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High Prevalence of Occult Heart Failure with Preserved Ejection Fraction among Patients with Atrial Fibrillation and Dyspnea

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Keywords

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Atrial fibrillation (AF) is common in patients with heart failure (HF) and preserved ejection fraction (HFpEF).[1, 2] Like people with HFpEF, patients with AF commonly describe exertional dyspnea. Treatments directed at AF are often undertaken using antiarrhythmic drugs, rate control or AF ablation with the ultimate goal of improving these symptoms. However, recent data indicate that some patients with apparently 'lone AF' display myocardial abnormalities that persist even when sinus rhythm has been restored, suggesting the coexistence of an underlying cardiomyopathic process.[3] Viewed in this light, AF might be conceptualized as a consequence rather than cause of symptoms of heart failure.

There is little information available regarding the prevalence of HFpEF among patients presenting with dyspnea, normal EF, and AF. Because history, physical examination, and echocardiography are insensitive to the diagnosis of HFpEF, the only method to accurately determine whether HFpEF is present or absent in this group is to ascertain disease status using the gold standard of invasive hemodynamic cardiopulmonary exercise testing.[4, 5]

We examined the relationships between AF and HFpEF among consecutive patients presenting with unexplained exertional dyspnea, normal EF (>50%), and no prior diagnosis of HF referred for invasive exercise testing between 2000 and 2014. The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. Patients were diagnosed with HFpEF based upon an increase in pulmonary capillary wedge pressure (PCWP) to ≥25 mmHg during exercise.[4, 5] Patients with no demonstrable cardiac pathology and an exercise PCWP <25 mmHg during exercise were diagnosed as having non-cardiac etiologies of dyspnea (NCD). Patients with alternative causes of HF, a prior history of tachycardia–mediated cardiomyopathy or any history of low EF (<50%) were excluded. The study was approved

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Disclosures

None.

by the Mayo Clinic institutional review committee and that all subjects gave informed consent.

Among 429 consecutive patients meeting these criteria, 154 (36%) were diagnosed as NCD and 275 (64%) were diagnosed with HFpEF (Table). As compared with NCD, HFpEF patients were older, heavier, and more likely to be have diabetes and hypertension. The majority of NCD patients (96.1%) were in sinus rhythm, with only 3.3% and 0.7% documented to have paroxysmal and persistent/permanent AF, respectively. Conversely, 17.5% and 17.1% of HFpEF subjects had paroxysmal or persistent/permanent AF, respectively ($p<0.0001$). HFpEF was highly prevalent among patients with AF and dyspnea: diagnosed in 98% of individuals with persistent/permanent AF and 91% those with paroxysmal AF. Using logistic regression, the odds ratio for HFpEF associated with permanent AF was 38.6 [95% CI, 8.3–688.0] ($p=0.0003$) and the odds ratio for HFpEF with paroxysmal AF was 7.9 [95% CI, 3.4–23.2] ($p<0.0001$). After adjusting for baseline characteristics, the presence of permanent AF (OR 22.1; 95% CI, 4.4–401) and paroxysmal AF (OR 4.86; 95% CI, 1.90–15.1) remained a highly significant predictor of HFpEF (both $p<0.001$). The prevalence rate ratio of HFpEF among patients with paroxysmal AF was 1.65 [95% CI 1.45–1.88], and among persistent/permanent AF was 1.78 [95% CI 1.59 −1.98], implying a 65% and 78% greater risk of HFpEF in these two AF groups.

It is currently unclear whether AF in general is merely a complication of unrecognized HFpEF, or whether AF is a separate disease that can cause a clinical syndrome mimicking HFpEF.[1, 2] The results of the current study demonstrate that the vast majority of patients undergoing hemodynamic evaluation and presenting with unexplained dyspnea, AF, and normal EF display classical hemodynamic derangements during exercise that are diagnostic of HFpEF.[4, 5] This suggests that AF may be a very specific marker suggesting the presence of underlying HFpEF among patients presenting with unexplained dyspnea. Further prospective study enrolling unselected AF patients is required to replicate these findings, because the current study was single-center limiting generalizability. In addition, all patients were referred for invasive exercise testing, introducing selection bias that increases the prevalence of disease and the odds ratio. This study population included only patients with exertional dyspnea; therefore the results may not be applicable to asymptomatic patients with AF.

Invasive cardiopulmonary exercise testing has emerged as a commonly used test in these patients, and the definitive ascertainment of the presence or absence of HFpEF would not have been possible without this assessment. A cross sectional study cannot prove causation, but there is strong biological plausibility supporting the theory that HFpEF may underlie both symptoms of dyspnea and cardiac derangements that lead to AF, since chronic elevation in filling pressures increases left atrial wall stress, resulting in atrial dilatation, scarring and fibrosis.[1]

Therefore, among patients with normal EF and unexplained dyspnea, the presence of AF should raise suspicion that underlying HFpEF is present. These results support a shift in focus in AF from the arrhythmogenic substrate to that of the underlying myocardium. This is important not only to reach the correct diagnosis, but also because therapies targeting AF

itself carry cost and risk that may not be warranted if symptoms are primarily caused by HFpEF rather than dysrhythmia.

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Table

Patient Characteristics and Prevalence of Atrial Fibrillation

	NCD(N=154)	HFpEF(N=275)
Age, years	56±15	68±11 *
Female, n (%)	90 (58)	171 (62)
Body mass index, kg/m^2	28.4±5.6	33.1±7.3 *
Diabetes, n (%)	20 (14)	76 (29) *
Hypertension, n (%)	84 (55)	232 (84) *
Sinus rhythm, n (%)	148 (96)	180 (65) *
Paroxysmal atrial fibrillation, n (%)	5 (3)	48 (18) *
Persistent or Permanent atrial fibrillation, n (%)	1 (1)	47 (17) *

NCD, non-cardiac dyspnea; HFpEF, heart failure with preserved ejection fraction,

* p<0.001 vs NCD by T test, Chi square, or Fisher's Exact Test