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Original Article

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Characteristics and Outcomes of Atrial Fibrillation in Chronic Heart Failure Patients: A Comprehensive Analysis of the Colombian Heart Failure Registry

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Abstract

Background: Heart failure (HF) and atrial fibrillation (AF) represent conditions that commonly coexist. The impact of AF in HF has yet to be well studied in Latin America. This study aimed to characterize the sociodemographic and clinical features, along with patients' outcomes with AF and HF from the Colombian Heart Failure Registry (RECOLFACA).

Methods: Patients with ambulatory HF and AF were included in RECOLFACA, mainly with persistent or permanent AF. A 6-month follow-up was performed. Primary outcome was all-cause mortality. To assess the impact of AF on mortality, we used a logistic regression model. A P value of < 0.05 was considered significant. All statistical tests were two-tailed.

Results: Of 2,528 patients with HF in the registry, 2,514 records included information regarding AF diagnosis. Five hundred sixty (22.3%) were in AF (mean age 73 ± 11, 56% men), while 1,954 had no AF (mean age 66 ± 14 years, 58% men). Patients with AF were significantly older and had a different profile of comorbidities and implanted devices compared to non-AF patients. Moreover, AF diagnosis was associated with lower quality of life score (EuroQol-5D), mainly in mobility, personal care, and daily activity. AF was prevalent in patients with preserved ejection fraction (EF), while no significant differences in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels were observed. Although higher mortality was observed in the AF group compared to individuals without AF (8.9% vs. 6.1%, respectively; P = 0.016), this association lost statistical significance after adjusting by age in a multivariate regression model (odds ratio (OR): 1.35; 95% confidence interval (CI): 0.95 - 1.92).

Conclusions: AF is more prevalent in HF patients with higher EF, lower quality of life and different clinical profiles. Similar HF severity and non-independent association with mortality were observed in our cohort. These results emphasize the need for an improved understanding of the AF and HF coexistence phenomenon.

Keywords: Heart Failure; Atrial fibrillation; Ejection fraction; Mortality; Registry; Comorbidity; Colombia; Treatment

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Introduction

Heart failure (HF) and atrial fibrillation (AF) represent prevalent conditions that commonly coexist, mainly derived from the mutual pathophysiological pathways on both diseases [1]. On one side, HF represents one of the most chronic non-trans-

missible diseases, with an estimated prevalence of around 100 cases per 1,000 population in individuals over 65 years, with about 5.7 million Americans over 20 years of HF diagnosis [2]. On the other side, AF is the most frequently observed type of arrhythmia in general clinical practice [3]. AF prevalence in the United States has been estimated at around 2.6 to even 6.1 million, suggesting an increase of 2.5 times by 2050 [2, 4]. Added to their high prevalence, both AF and HF carry a significant burden of healthcare costs and morbimortality worldwide [5-7].

The close interrelationship between AF and HF was initially suggested by the results of the Framingham study, which reported a higher incidence of HF in AF patients (33 per 1,000 person-years) compared to those without AF and a high incidence of AF in patients with HF [8]. Furthermore, the coexistence of these two conditions was associated with increased mortality, especially in AF patients who subsequently developed HF [8]. After this, several studies have aimed to understand the prognostic significance of AF in patients with HF; nevertheless, there is still controversy regarding the role of AF as a risk factor for adverse outcomes in the context of HF [9]. The present study aimed to characterize the sociodemographic and clinical features, and outcomes of patients with AF and HF from the Colombian Heart Failure Registry (RECOLFACA).

Materials and Methods

Study design and population

RECOLFACA is a prospective cohort study that enrolled patients with a clinical diagnosis of HF based on international guidelines, from 60 medical institutions in Colombia. Recruitment period comprehended between February 2017 and October 2019. A 6-month follow-up after recruitment was performed. Details on inclusion and exclusion criteria are described elsewhere [10, 11]. Our study was approved by the Ethics Committee of the Fundacion Valle del Lili under act number 174-2017. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Data collection and outcomes

We registered all sociodemographic, clinical, and laboratory data at baseline. The diagnosis of AF was based on a 12-lead electrocardiogram (ECG) or previous documentation of this condition in the clinical record, which could have led to the possibility of missing patients with paroxysmal AF. HF severity was evaluated using the American Heart Association (AHA)/American College of Cardiology (ACC) stages stratification and the New York Heart Association (NYHA) classification. Description of all comorbidities assessed can be found in a previous report [10]. We considered triple therapy for HF treatment as the presence of the prescription of an angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor neprilysin inhibitor (ARNI), plus a mineralocorticoid receptor antagonist (MRA) and a beta-blocker. In this study we present the data from the first follow-up performed 6 months post-enrollment into RECOLFACA (median follow-up time was 215 days).

Statistical analysis

At first, the total sample was divided into two groups (AF vs. non-AF patients). Continuous variables were reported as medians and quartiles, while categorical variables as proportions and absolute counts. Pearson's Chi-squared, Fisher's exact test or Mann-Whitney U test were used to find differences between groups according to the type of variable analyzed. The cumulative incidence of the mortality events was assessed with 95% confidence intervals (CIs). A multivariable logistic regression model was fitted to evaluate the prognostic role of AF diagnosis. A P value of < 0.05 (two-tailed test) was considered statistically significant. Statistical Package STATA version 15 (Station College, Texas, USA) was used for all statistical analyses.

Results

Of 2,528 patients in the RECOLFACA between 2017 and 2019, 2,514 records included information regarding AF diagnosis. The prevalence of AF among these patients was 22.3% (n = 560). Moreover, from a total of 66 patients (2.6% of the total) with a diagnosis of tachycardia-induced cardiomyopathy as HF etiology, 53 (80.3%) had AF.

Sociodemographic factors and comorbidities

No significant differences regarding sex and population were observed. Patients with AF were significantly older and had substantially higher rates of arterial hypertension, chronic obstructive pulmonary disease, thyroid disease, chronic kidney disease, and valvular disease. On the other hand, patients without AF were most frequently diagnosed with type 2 diabetes mellitus (Table 1).

Clinical, laboratory, and echocardiographic differences

There were no significant differences regarding NYHA and AHA/ACC classifications between both groups, and they also had similar heart rates and QRS duration. On the other hand, AF diagnosis was associated with a significantly lower quality of life (QoL) score (Euro Qol-5D), mainly in the areas of mobility, personal care, and daily activity. This difference in the QoL score was still present even after accounting for differences in age, sex, and chronic kidney disease (variables also associated with QoL). Although the rates of an implantable cardioverter defibrillator (ICD) were similar between the two groups, patients with AF had a higher rate of ICD with cardiac resynchronization therapy (CRT) and a higher rate of implanted pacemakers (Table 1).

Table 1. Sociodemographic and Clinical Characteristics Based on Atrial Fibrillation Diagnosis

	No AF (n = 1,954) n (%)	AF (n = 560), n (%)	Total (n = 2,514), n (%)	P value
Demographics				
Age (years), mean ± SD	66.00 ± 14.00	73.00 ± 11.00	67.00 ± 14.00	< 0.001*
Sex				0.272
Female	818 (41.9)	249 (44.5)	1,067 (42.4)	
Male	1,136 (58.1)	311 (55.5)	1,447 (57.6)	
Population				0.824
Asian	1 (0.1)	0 (0.0)	1 (0.0)	
European	86 (4.4)	30 (5.4)	116 (4.6)	
Native American	9 (0.5)	1 (0.2)	10 (0.4)	
Hispanic	1,444 (73.9)	409 (73.0)	1,853 (73.7)	
Mestizo	354 (18.1)	104 (18.6)	458 (18.2)	
African-American	60 (3.1)	16 (2.9)	76 (3.0)	
Insurance information				
Contributive	1,115 (57.1)	355 (63.4)	1,470 (58.5)	< 0.001*
Subsidized	748 (38.3)	149 (26.6)	897 (35.7)	
Additional insurance policy	91 (4.7)	56 (10.0)	147 (5.8)	
Comorbidities				
Hypertension	1,382 (70.7)	429 (76.6)	1,811 (72.0)	0.006
Type 2 diabetes mellitus	516 (26.4)	104 (18.6)	620 (24.7)	< 0.001*
Cancer	78 (4.0)	23 (4.1)	101 (4.0)	0.902
Coronary artery disease	565 (28.9)	141 (25.2)	706 (28.1)	0.083
COPD	315 (16.1)	126 (22.5)	441 (17.5)	< 0.001*
Thyroid disease	257 (13.2)	131 (23.4)	388 (15.4)	< 0.001*
Chronic kidney disease	307 (15.7)	127 (22.7)	434 (17.3)	< 0.001*
Valvular disease	297 (15.2)	132 (23.6)	429 (17.1)	< 0.001*
Smoking	362 (18.5)	90 (16.1)	452 (17.9)	0.182
CABG	139 (7.1)	31 (5.5)	170 (6.8)	0.190
Dyslipidemia	513 (26.3)	134 (23.9)	647 (25.7)	0.267
Chagas disease	70 (3.6)	18 (3.2)	88 (3.5)	0.676
Heart failure information				
NYHA classification				0.488
I	242 (12.4)	56 (10.0)	298 (11.9)	
II	1042 (53.3)	308 (55.0)	1,350 (53.7)	
III	577 (29.5)	170 (30.4)	747 (29.7)	
IV	93 (4.8)	26 (4.6)	119 (4.7)	
AHA/ACC stage				0.171
C	1,854 (94.9)	523 (93.4)	2,377 (94.6)	
D	100 (5.1)	37 (6.6)	137 (5.4)	
Bicameral PM	60 (3.1)	38 (6.8)	98 (3.9)	< 0.001*
Unicameral PM	28 (1.4)	21 (3.8)	49 (1.9)	< 0.001*
CRT	39 (2.0)	9 (1.6)	48 (1.9)	0.553
ICD	184 (9.4)	59 (10.5)	243 (9.7)	0.429
CRT + ICD	84 (4.3)	43 (7.7)	127 (5.1)	0.001*

Table 1. Sociodemographic and Clinical Characteristics Based on Atrial Fibrillation Diagnosis - *(continued)*

	No AF (n = 1,954) n (%)	AF (n = 560), n (%)	Total (n = 2,514), n (%)	P value
HR (bpm), median (IQR)	72 (65, 80)	70 (64, 83)	72 (65, 81)	0.832
QRS complex				0.190
< 120 ms	635 (61.4)	198 (65.6)	833 (62.4)	
> 120 ms	399 (38.6)	104 (34.4)	503 (37.7)	
LVDD mm	56.595 (12.493)	55.089 (12.626)	56.270 (12.532)	0.032
LVEF %	33.978 (13.432)	35.293 (13.672)	34.261 (13.491)	0.067
Pulmonary hypertension on echocardiogram	649 (45.5)	241 (59.5)	890 (48.6)	< 0.001*
Quality of life score	79.742 (20.383)	75.616 (22.487)	78.823 (20.936)	< 0.001*
Laboratory results				
Hemoglobin, mg/dL	12.966 (2.098)	12.944 (2.041)	12.961 (2.084)	0.980
Creatinine, mg/dL	1.349 (1.050)	1.310 (0.690)	1.340 (0.979)	0.010
GFR	63.729 (35.912)	59.116 (26.455)	62.666 (34.016)	0.031
Hyperkalemia	142 (9.9)	34 (7.7)	176 (9.4)	0.146
Hyponatremia	193 (14.8)	47 (11.6)	240 (14.1)	0.111
Blood urea nitrogen	25.965 (14.052)	27.937 (14.087)	26.413 (14.080)	0.002*
NTproBNP, pg/mL	5,506.983 (8,508.236)	5,925.434 (10,806.911)	5,625.510 (9,205.680)	0.417

*P < 0.05. This table contains absolute counts and percentages (%) for categorical variables and mean and SD for continuous variables. n: refers to the total number of patients that report having/not having each condition. ACC: American College of Cardiology; AHA: American Heart Association; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; GFR: glomerular filtration rate; HR: heart rate; bpm: beats per minute; ICD: implantable cardioverter defibrillator; LVDD: left ventricular diastolic diameter; LVEF: left ventricle ejection fraction; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; NYHA: New York Heart Association; PM: pacemaker; SD: standard deviation; IQR: interquartile range.

Regarding echocardiographic measures, the prevalence of HF with reduced ejection fraction (HFrEF) (< 40%) was significantly lower in AF patients (50.9% vs. 55.8% in non-AF patients, P = 0.040). AF patients reported a considerably lower diastolic diameter of the left ventricle while reporting a higher rate of pulmonary hypertension. Finally, AF patients had substantially lower creatinine values; the glomerular filtration rate was also lower in this group, while the blood urea nitrogen value was considerably higher. No significant differences in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels were observed (Table 1).

HF treatment

Patients with AF had similar prescription rates of ARNI/ACEI/ARB and MRAs compared to non-AF patients. However, they were most frequently prescribed with beta-blockers, diuretics, and digoxin (Fig. 1). Finally, 93% of the total AF patients had at least one rate-control drug prescribed. Unfortunately, we could not assess the prescription of rhythm control medications, as the RECOLFACA registry did not include information regarding this type of drug.

Mortality

During the follow-up we registered the death of 170 patients (6.76%), representing a mortality rate of 0.29 per 1,000 person-years (95% CI: 25.4 - 34.5). The AF group had significantly higher mortality than individuals without AF (8.9% vs. 6.1%, respectively, P = 0.016). However, this association was insignificant after age adjustment in a multivariate logistic regression model (odds ratio (OR): 1.35; 95% CI: 0.95 - 1.92).

AF and left ventricle ejection fraction (LVEF)

Prevalence of AF varies according to the LVEF, with a higher trend in its prevalence with higher values of LVEF. In HFrEF (< 40% LVEF), it is 20.7%; in HF with mildly reduced ejection fraction (HFmrEF) (41-49% LVEF), it is 22.6% and in HF with preserved ejection fraction (HFpEF) (> 50% LVEF), it is 24.8%.

Patients with AF and HFrEF or HFmrEF were significantly younger, had lower rates of thyroid disease, and were most frequently diagnosed with Chagas disease than patients with AF and HFpEF (Table 2). There were no significant differences in HF etiology between both groups except for chagasic (P = 0.014) and valvular (P = 0.027) etiology. There were no significant differences in the prescription rates of ACEI or ARB between the two groups. Interestingly, the beta-blocker prescription was not significantly higher in the HFrEF group. Finally, only MRAs prescription was higher in patients with HFrEF (Table 2). Mortality was similar in patients with AF despite the ejection fraction classification (HFpEF: 8.4% vs.

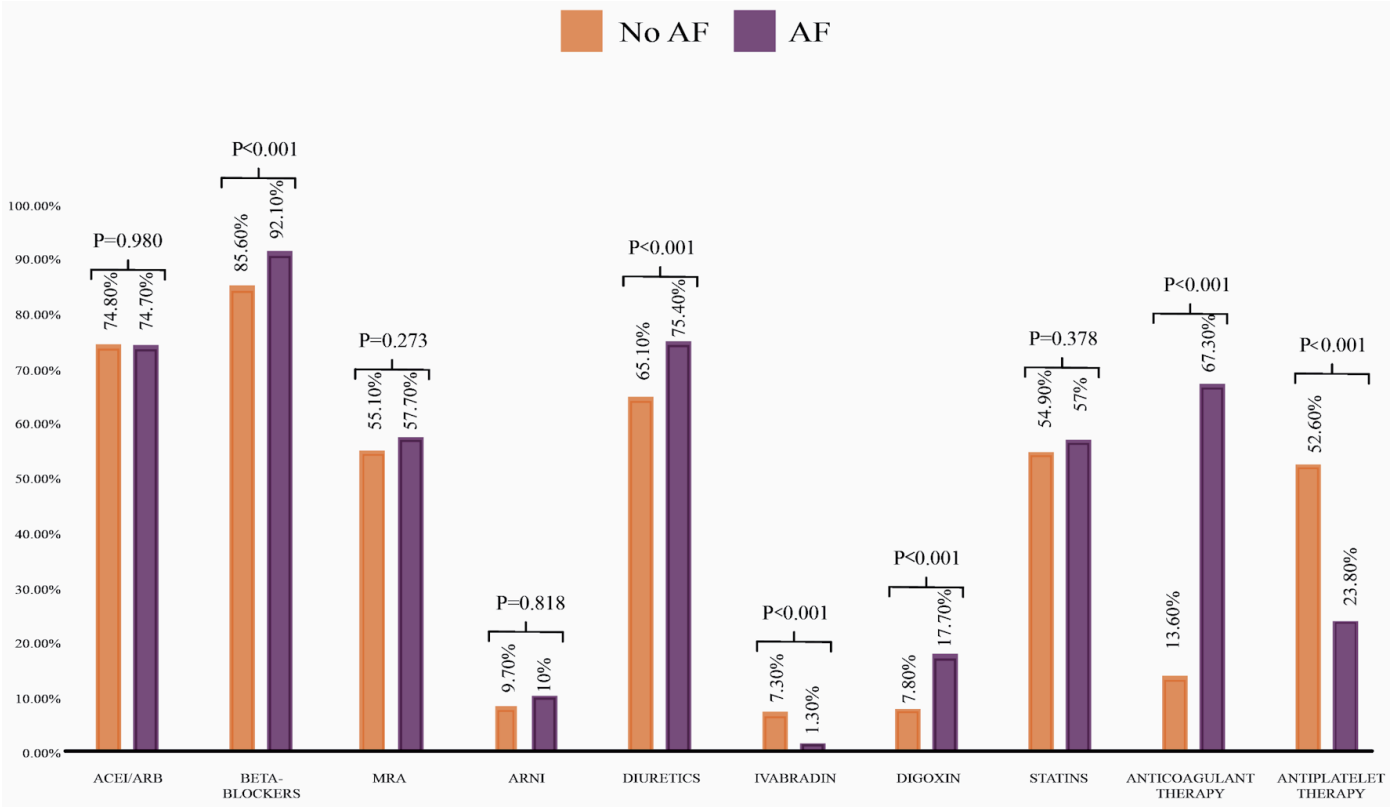

Figure 1. Prescription rates of HF medications based on AF diagnosis. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor; AF: atrial fibrillation; HF: heart failure; MRA: mineralocorticoid receptor antagonist.

HFrEF: 9.5%, P = 0.645). Nevertheless, AF diagnosis was associated with an increased mortality risk in HFrEF patients (OR: 1.71; 95% CI: 1.07 - 2.73), while no significant difference was observed in individuals with HFpEF (OR: 1.29; 95% CI: 0.78 - 2.14).

Discussion

In the present study, we observed a prevalence of AF in patients with HF of 22.3%, highlighting essential sociodemographic, clinical, medication prescriptions, and laboratory differences between patients with and without AF. Moreover, patients with AF had a significantly higher mortality rate than non-AF individuals; however, this difference lost statistical significance when adjusted by age (as patients in the AF group were significantly older).

The complex inter-relationship between HF and AF has been a matter of interest during the last decades. Initial study results revealed the increased risk of complications attributed to the simultaneous presence of these two entities [8]. Since 1937, causal associations have been proposed when addressing the AF-HF interplay [12]. At first, AF can induce the appearance of HF due to an increase in the ventricular rate, a loss of atrial systole, increased irregularity of the ventricular response, poorly controlled ventricular rates, and worsened regurgitation of the mitral and tricuspid valves, finally leading to a reduction of the cardiac output [13, 14]. All of these factors are responsible for the development of HF, better known as tachycardia-induced cardiomyopathy, from which AF represents the most common etiology [9].

Conversely, HF promotes atrial changes that predispose the development of AF, mainly through processes such as the dysregulation of intracellular calcium, neuroendocrine dysfunction, and the elevation of cardiac filling pressures, among others [14]. The resulting increase in atrial stretch due to increased volumes and pressures promotes the activation of ionic currents, which favor alterations in physiological conduction pathways [15]. Finally, increased interstitial fibrosis of the atria has been consistently observed during HF in animal models, thus creating a relevant substrate for AF [16].

The prevalence of AF observed in the present study is similar to that reported in other registry-based studies and randomized clinical trials [13, 17-25]. However, substantial heterogeneity in the prevalence data was observed in the literature, ranging from 6% in the Studies of Left Ventricular Dysfunction (SOLVD) trials to 35% in the Japanese Cardiac Registry of HF [13, 24]. Furthermore, the higher prevalence of AF in patients with HFpEF compared to those with HFrEF observed in our study has also been described in other clinical studies [26-30], potentially being attributed to common risk factors for HFpEF and AF; however, this difference in our study was

Table 2. Sociodemographic and Clinical Characteristics of Patients With HF and Atrial Fibrillation Based on Ejection Fraction

	HFpEF (n = 275), n (%)	HFrEF (n = 285), n (%)	Total (n = 560), n (%)	P value
Demographics				
Age (years), mean ± SD	75.21 ± 10.06	70.95 ± 10.61	73.04 ± 10.55	< 0.001
Sex				
Female	136 (49.5)	113 (39.6)	249 (44.5)	
Males	139 (50.5)	172 (60.4)	311 (55.5)	0.020
Population				0.661
European	15 (5.5)	15 (5.3)	30 (5.4)	
Indigenous	0 (0.0)	1 (0.4)	1 (0.2)	
Hispanic	197 (71.6)	212 (74.4)	409 (73.0)	
Mestiza	53 (19.3)	51 (17.9)	104 (18.6)	
African-American	10 (3.6)	6 (2.1)	16 (2.9)	
Comorbidities				
Hypertension	217 (78.9)	212 (74.4)	429 (76.6)	0.206
Type 2 diabetes mellitus	57 (20.7)	47 (16.5)	104 (18.6)	0.198
Coronary disease	72 (26.2)	69 (24.2)	141 (25.2)	0.591
COPD	68 (24.7)	58 (20.4)	126 (22.5)	0.215
Thyroid disease	76 (27.6)	55 (19.3)	131 (23.4)	0.020
Chronic kidney disease	57 (20.7)	70 (24.6)	127 (22.7)	0.279
Valvular disease	71 (25.8)	61 (21.4)	132 (23.6)	0.219
Smoking	50 (18.2)	40 (14.0)	90 (16.0)	0.182
CABG	17 (6.2)	14 (4.9)	31 (5.5)	0.511
Dyslipidemia	59 (21.5)	75 (26.3)	134 (23.9)	0.178
Chagas disease	4 (1.5)	14 (4.9)	18 (3.2)	0.020
Heart failure information				
HF etiology				
Hypertensive	118 (42.9)	103 (36.1)	221 (39.5)	0.101
Toxic	3 (1.1)	1 (0.4)	4 (0.7)	0.365
Ischemic	108 (39.3)	109 (38.2)	217 (38.8)	0.803
Unknown	0	0	0	
Valvular	78 (28.4)	58 (20.4)	136 (24.3)	0.027
Other	0	0	0	
Chemotherapy	2 (0.7)	2 (0.7)	4 (0.7)	1.000
Idiopathic	19 (6.9)	19 (6.7)	38 (6.8)	0.909
Tachycardiomyopathy	58 (21.1)	73 (25.6)	131 (23.4)	0.206
Metabolic	5 (1.8)	8 (2.8)	13 (2.3)	0.437
Chagasic	3 (1.1)	13 (4.6)	16 (2.9)	0.014
Congenital	2 (0.7)	2 (0.7)	4 (0.7)	1.000
Viral	1 (0.4)	0 (0.0)	1 (0.2)	0.491
Genetic	1 (0.4)	0 (0.0)	1 (0.2)	0.491
Peripartum	0 (0.0)	1 (0.4)	1 (0.2)	1.000
Alcoholic	0 (0.0)	1 (0.4)	1 (0.2)	1.000
NYHA classification				0.153
I	25 (9.1)	31 (10.9)	56 (10.0)	

Table 2. Sociodemographic and Clinical Characteristics of Patients With HF and Atrial Fibrillation Based on Ejection Fraction - (continued)

	HFpEF (n = 275), n (%)	HFrEF (n = 285), n (%)	Total (n = 560), n (%)	P value
II	151 (54.9)	157 (55.1)	308 (55.0)	
III	91 (33.1)	79 (27.7)	170 (30.4)	
IV	8 (2.9)	18 (6.3)	26 (4.6)	
AHA/ACC stage				0.079
C	262 (95.3)	261 (91.6)	523 (93.4)	
D	13 (4.7)	24 (8.4)	37 (6.6)	
Bicameral PM	25 (9.1)	13 (4.6)	38 (6.8)	0.033
Unicameral PM	13 (4.7)	8 (2.8)	21 (3.8)	0.232
CRT	4 (1.5)	5 (1.8)	9 (1.6)	0.957
ICD	24 (8.7)	35 (12.3)	59 (10.5)	0.171
CRT + ICD	8 (2.9)	35 (12.3)	43 (7.7)	< 0.001
Prolonged QRS	43 (31)	61 (37)	104 (34.4)	0.237
LVDD, mm	48.516 (10.170)	58.220 (12.499)	55.089 (12.626)	< 0.001
LVEF	50.406 (8.634)	27.074 (7.487)	35.293 (13.672)	< 0.001
Pulmonary hypertension on echocardiogram	94 (64.4)	147 (56.8)	241 (59.5)	0.133
Quality of life score	77.018 (21.525)	74.263 (23.335)	75.616 (22.487)	0.195
Pharmacological treatment				
ACE inhibitors	77 (28.0)	95 (33.3)	172 (30.7)	0.171
ARB	136 (49.5)	119 (41.8)	255 (45.5)	0.067
Diuretics	205 (74.5)	217 (76.1)	422 (75.4)	0.661
Beta-blockers	248 (90.2)	268 (94.0)	516 (92.1)	0.090
Sacubitril/valsartan	17 (6.2)	39 (13.7)	56 (10.0)	0.003
MRAs	131 (47.6)	192 (67.4)	323 (57.7)	< 0.001
Ivabradine	2 (0.7)	5 (1.8)	7 (1.2)	0.274
Digoxin	41 (14.9)	58 (20.4)	99 (17.7)	0.091
Nitrates	11 (4.0)	5 (1.8)	16 (2.9)	0.111
Antiaggregants	67 (24.4)	66 (23.2)	133 (23.8)	0.737
Statins	148 (53.8)	171 (60.0)	319 (57.0)	0.140
Anticoagulants	194 (70.5)	183 (64.2)	377 (67.3)	0.110
Laboratory findings				
Hemoglobin, mg/dL	12.631 (2.152)	13.243 (1.886)	12.944 (2.041)	0.005
Serum creatinine, mg/dL	1.255 (0.630)	1.361 (0.739)	1.310 (0.690)	0.013
GFR	61.905 (25.763)	56.499 (26.877)	59.116 (26.455)	0.007
Blood urea nitrogen	26.717 (13.971)	29.033 (14.139)	27.937 (14.087)	0.050
Hyperkalemia	16 (7.3)	18 (7.9)	34 (7.7)	0.804
Hyponatremia	28 (13.9)	19 (9.4)	47 (11.6)	0.152
NT-proBNP, pg/mL	4,975.927 (12,335.601)	6,795.815 (9,207.515)	5,925.434 (10,806.911)	0.177

This table contains absolute counts and % for categorical variables and mean and SD for continuous variables. n: refers to the total number of patients that report having/not having each condition. SD: standard deviation; ACC: American College of Cardiology; AHA: American Heart Association; ARB: aldosterone receptor blocker; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; GFR: glomerular filtration rate; ICD: implantable cardioverter defibrillator; LVDD: left ventricle diastolic diameter; LVEF: left ventricle ejection fraction; MRA: mineralocorticoid receptor antagonist; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; NYHA: New York Heart Association; PM: pacemaker; ACE: angiotensin-converting enzyme; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction.

small and probably not clinically significant. The reasons behind the differential profile of AF by LVEF classification are still unclear [26].

Furthermore, considering the pathophysiological background, the coexistence of these two entities could also increase the severity of the cardiac involvement, thus, increasing the risk of adverse outcomes [8]. Several randomized clinical trials have evaluated the prognostic value of AF in the context of HF. For example, the SOLVD trial observed that AF was an independent predictor for all-cause mortality, being this effect mainly due to an increase in the risk of pump failure [13]. Similarly, in the Valsartan in Acute Myocardial Infarction (VALIANT), AF was associated with a higher risk of long-term morbidity and mortality in patients with myocardial infarction complicated by HF [22]. This added risk has also been observed in patients with HFpEF, as evidenced in the study of Aronow et al [31], in which patients with prior myocardial infarction and HF diagnosed with AF had a significantly higher 6-month mortality rate than those in sinus rhythm [31]. In the present study, patients with AF and HFrEF had a higher mortality risk than those with HFrEF without AF; nonetheless, AF was not an independent predictor of mortality, as it lost statistical significance as a risk factor after adjusting by age. Several studies have also suggested that AF may not confer a higher risk of mortality in the context of AF, while others report an increased risk of this adverse outcome only in HFpEF patients. Nevertheless, an adjusted meta-analysis of 16 studies (nine observational studies and seven randomized trials) assessing 53,969 patients suggested that patients with AF had a worse prognosis irrespective of the systolic function, with an increased risk of mortality both in the randomized trials (OR: 1.40, 95% CI: 1.32 - 1.48) and observational studies (OR: 1.14, 95% CI: 1.03 - 1.26). The reason behind the lack of significance in our study may be the small sample size, along with the short follow-up. We expect to reevaluate the prognostic impact of AF as the RECOLFACA registry continues the follow-up of the enrolled patients.

Study limitations

First, the RECOLFACA registry did not include information regarding rhythm control therapy, or the type of anticoagulant treatment prescribed. Second, the present study should have accounted for several potential confounders. Nonetheless, we intended to overcome this limitation by including prior medical history data, sociodemographic variables, echocardiographic measures, laboratory tests, and device therapy information. Third, the way of diagnosing AF used in this study might have induced a potential of missing patients with paroxysmal AF. Fourth, this study was conducted between 2017 and 2019, which explains the low percentage of patients receiving ARNI and the absence of information on sodium-glucose cotransporter 2 inhibitor (SGLT2i) prescriptions in patients with HF. When the registry ended recruitment (2019), SGLT2i were not approved for this indication in our country. These two conditions could affect the clinical outcomes of patients.

Conclusions

In this study, AF represents a common comorbidity in patients with HF, highlighting a higher prevalence with increasing LVEF, a differential clinical profile, similar HF severity, and a non-independent association with mortality in our cohort (Fig. 2). These results show the need for an improved understanding of the AF and HF coexistence phenomenon. Analyzing large HF registries may help elucidate relevant differences in the trends by region.

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Financial Disclosure

None to declare.

Conflict of Interest

The authors declare that they do not have any competing interests.

Informed Consent

Not applicable.

Author Contributions

JEG contributed to the conceptualization, data curation, formal analysis, investigation, methodology, project administration, software, supervision, validation, visualization, writing the original draft and writing, reviewing, and editing of the final version of the manuscript. CS and LEE contributed to conceptualization, investigation, methodology, supervision, writing the original draft, and writing, reviewing, and editing of the final version of the manuscript. ART, JBH, BR, FMJ, JIM, OAP, AHR, PRG, FRT, GTG, MAD and EEC contributed to the investigation and writing, reviewing, and editing of the final version of the manuscript. All authors critically revised and approved the manuscript.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Abbreviations

ACC: American College of Cardiology; ACEI: angiotensin-

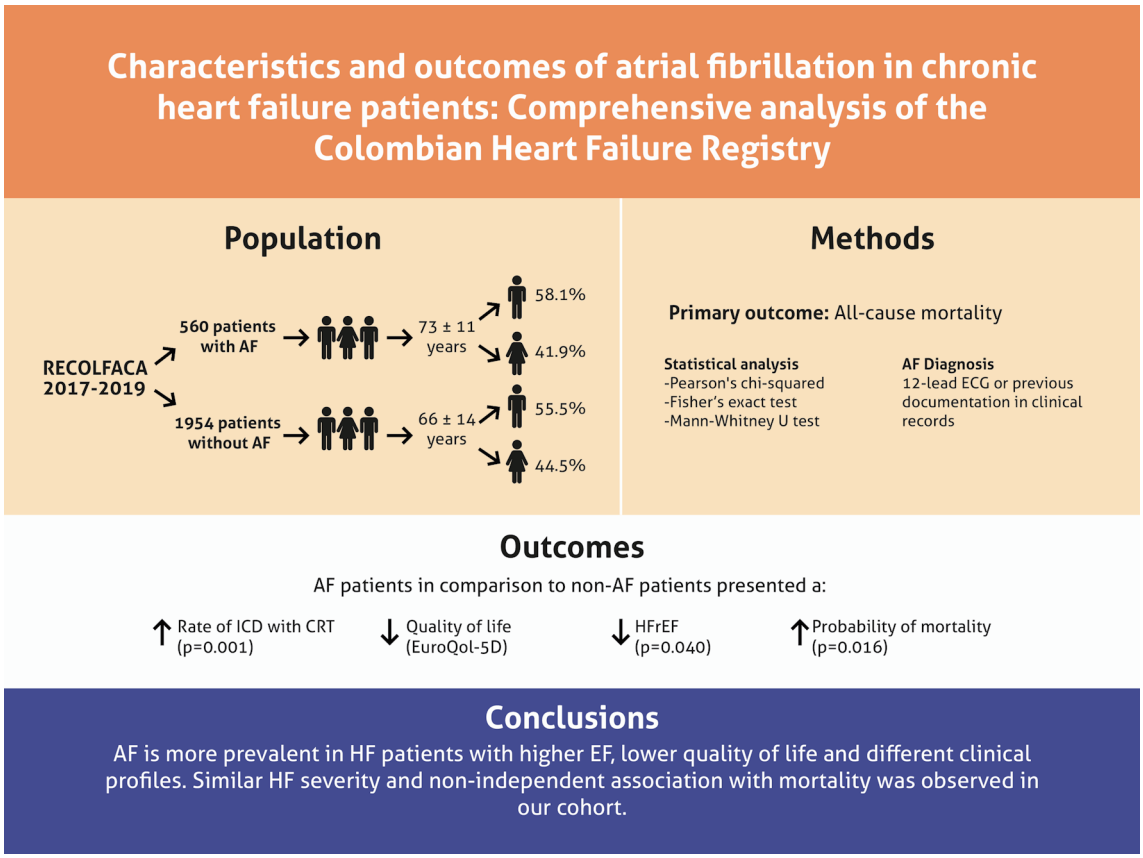

Figure 2. Summary of findings from the RECOLFACA study regarding atrial fibrillation (AF) in chronic HF patients. RECOLFACA: the Colombian Heart Failure Registry; ECG: electrocardiogram; ICD: implantable cardioverter defibrillator; CRT: cardiac resynchronization therapy; HFrEF: heart failure with reduced ejection fraction.

converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor; AF: atrial fibrillation; AHA: American Heart Association; HF: heart failure; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; ICD: implantable cardioverter defibrillator; LVEF: left ventricle ejection fraction; MRA: mineralocorticoid receptor antagonist; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; NYHA: New York Heart Association; QoL: quality of life; RECOLFACA: Colombian Heart Failure Registry; VALIANT: Valsartan in Acute Myocardial Infarction

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