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Atrial Fibrillation in Heart Failure with Preserved Ejection Fraction

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Keywords: Heart failure; Preserved ejection fraction; Atrial fibrillation; Prognosis.

Abstract

Background: Heart Failure with Preserved Ejection Fraction (HFPEF) accounts for more than half of the cases of heart failure with similar prognsis that HF with Reduced Ejection Fraction (HfrEF). Because Atrial Fibrillation (AF) and HFpEF share common risk factors, they frequently coexist, suggesting a worse prognosis than either of these conditions alone.

Objective: This study aims to evaluate the pronostic role of AF in HFpEF in an Algerian cohort.

Patients and methods: Prospective observational study from April 2018 to April 2020, including patients aged 18 and over, presnting chronic or acute heart failure with preserved ejection fraction defined according to the ESC 2016 criteria, with a follow-up of one year.

Results: 153 patients were collected. The average age of our patients is 73 years +/- 11 ranging from 42 to 91 years with 67% female. 86% of patients are hypertensive and 64% diabetic with a history of Atrial Fibrillation (AF) in 46% of cases. LA dilation is found in 80% of cases. Patients with AF were older and less likely to be current smokers or have coronary artry diseases than those without AF. Left ventricular mass, left atrial volume and pulmonary artery systolic pressure increased in patients with AF. Regarding outcome, AF is significally associated with poor fonctional statute and increased of acute decompensation heart failure.

Conclusion: Near of half of our HFpEF patient population had AF. Patients with AF were older, and less likely to have coronary artery diseases, with a higher left ventricular mass, left atrial volume, and pulmonary artery systolic pressure, than those without AF. Regarding outcome, atrial fibrillation is significally associated with poor fonctional statute and increased of acute decompensation heart failure.

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Introduction

Heart failure with preserved ejection fraction, account 40% -70% of heart failure [1,2], with a considerable impact on outcome as than of Heart Failure With Reduced Ejection Fraction (HFrEF) [3,45,67]. Atrial fibrillation (AF) is frequently associated with HFpEF with a prevalence of 15% to 65% [8,9,10].

AF and HFpEF share common 11risk [12,13] leading to endothelial dysfunction, with inflammatory response and fibrosis [14,15,16,17,18], and reflects a common underlying atrial and ventricular myopathy [19,20, 21, 22]. Structural abnormalities of left atrium precede those of left ventricle, so AF is considered as a mirror of LV abnormalities and could be considered as the "natural" consequence of HFpEF [23]. The impact on outcome of AF and HFpEF, suggests that patients with AF and HFpEF have a worse prognosis than those with either of these conditions alone. This study aims to evaluate the impact of AF on outcome in patients with HFpEF in an Algerian cohort.

Population study

Our monocenter study had included, prospectively, 153 adult patients with HFpEF between April 2018 to April 2020, and folled-up for one year. HFpEF diagnosis was made according to ESC 2016 criteria [24]. Excluded from the study were all patients with HFpEF but who have more than moderate valvulopathy, WHO class 1, 3, 4, or 5 Pulmonary arterial hypertension, right ventricular arrhythmogenic dysplasia, congenital heart disease, right ventricular infarction, pericardium disease: Tamponnade, constrictive pericarditis, specific cardiomyopathy: viral, inflammatory (Sarcoidosis), genetic (Hypertrophic Cardiomyopathy), and restrictive cardiomyopathy.

Results

The average age of our patients is 73 years +/- 11 ranging from 42 to 91 years with 67% female. 86% of patients are hypertensive and 64% diabetic with a history of Atrial Fibrillation (AF) in 46% of cases**.** 71% of patients had chronic heat failure and 29% acute heart failure.

Patients with AF were older and less likely to have ischemic heart disease than those without AF. Left ventricular mass, left atrial volume and pulmonary artery systolic pressure increased in patients with AF. AF wasalso significally associated with poor fonctional statute and increased of acute decompensated heart failure. (**Table 1**).

Regarding outcome, the rate of mortality at one year was 14%, and hospitalization for HF was 5.9%. There were 21 deaths from any cause, representing a rate of 13.73%. Atrial fibrillation was associated with the one year outcome in univariate analysis (P= 0,01471; OR= 2,362) but not in multivariate analysis. Acute decompensated hear failure, anemia and pulmonary hypertension are the independent prognostic factors at one year.

Figure 3: Baseline characteristics of the HFpEF study population according to AF (unmatched cohort).

Characteristics	Without AF (n=83; 54.25%)	With AF (n=70; 45.75)	OR	CI 95%	P value
Age,	70.11 (12.14)	75.9 (9.068)	1.052	1.019- 1.087	0.0019
Sex male	31 (59.62)	21 (40.38)	0.719	0.363- 1.423	0.3397
Diabetes	51 (51)	49 (49)	1.464	0.741- 2.893	0.2689
Hypertention	69 (51.88)	64 (48.12)	2.164	0.778- 6.021	0.1360
Dyslipidemia	34 (56.67)	26 (43.33)	0.852	0.441- 1.645	0.6297
Obesity	26 (48.15)	28 (51.85)	1.462	0.747- 2.861	0.2642
Ischaemic heart disease	31 (79.49)	8 (20.51)	0.216	0.091- 0.515	<0.001
COPD	12 (38.71)	19 (61.29)	2.204	0.977- 4.974	0.0550
Anemia	32 (49.23)	33 (50.77)	1.421	0.742- 2.723	0.2850
Chronic renal failure	30 (50.85)	29 (49.15)	1.250	0.647- 2.414	0.5038
Current smoking	55 (83.33)	1 (16.67)	0.226	0.025- 2.018	0.1796
Acute decompensated HF	9 (25.71)	26 (74.29)	4.088	1.424 11.74	0.00888
Left ventricular mass (g/m2)	129.2 (39.27)	111.8 (33.28)	0.985	0.975- 0.996	0.0058
Left atrial dilatation (>34ml/m2)	58 (47.15)	65 (52.85)	5.603	1.997- 15.72	<0.001
PASP (mmHg)	39.2 (12)	45.49 (13.08)	1.041	1.013- 1.07	0.0034
E/e'	15.34 (5.40)	16.07 (5.23)	1.026	0.966- 1.091	0.3955
LVEF (%)	58.17 (6.20)	60.16 (7.06)	1.047	0.996- 1.1	0.0676
GLS (%)	14.72 (3.77)	13.79 (4.17)	0.942	0.868- 1.023	0.1537
NT-ProBNP (pg/ml)	2977 (61)	2866 (341)	0.995	0.933- 1.062	0.8923
GDF 15 (pg/ml)	3531 (456)	4629 (4096)	1.062	0.968- 1.164	0.1952
6-MWT (meters)	334 (143)	191 (118)	0.992	0.988- 0.996	<0.001

Discussion

Prevalence of AF in HFpEF: AF is common in HFpEF and its prevalence varies betweenstudies from 15 to 41% depending on the design of the study and the diagnostic methods (clinical diagnosis or Holter screening) [26,27,28,29]. The prevalence of AF in our study is 45.75% in line with results of KaRen andthe Korean acute heart Failure registry [31,32].

The prevalence of AF in HFrEF is significantly lower (24.6%) in patients with HFrEF in an Algerian cohort [33]. Our patients with AF were older and less likely to have coronary artery disease or

current smokers thanthose without AF. Regarding echographic features, left ventricular mass, left atrial volume and pulmonary artery systolic pressure increased in patients with AF. Regarding outcome, AF is significally associated with poor fonctional statute and increased of acute decompensation heart failure. Our results are in concordance with pathophysiiology explainig the role of the left atrium in HFpEF, so preservation of atrial function could be an important adaptation that protects the lungs and right heart in HFpEF, since the development of atrial dysfunction is associated with poor exercise capacity, pulmonary vascular disease, right heart failure, and an increased risk of mortality [34,3536,37,38].

AF may be the first indicator of inflammatory or metabolic "atrial myopathy" causing HFpEF [33]. Myocardial inflammation, fibrosis, and hypertrophy are identified in left atrium and left ventricle, in both AF and HFpEF, [34] hence higher LA volume and LV mass in our patients with AF than those without AF, and consequently higher PASP and more acute decompensation HF as found in our study. Moreover, Gavin et al, in their analysis of the TOPCAT trial substudy, found that patients with high NT-Pro BNP levels had significantly higher LV volume and LV mass than patients with low LV mass and low prevalence of LVH [35].

AF and outcome in HFpEF

A growing numer of evidence suggests that the combination of AF and HFpEF predicts increased morbidity and mortality compared to either condition alone. An increase in mortality, hospitalizations for HF and strokes has been observed in the Swedish Heart Failure Registry (SwedeHF), and other studies, such as the population-based cohort study of the county of Olmsted, the CHARM program and the Framingham Heart Study [36,37].

However, in the post-ad hoc analysis of the I-PRESERVE trial, AF predicted outcomes only in univariate analysis, similar to our results [38].

Conclusion

Near of half of our HFpEF patient population had AF. Sharing common risk factors, patients with AF were older, and less likely to have coronary artery diseases, with a higher left ventricular mass, left atrial volume, and pulmonary artery systolic pressure, than those without AF.The coexistence of AF and HFpEF is associated with a worse prognosis with poor fonctional statute and increased of acute decompensation heart failure but not of mortality at one year.

Abbreviations

ACE: Angiotensin Conversion Enzym; ADHF: Acute Decompensation of Heart Failure; AF: Atrial Fibrillation; ARB: Angiotensin Receptors Blockers; ARNI: Angiotensin Receptors Neprilysin Inhibitors; BMI: Body Mass Index; BNP: Brain Natriuretic Peptide; COPD: Chronic Obstructive Pulmonary Disease; CRI: Chronic Renal Insufficiency; EF: Ejection Fraction; ESC: European Society Of Cardiology; GDF: Growth Differentiation Factor; GLS: Global Longitudinal Strain; HF: Heart Failure; Hfpef: Heart Failure With A Preserved Ejection Fraction; Hfref: Heart Failure With A Reduced Ejection Fraction; LA: Left Atrium; LAV: Left Atrial Volume; LV: Left Ventricle; LVEF: Left Ventricular Ejection Fraction; LVH: Left Ventricular Hypertrophy; LVM: Left Ventricular Mass; MACE: Major Acute Cardiovascular Events; 6M-WT: 6 Minutes' Walk Test; NT-Probnp: N Terminal Pro Brain Natriuretic Peptide; PASP: Pulmonary Artery Systolic Pressure; TR: Tricuspid Regurgitation; WHO : Word Heart Organizaton.

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