High Prevalence of Occult Heart Failure With Preserved Ejection Fraction Among Patients With Atrial Fibrillation and Dyspnea

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Atrial fibrillation (AF) is common in patients with heart failure 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 by 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 a cause of symptoms of heart failure.

There is little information available regarding the prevalence of HFpEF among patients presenting with dyspnea, normal ejection fraction (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 by 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 heart failure referred for invasive exercise testing between 2000 and 2014. Patients were diagnosed with HFpEF based on an increase in pulmonary capillary wedge pressure to ≥25 mm Hg during exercise.[4,5] Patients with no demonstrable cardiac pathology and an exercise pulmonary capillary wedge pressure <25 mm Hg during exercise were diagnosed as having noncardiac etiologies of dyspnea. Patients with alternative causes of heart failure, a prior history of tachycardia-mediated cardiomyopathy, or any history of low EF (<50%) were excluded. The study was approved by the Mayo Clinic institutional review committee, and all subjects gave informed consent.

Among 429 consecutive patients meeting these criteria, 154 (36%) were diagnosed with noncardiac etiologies of dyspnea, and 275 (64%) were diagnosed with HFpEF (Table). In comparison with patients with noncardiac etiologies of dyspnea, patients with HFpEF were older, heavier, and more likely to have diabetes mellitus and hypertension. The majority of patients with noncardiac etiologies of dyspnea (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 subjects with HFpEF 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% of those with paroxysmal AF. With the use of logistic regression, the odds ratio (OR) for HFpEF associated with permanent AF was 38.6 (95% confidence interval [CI], 8.3–688.0; P=0.0003), and the OR 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

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Key Words: atrial fibrillation ■ cardiomyopathies ■ dyspnea ■ exercise ■ heart failure

Table. Patient Characteristics and Prevalence of Atrial Fibrillation

	NCD (n=154)	HFpEF (n=275)
Age, y	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 mellitus, 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)*

Values indicated in mean ± SD. NCD indicates noncardiac dyspnea; and HFpEF, heart failure with preserved ejection fraction.

*P<0.001 vs. NCD by t test, χ^2, or Fisher exact test.

paroxysmal AF was 1.65 (95% CI, 1.45–1.88), and among patients with persistent/permanent AF, it was 1.78 (95% CI, 1.59–1.98), implying a 65% and 78% greater risk of HFpEF in these 2 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 studies enrolling unselected AF patients are required to replicate these findings, because the current study was conducted in a 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 OR. 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, because 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 costs and risks that may not be warranted if symptoms are primarily caused by HFpEF rather than dysrhythmia.

SOURCES OF FUNDING

Dr Borlaug is supported by U10 HL110262 and RO1 HL128526, and Dr Reddy is supported by T32 HL007111, all from the National Institutes of Health.

DISCLOSURES

None.

AFFILIATION

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FOOTNOTES

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.

Circulation is available at http://circ.ahajournals.org.

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Circulation. 2018;137:534-535
doi: 10.1161/CIRCULATIONAHA.117.030093
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539