic has major consequences for public health and expenditure because of the symptom burden and frequent hospital admissions.[1,4] Overall, patients with AF are at increased risk of mortality and morbidity from stroke and thromboembolism.[5]

The association of HF with AF control, symptoms, and hospital admissions is unclear. Using data from the RealiseAF[6] survey, we examined the association of the presence/absence of HF and of HF type (with or without reduced left ventricular ejection fraction [LVEF]) with AF management and control, symptoms, and hospitalizations.

Methods

Design, Patients, and Data Collection

RealiseAF was an international, cross-sectional, observational survey of >10 000 patients with all types of AF, involving >800 sites. It was designed to provide reliable contemporary information on patient characteristics, CV risk, AF types, symptoms, medical history, impact on quality of life (QoL), and AF management worldwide. The survey has been described in detail previously.[6] Briefly, RealiseAF includes data from men and women with documented current AF or a history of ≥1 AF episode documented in the previous 12 months by standard electrocardiogram (ECG) or by ECG Holter monitoring.

Definitions

HF was defined as a history of HF at any time based on physician judgment; the physician recorded when HF was first diagnosed (before/after AF/unable to state), NYHA class, and etiology (ischemic, valvular, or hypertensive). AF control was defined as being either in sinus rhythm (SR) or in AF with a heart rate (HR) ≤ 80 beats per minute (bpm)[7] at the time of the visit on resting ECG. HF with reduced ejection fraction (HF-REF) was defined as HF and LVEF ≤ 50%, and HF with preserved ejection fraction (HF-PEF) was defined as HF and LVEF > 50%.[8] LVEF was assessed within 12 months (unless the patient had a myocardial infarction), depending on what techniques were available to the physician at the time, by ECG, multiple-gated acquisition scan, cardiac catheterization, magnetic resonance imaging, or a computed tomographic scan. HF symptoms were classified according to the NYHA.[9]

The reasons for hospitalization relating to a CV event in the prior 12 months were collected without additional information, and based purely on physician judgment.

Goals

The primary aims of RealiseAF were to determine the frequency of AF control and describe the CV risk profile for AF patients.[6] The present post hoc analysis assessed the association between a history of HF and AF control, symptoms, management, and hospitalizations in the year before the visit.

Statistical Analysis

Population characteristics were summarized into mean, standard deviation for continuous variables, and count and percentages for qualitative variables, unless otherwise indicated. Percentages reported were based only on those patients with data available for each given variable. Descriptive analyses were conducted according to history of HF and within HF patients according to LVEF. Comparisons between subgroups were made using χ^2 tests, trend tests (for ordinal variables), or Student t test. Analyses were performed using SAS statistical software, version 9.2 (SAS Institute, Cary, NC).

Results

Study Population

From October 2009 to May 2010, 831 sites included 10 523 patients (Supplementary Figure 1) from 26 participating countries. Mean patient age was 66.6 ± 12.2 years, and 56.4% were male. AF was paroxysmal in 2606 (24.8%), persistent in 2341 (22.3%), and permanent in 4869 (46.4%) patients. In the remaining 675 patients (6.4%), AF was classified as first episode.

Prevalence and Clinical Characteristics of HF

Information regarding HF was missing in 57 (0.5%) patients. A history of HF was present in 45.8% of the remaining 10 466, of whom the majority were classified as having NYHA class I/II HF. AF patients with a history of HF were slightly older, had AF for longer, and were more frequently female than AF patients with no HF history. In addition, AF patients with a history of HF were more likely to have a high symptom burden (European Heart Rhythm Association [EHRA] class II–IV), known CV risk factors, comorbidities, or a $CHADS_2$ score of ≥2 than those with no history of HF (Table 1). AF patients with HF had a higher HR than patients without HF, but blood pressure was similar between the groups. Permanent AF was more frequently present in patients with HF (56.4%) than in patients without HF (38.0%; Table 1).

HF With Preserved LVEF

Among patients with HF, information about LVEF within the past 12 months was available in 3766 (78.6%); 1905 (50.6%) were diagnosed as having HF-PEF (ie, LVEF > 50%). Patients with AF and HF-PEF were similar in age and body mass index compared to those with AF and HF-REF (Table 1). However, HF-PEF patients had longer time since AF diagnosis, were more frequently female, and were less likely to have CV risk factors or a high symptom burden (EHRA class II–IV). HF-PEF was associated with a lower prevalence of coronary artery disease, but a similar prevalence of cerebrovascular disease, and a higher prevalence of valvular heart disease than HF-REF. In addition, HF-PEF patients were more likely to have paroxysmal AF than those

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DOI:10.1002/clc.22209

Table 1. Clinical Characteristics of Patients With AF According to Presence or Absence of HF and of LVEF[a]

Characteristic	All HF, n = 4790	No HF, n = 5676	*P*, HF vs No HF	HF-REF, n = 1861[b]	HF-PEF, n = 1905[b]	*P*, HF-REF vs HF-PEF
Age, y, mean (SD)	67.6 (11.7)	65.7 (12.5)	<0.0001	66.9 (11.4)	67.0 (11.9)	0.72
Males, %	54.7	57.9	0.0009	65.4	46.2	<0.0001
BMI, kg/m², mean (SD)	28.6 (5.4)	28.1 (5.0)	<0.0001	28.7 (5.4)	28.6 (5.4)	0.72
HR, bpm, mean (SD)	84.4 (22.7)	81.3 (23.4)	<0.0001	87.4 (24.3)	81.4 (21.1)	<0.0001
SBP, mmHg, mean (SD)	132.6 (20.2)	133.1 (18.8)	0.17	132.5 (21.6)	132.8 (19.0)	0.66
DBP, mmHg, mean (SD)	79.9 (11.9)	79.8 (10.9)	0.61	80.6 (12.6)	79.7 (11.3)	0.02
CV risk factors, %						
Physical inactivity	64.6	58.1	<0.0001	67.1	60.0	<0.0001
Hypertension	76.8	68.3	<0.0001	76.7	76.8	0.93
Diabetes mellitus	24.3	18.8	<0.0001	27.0	20.6	<0.0001
Dyslipidemia	53.1	40.7	<0.0001	56.5	50.1	0.0001
Comorbidities, %						
CAD	48.4	19.2	<0.0001	56.1	39.8	<0.0001
CVD	18.6	10.3	<0.0001	18.0	17.1	0.50
Valvular heart disease	37.4	17.7	<0.0001	37.9	42.0	0.01
CPD	15.4	7.2	<0.0001	15.0	14.6	0.69
Chronic advanced renal failure[c]	6.0	2.1	<0.0001	8.4	4.2	<0.0001
Liver disease	6.2	3.0	<0.0001	7.2	5.4	0.02
Malignancies	4.7	4.4	0.56	4.5	4.0	0.51
$CHADS_2$ score ≥ 2, %	85.6	38.2	<0.0001	85.9	84.2	0.15
Time since AF diagnosis, mo, mean (SD)	61.0 (75.8)	46.5 (65.2)	<0.0001	56.3 (73.2)	61.5 (76.2)	0.03
Type of AF, %			<0.0001			<0.0001
Paroxysmal	17.9	30.8		14.7	22.0	
Persistent	21.5	22.9		24.9	21.9	
Permanent	56.4	38.0		56.4	52.8	
First episode	4.2	8.3		4.0	3.3	
EHRA classes, %			<0.0001			<0.0001
I	11.2	38.8		9.2	13.5	
II	53.0	50.8		46.4	57.4	
III	32.4	9.7		39.5	27.0	
IV	3.4	0.7		4.9	2.0	
EHRA class II, III, and IV, %	88.8	61.2	<0.0001	90.8	86.5	<0.0001
HF characteristics						
Current NYHA class, %			NA			<0.0001

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DOI:10.1002/clc.22209

Table 1. Continued

Characteristic	All HF, n = 4790	No HF, n = 5676	P, HF vs No HF	HF-REF, n = 1861[b]	HF-PEF, n = 1905[b]	P, HF-REFvs HF-PEF
I	12.1	—		15.3	8.3	
II	55.0	—		60.0	47.6	
III	29.3	—		22.2	38.5	
IV	3.7	—		2.4	5.6	
LVEF, mean (SD)	50.2 (12.9)[d]	59.5 (9.0)[e]	<0.0001	39.7 (8.7)[f]	60.5 (6.3)[g]	<0.0001

Abbreviations: AF, atrial fibrillation; BMI, body mass index; bpm, beats per minute; CAD, coronary artery disease; CPD, chronic pulmonary disease; CV, cardiovascular; CVD, CV disease; DBP, diastolic blood pressure; EHRA, European Heart Rhythm Association; HF, heart failure; HF-PEF, HF with preserved ejection fraction; HF-REF, HF with reduced ejection fraction; HR, heart rate; LVEF, left ventricular ejection fraction; NA, not applicable; NYHA, New York Heart Association; SBP, systolic blood pressure; SD, standard deviation.
[a]Data are not complete for all patients: the reported percentage is for the number of patients with data available for each given variable. [b]Records with missing values were excluded from statistical analysis. [c]Creatinine clearance <30 mL/min, as reported by the physician. [d]n = 3766. [e]n = 3988. [f]n = 1861. [g]n = 1905.

with HF-REF (Table 1). HF-PEF patients were less symptomatic (based on the NYHA class) than those with HF-REF.

Etiology of HF and NYHA Functional Class According to Type of AF

Patients with permanent AF had a history of more severe HF symptoms than other forms of AF, as reflected by a higher prevalence of patients in NYHA classes III or IV (Table 2). Additional results relating to etiology are shown in Table 2.

AF Control and Treatment

On the day of the visit, AF was controlled in ~60% of patients, with better control rates seen in patients with no HF vs HF, and in patients with HF-PEF vs those with HF-REF (Table 3). In HF patients, control of AF was mainly due to being in AF with an HR ≤ 80 bpm, whereas in patients without HF, AF control was almost equally divided between being in SR or in AF with a HR ≤ 80 bpm.

Prior to the visit, antiarrhythmic drugs (AADs), including amiodarone and digoxin, antithrombotic agents (Table 3), and other medications such as aldosterone antagonists, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, and diuretics, were prescribed more frequently to patients with HF than without (all $P < 0.0001$); however, angiotensin II receptor blockers (ARBs) were prescribed more frequently to patients without HF than with HF ($P = 0.04$).

Prior to the visit in patients with HF-REF and HF-PEF, the prescription frequency of antithrombotic agents, AADs (Table 3), and ARBs was similar. Digoxin, amiodarone (Table 3), ACE inhibitors, β-blockers, and diuretics were prescribed less frequently to patients with HF-PEF than with HF-REF (all $P < 0.0001$). Of the antithrombotic agents prescribed, the prescription frequency of oral and injectable anticoagulants was similar; however, antiplatelets were prescribed less frequently to patients with HF-PEF than with HF-REF ($P = 0.014$; Table 3).

Table 2. Etiology of HF and NYHA Functional Class According to the Type of AF (%)[a]

HF/NYHA Class	First Episode of AF, n = 675	Paroxysmal AF, n = 2606	Persistent AF, n = 2341	Permanent AF, n = 4869	P
HF	29.8	32.9	44.3	55.6	<0.0001
Main cause of HF					<0.0001
Ischemic	38.2	48.5	44.0	40.0	
Valvular	31.2	12.7	18.2	31.9	
Hypertensive	30.6	38.9	37.8	28.0	
HF NYHA classes					<0.0001
I	11.8	16.2	13.4	10.2	
II	49.7	61.4	55.3	53.3	
III or IV	38.5	22.4	31.3	36.5	

Abbreviations: AF, atrial fibrillation; HF, heart failure; NYHA, New York Heart Association.
[a]Data are not complete for all patients; the reported percentage is for the number of patients with data available for each given variable.

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DOI:10.1002/clc.22209

Table 3. Control of AF (in Sinus Rhythm or in AF with HR ≤ 80 bpm) and Management Strategy (Medication), According to Presence or Absence of HF and of LVEF (%)[a]

Characteristic	All HF, n = 4790	No HF, n = 5676	*P*, HF vsNo HF	HF-REF, n = 1861	HF-PEF, n = 1905	*P*, HF-REF vs HF-PEF
Control of AF	54.6	62.8	<0.0001	49.3	60.3	<0.0001
In sinus rhythm	19.8	32.3		16.1	26.1	
In AF with HR ≤ 80 bpm	34.8	30.6		33.1	34.2	
Prior to the visit						
Therapeutic strategy			<0.0001			<0.0001
Rhythm control	28.0	40.2		25.4	33.2	
Rate control	63.3	45.8		65.9	58.7	
None	8.6	14.0		8.5	8.1	
Both	<0.1	<0.1		0.2	0.0	
Medication						
At least 1 AAD[b]	91.8	84.1	<0.0001	93.1	91.8	0.15
Class Ia	0.5	0.4	0.66	0.3	0.8	0.06
Class Ic	3.7	9.2	<0.0001	2.5	5.5	<0.0001
Class II	61.4	52.9	<0.0001	67.6	59.4	<0.0001
Class II for AF reason	44.4	41.3	<0.01	45.7	45.8	0.95
Class III	24.9	23.2	0.04	27.6	24.2	0.02
Amiodarone	22.8	19.4	<0.0001	26.6	20.9	<0.0001
Class IV	15.4	17.2	0.01	13.3	16.8	<0.01
Class IV for AF reason	6.2	7.7	<0.01	4.7	7.0	<0.01
Digoxin	40.9	20.1	<0.0001	45.1	36.1	<0.0001
Antithrombotic agents	91.5	82.8	<0.0001	92.2	91.5	0.50
Antiplatelet agents	42.7	36.2	<0.0001	43.8	39.9	0.014
Oral anticoagulants	56.2	52.2	<0.0001	58.7	56.7	0.22
Injectable anticoagulants	7.5	4.5	<0.0001	8.1	7.5	0.53
At the end of the visit						
Therapeutic strategy			<0.0001			<0.0001
Rhythm control	29.2	44.1		26.8	33.9	
Rate control	67.2	49.5		70.0	62.2	
None	3.5	6.3		2.9	3.8	
Both	0.2	0.2		0.3	0.1	
Medication						
At least 1 AAD[b]	85.0	77.5	<0.0001	85.4	85.3	0.91
Class Ia	0.4	0.4	0.10	<0.1	0.8	<0.01
Class Ic	3.1	9.4	<0.0001	2.0	4.5	<0.0001
Class II	56.3	45.2	<0.0001	61.7	54.8	<0.0001
Class II for AF reason	42.3	37.4	<0.0001	43.8	43.3	0.75

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DOI:10.1002/clc.22209

Table 3. Continued

Characteristic	All HF, n = 4790	No HF, n = 5676	P, HF vsNo HF	HF-REF, n = 1861	HF-PEF, n = 1905	P, HF-REF vs HF-PEF
Class III	26.4	25.4	0.23	29.8	25.1	<0.01
Amiodarone	24.1	20.7	<0.0001	29.0	21.7	<0.0001
Class IV	13.0	14.6	0.02	10.8	14.3	<0.01
Class IV for AF reason	5.4	6.9	<0.01	4.0	5.9	<0.01
Digoxin	38.0	18.4	<0.0001	41.5	33.3	<0.0001
Antithrombotic agents	86.0	75.9	<0.0001	86.3	86.6	0.78
Antiplatelet agents	37.1	32.0	<0.0001	36.6	34.2	0.12
Oral anticoagulants	54.0	47.0	<0.0001	57.0	55.5	0.36
Injectable anticoagulants	10.2	8.9	0.03	12.4	8.3	<0.0001

Abbreviations: AAD, antiarrhythmic drug; AF, atrial fibrillation; bpm, beats per minute; HF, heart failure; HF-PEF, HF with preserved ejection fraction; HF-REF, HF with reduced ejection fraction; HR, heart rate; LVEF, left ventricular ejection fraction.
[a]Data are not complete for all patients; the reported percentage is for the number of patients with data available for each given variable. [b]Class Ia, Ic, II, III, and IV; includes digoxin.

At the end of the visit, fewer patients were on medication than prior to the visit in all categories; however, as described above the prescription pattern remained the same between HF and no HF, and between HF-REF and HF-PEF. The only exception was in the prescription of injectable anticoagulants, which increased at the end of the visit, and were prescribed less frequently to patients with HF-PEF than with HF-REF ($P < 0.0001$). In addition, at the end of the visit, prescription of antiplatelets was similar between HF-REF and HF-PEF (Table 3).

Rhythm-Control vs Rate-Control Strategies

Overall, rate control was preferred over rhythm control. Rhythm control was used more frequently in patients without HF or HF-PEF than with HF or HF-REF, both prior to and at the end of the visit (Table 3).

As the presence and severity of HF increased, rhythm control was less frequently used, ranging from 43.5% in patients with no HF or with NYHA class I HF, to 31.1% in patients with NYHA class II HF, and to 22.8% in patients with NYHA classes III or IV HF ($P < 0.001$; Figure 1).

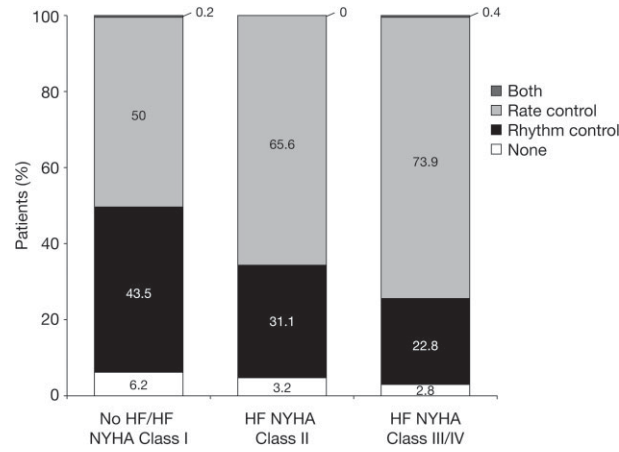

Figure 1. Choice of rhythm-control or rate-control strategy at the end of the visit according to existence of heart failure (HF) and New York Heart Association (NYHA) functional class.

Burden of AF and CV Interventions

Overall, 28.7% of all patients underwent ≥1 hospital admission relating to a CV event in the prior 12 months. The rate of CV hospitalizations was higher in patients with HF than in those without (41.8% vs 17.5%; $P < 0.001$), across all types of AF (paroxysmal AF: 42.5% vs 20.1%; persistent AF: 46.5% vs 16.9%; permanent AF: 39.6% vs 16.2%). Hospitalization rates were the same, regardless of whether AF preceded or followed the occurrence of HF (both 41.4%). Among patients with HF, hospital admissions in the prior 12 months were more frequent in patients with HF-REF than with HF-PEF (51.6% vs 35.6%; $P < 0.001$). AF patients with ischemic HF had more frequent CV hospitalizations than those with valvular or hypertensive HF (48.4% vs 40.8% vs 34.1%, respectively; $P < 0.001$). Reasons for hospitalization in patients according to presence or absence of HF and LVEF are described in Figure 2A. Acute decompensated HF was the main reason for hospitalization in patients with HF (around a quarter of all patients). Specifically, over one-third of patients with HF-REF and around one-fifth of patients with HF-PEF were hospitalized for this reason. Arrhythmic or proarrhythmic events were the main reasons for hospitalization in patients with no HF (6.4% of patients). In addition, 9.6% of patients with HF were hospitalized due to an arrhythmic or proarrhythmic event. In patients with HF-REF and patients with HF-PEF, supraventricular tachycardia and clinically significant bradycardia/atrioventricular block were the most frequently recorded events (ranging from 3.2% to 4.5% of patients; Figure 2B).

A history of CV interventions in the past 12 months was more frequent in patients with HF compared with no HF (14.7% vs 10.4%; $P < 0.0001$) and more frequent

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DOI:10.1002/clc.22209

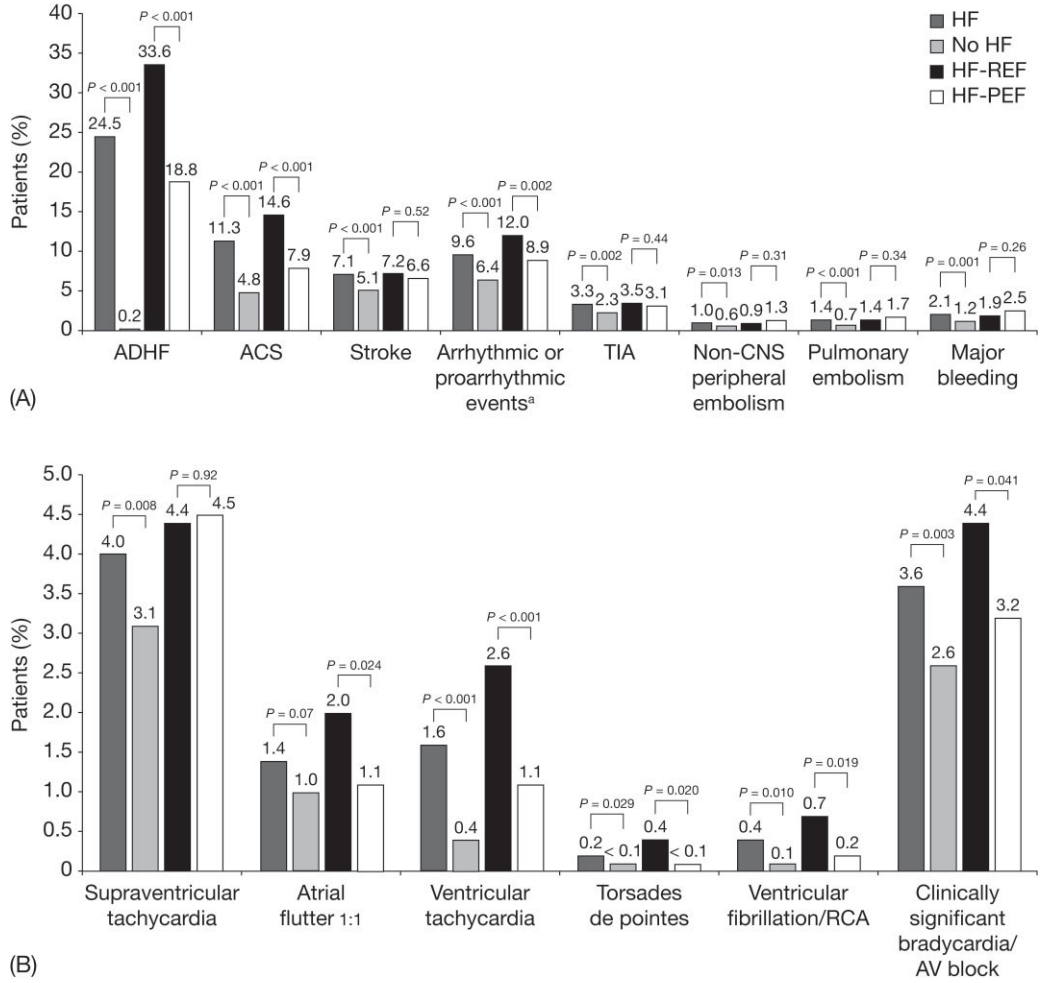

Figure 2. (A) Cardiovascular events leading to hospitalizations in the past 12 months according to presence or absence of heart failure (HF), HF-REF, and HF-PEF. (B) Arrhythmic or proarrhythmic events leading to hospitalizations in the past 12 months according to presence or absence of HF, HF-REF, and HF-PEF. [a] Supraventricular tachycardia, atrial flutter 1 to 1, ventricular tachycardia, torsades de pointes, ventricular fibrillation/RCA, clinically significant bradycardia/AV block. Abbreviations: ACS, acute coronary syndrome; ADHF, acute decompensated heart failure; AV, atrioventricular; CNS, central nervous system; HF, heart failure; HF-PEF, HF with preserved ejection fraction; HF-REF, HF with reduced ejection fraction; RCA, resuscitated cardiac arrest; TIA, transient ischemic attack.

in HF-REF than in HF-PEF (18.9% vs 12.8%; $P < 0.0001$). Intervention types according to HF and LVEF are shown in Supplementary Figure 2.

Discussion

The present post hoc analysis of the RealiseAF survey examined the association of HF with AF control, symptoms, and CV hospitalizations. The main finding was that a history of HF is extremely common in patients with AF, and was most frequently reported in patients with permanent AF. AF accompanied by HF is associated with more comorbidities and a higher CV risk profile than AF without HF; the latter is more pronounced in patients with HF-REF than HF-PEF. Patients with AF and concomitant HF vs patients without HF and patients with HF-REF vs patients with HF-PEF had more severe symptoms, less frequently controlled AF, and more CV events leading to hospitalizations. The latter was true across all types of AF and regardless of whether AF preceded HF or the reverse. Acute decompensated HF, acute coronary syndrome, arrhythmic or proarrhythmic events, and transient ischemic attack were the leading causes of hospitalization.

In the Framingham Heart Study, left ventricular systolic dysfunction increased the risk of de novo appearance of AF in men and women by 4.5 and 5.9 times, respectively.[10] Similarly, in the Euro Heart Survey on AF, new HF appeared during 1 year of follow-up in 5.0% of patients with AF, whereas deterioration of HF was registered in 24.7% patients.[11] Our results are in accordance with recent studies, which indicate that, in AF patients, the coexistence of HF identifies a population at particularly high risk of CV complications, particularly HF hospitalizations.[12–14]

There are several possible reasons for this increased risk; HF can aggravate AF because it is associated with neurohormonal activation, ventricular and atrial interstitial

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DOI:10.1002/clc.22209

fibrosis, dysregulation of myocardial intracellular calcium, and increased atrial filling pressures leading to increased atrial size.[1] Conversely, AF can impair myocardial function due to the reduction of cardiac output consecutive to irregular and/or rapid HR, loss of atrial contraction, and increased mitral or tricuspid regurgitation.[1]

Additionally, HF is known to be closely associated with the potentially fatal effects of AADs used in AF.[15,16] AADs were more frequently prescribed to our patients with AF and HF than to those with AF and no HF.

In our study, patients in whom HF coexisted with AF were older and had more frequent CV risk factors and comorbidities than those with AF and no history of HF. These patients, and in particular those with HF-REF, also had a higher HR, more frequent permanent AF, a higher symptom burden, and less frequently controlled AF than patients without HF or HF-PEF. Our findings are clinically relevant because all these factors identify patients with AF and HF as a sicker population at exceedingly high CV risk.

In this survey of AF patients, the concomitance of HF increased thromboembolic risk, evidenced by the higher percentage of patients having a $CHADS_2$ score ≥ 2 compared to those with AF and no HF. However, in these high-risk patients, oral anticoagulation both prior to and at the end of the visit was relatively low, at around 55%. The underuse of oral anticoagulants in high-risk AF patients (where undertreatment is defined as treatment of <70% of high-risk patients) has been documented previously in a 2010 systematic review.[17] Underuse of oral anticoagulation in patients at high risk of thromboembolic events could account for the increase in hospital admissions due to stroke, TIAs, and pulmonary embolism observed in our population. This is pertinent because, in some older patients with AF and HF, nontreatment with the anticoagulant warfarin has been associated with a higher mortality rate than if warfarin was prescribed.[18]

AF and HF share a high prevalence, an increased morbidity and mortality, and a high economic impact.[8,15] In both conditions, the main outcomes include death and hospitalizations. The prevention of these outcomes and the improvement of symptoms constitute major therapeutic goals, although the fulfillment of many of them remains elusive in the case of AF. Hospital admissions are particularly important, not only because they are the main drivers of cost but also because they are important markers for adverse outcomes.

The optimal management strategy for AF in patients with HF remains unclear due to possible causative links between AF and HF.[19] Rhythm control is recommended in symptomatic AF patients in the current guidelines,[15,20] largely based on the possible QoL benefits rather than changes in hard endpoints. Rate-control strategy is typically used for patients with HF and worsening of its functional class. The large prospective clinical trial Atrial Fibrillation and Congestive Heart Failure directly compared rate-control and rhythm-control strategies, and found no difference in CV mortality (the primary outcome) in patients with an LVEF $\leq$ 35%, symptoms of congestive HF, and a history of AF, or in secondary outcomes, including all-cause mortality and worsening of HF.[21] Other large clinical trials comparing rate and rhythm control for AF management strategies have not shown superiority of either approach in terms of major clinical outcomes[7,21–23] and have failed to confirm the apparent benefits of long-term maintenance of SR as seen in retrospective analyses.[24] This notwithstanding, retrospective data from large clinical trials suggest that long-term maintenance of SR is associated with improved long-term outcomes in patients with HF and paroxysmal or persistent AF.[25] However, recent data show that in AF patients with signs of HF, 2 distinct clinical conditions can be recognized based on the chronologic sequence of AF and HF development. This should be considered before making a decision regarding SR restoration and maintenance.[26]

There are important limitations to keep in mind when interpreting our observations. Due to the cross-sectional nature of this study, it is not possible to extract data to support or contradict the idea of restoration and maintenance of SR in patients with AF.

Nevertheless, these data call to our attention the high risk inherent in patients with AF and a history of HF. Due to the contraindications of many AADs, existing antiarrhythmic strategies are of limited value to these patients; as such, there is a need to develop targeted strategies for the monitoring and treatment of these patients to avoid symptomatic deterioration and reduce hospitalization burden.

The prevalence of severe class IV HF was low at 3.7%, presumably reflecting a low prevalence in real life among outpatients. As in all observational studies, associations between clinical characteristics and events or symptoms may be confounded. In addition, events were not adjudicated, and collection of biological variables and performance of functional tests was left to the physician's discretion; thus, the evaluation of HF and determination of LVEF were based on physician judgment and available techniques, respectively. In addition, the cross-sectional nature of this survey prevents analysis of a direct link with outcomes and is prone to reverse causality. Conversely, the contemporary nature, the geographic scope, and the large size constitute strengths of the current data set.

In conclusion, in this large, international, observational survey, HF was highly prevalent among patients with AF. Furthermore, HF appeared strongly associated with more symptoms, less frequently controlled AF, and increased CV-related hospitalizations. Further studies will be needed to identify the optimal management strategy for this very high-risk patient population.

Acknowledgments

The authors thank Leigh Prevost, BSc (PPSI, a PAREXEL company) for editing the manuscript.

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DOI:10.1002/clc.22209

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Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22209