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EDITORIAL COMMENT

Left Atrial Pressure

The Key to Understand and Treat HFpEF?*

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Heart failure with preserved ejection fraction (HFpEF) is a frequent disease, with a prevalence of 1% to 5% in Western countries (1). No specific evidence-based treatment is yet available to manage this common disease, partly because its pathophysiology is poorly understood. Limitation of exercise capacity in patients with HFpEF may result from the diminished increase of cardiac output and/or from elevated left atrial pressure with increased pressure in the pulmonary capillaries. Increasing data indicate that pulmonary capillary wedge pressure (PCWP) and its rise during exercise may be the key components limiting exercise capacity and even prognosis in patients with HFpEF (2).

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The paper by Reddy et al. (3) in this issue of *JACC: Heart Failure* adds more important information on the determinants of exercise in HFpEF. The study has 2 goals: 1) to evaluate hemodynamic correlates of exercise capacity in patients with HFpEF as measured by peak oxygen consumption (Vo_2); and 2) to define peak Vo_2 diagnostic value. The basis of the paper is a retrospective analysis of 134 patients with HFpEF and 72 patients with noncardiac etiologies of dyspnea. Patients underwent noninvasive measurements of peak Vo_2, as well as invasive exercise hemodynamic measurements. The study has 2 major findings: 1) exercise PCWP as a surrogate for elevated left ventricular filling pressure and elevated left atrial pressure is an independent correlate of peak Vo_2; and 2) peak Vo_2 itself is of limited value in the diagnostic algorithm of HFpEF. The first finding is an important message and adds significantly to our understanding of HFpEF pathophysiology. Although an inadequate rise of cardiac output may be the major factor limiting exercise in heart failure with reduced ejection fraction, the rise of PCWP may be the dominant mechanism in HFpEF (4).

The second finding is also important because it tells us that noninvasive cardiopulmonary exercise testing alone, if done in in the supine or upright position, is of very limited value. There was good discrimination of HFpEF from noncardiac etiologies of dyspnea by using peak Vo_2 values lower and higher than cutoffs of <14 and >20 ml/min/kg, but 50% of patients with HFpEF diagnosed by the gold standard of exercise hemodynamics were between these values. Accordingly, Reddy et al. (3) suggest a very useful diagnostic algorithm for testing patients with unexplained dyspnea that puts hemodynamic exercise testing strongly in the foreground. Obviously, invasive exercise hemodynamic measurements identify the key mechanism that limits exercise: the rise of PCWP. This finding is consistent with previous work showing that guideline-recommended diagnostic methods of HFpEF during rest are poorly sensitive for diagnosing HFpEF and that exercise hemodynamic measurements are superior to exercise echocardiographic data (5). As Reddy et al. (3) state in the discussion, elevated left ventricular filling pressure increases PCWP and forces fluid movement into the interstitium, thereby altering lung compliance and inducing dyspnea.

The findings of Reddy et al. (3) also support current therapeutic approaches to reduce pulmonary pressures in patients with HFpEF. It was shown that management of patients with HFpEF

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according to sensor-based pulmonary artery pressure measurement significantly reduced pulmonary congestion and heart failure-related hospitalization (6). More recently, a therapeutic approach was developed to reduce PCWP by creating an atrial left-to-right shunt. Patients treated with this interatrial shunt device for 6 months improved clinically and showed increased duration of exercise and walking distance, together with reduced exercise PCWP (7).

In summary, the paper by Reddy et al. (3) strongly supports exercise hemodynamic testing as the diagnostic gold standard in patients with suspected HFpEF, as well as in patients with unexplained dyspnea in general. Moreover, together with recent therapeutic approaches, the findings of Reddy et al. (3) suggest that elevated PCWP may be an important therapeutic target in future attempts to manage HFpEF.

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