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CME

Clinical Features, Hemodynamics, and Outcomes of Pulmonary Hypertension Due to Chronic Heart Failure With Reduced Ejection Fraction

Pulmonary Hypertension and Heart Failure

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JACC: HEART FAILURE CME

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CME Objective for This Article: After reading this article, the reader should be able to: 1) discuss the causes of pulmonary hypertension in patients with systolic heart failure; 2) have an understanding of the differences between passive and mixed pulmonary hypertension; and 3) discuss the impact of pulmonary hypertension subtypes on disease severity and risk of death.

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Objectives The purpose of this study was to assess the clinical, functional, and hemodynamic characteristics of passive and mixed pulmonary hypertension (PH), compare outcomes, and contrast conventional and novel hemodynamic partition values in patients with chronic heart failure of reduced left ventricular ejection fraction (HFREF).

Background PH in HFREF may develop from left-sided venous congestion (passive PH) or the combination of pulmonary arterial disease and venous congestion (mixed PH). Subgroup outcomes are not well defined, and the partition values used to define risk are based largely on consensus opinion rather than outcome data.

Methods Ambulatory patients referred for hemodynamic catheterization were analyzed retrospectively (N = 463).

Results Comparing patients with no PH to those with passive PH and mixed PH, a progressive gradient of more severely deranged hemodynamics, diastolic dysfunction, and mitral regurgitation was observed. In multivariate analysis, the presence of any PH or mixed PH was associated with older age, diuretic use, atrial fibrillation, and lower pulmonary artery compliance (PAC). Over a median follow-up of 2.1 years, patients with PH displayed greater risk of death (hazard ratio [HR]: 2.24; confidence limits [95% CL]: 1.39, 3.98; $p < 0.001$) with mixed PH demonstrating greater risk than passive PH (HR: 1.55; 95% CL: 1.11, 2.20; $p < 0.001$). Partition values identifying highest risk were pulmonary vascular resistance >4 Wood units, systolic pulmonary artery pressure >35 mm Hg, pulmonary wedge pressure >25 mm Hg, and PAC <2.0 ml/mm Hg.

Conclusions Among stable HFREF outpatients, PH was associated with markers of greater disease severity and risk of death. However, the presence of pulmonary arterial disease (mixed PH) carries incremental risk. Abnormalities in pulmonary vascular resistance and compliance may serve as novel therapeutic targets. (J Am Coll Cardiol HF 2013;1:290–9) © 2013 by the American College of Cardiology Foundation

The development of pulmonary hypertension (PH) is an important marker in the progression of heart failure with reduced left ventricular (LV) ejection fraction (HFREF) (1–4). Initially, an increase in LV filling pressure causes an elevation in pulmonary venous pressures (5–7), resulting in post-capillary or passive PH (8–10). Some patients also develop abnormalities in pulmonary arterial structure and function resulting in a superimposed pulmonary arterial (pre-capillary) vasoconstrictor component that produces a "mixed" PH characterized by high LV filling pressure and elevated pulmonary vascular resistance (11–13). While PH is well established as an important risk factor for poor outcome in HFREF (8–10), the available data regarding passive and mixed PH subgroups are variable and limited by relatively short-term follow-up, incomplete characterization of left and right ventricular function, and limited data on coexisting valvular pathology (11–15).

Accordingly, the aim of this study was to comprehensively assess the clinical, functional, and hemodynamic characteristics of passive and mixed PH in a large cohort of ambulatory patients with chronic HFREF. Additional aims were to compare long-term outcomes in these subgroups of PH, contrast conventional and novel hemodynamic parameters of PH severity, and to propose partition values that might better stratify mortality risk and potentially serve as novel therapeutic targets in HFREF.

Methods

Ambulatory outpatients with HFREF referred by their primary cardiologist to the Mayo Clinic Rochester Cardiovascular Catheterization Laboratory for resting right heart hemodynamic catheterization for the period January 1, 2002, to December 31, 2008, were studied retrospectively. Inclusion criteria were age >18 years, LVEF ≤40%, and measurable LV diastolic and mitral valve function by echocardiography-Doppler evaluation at the time of the index catheterization. Exclusion criteria were primary parenchymal lung disease; chronic obstructive pulmonary disease other than mild as defined by pulmonary spirometry testing (forced expiratory volume in 1 s [FEV1] ≥80% of expected normal and the FEV1/forced vital capacity [FVC] ratio <70%) or clinical records description; prior valvular surgery; infiltrative, constrictive, or hypertrophic cardiomyopathy; myocardial infarction within 6 months; any history of risk factors associated with group 1 or group 3 PH (idiopathic, familial or pulmonary thromboembolic disease); congenital heart disease; tachycardia-related dysrhythmia; serum creatinine level ≥2.5 mg/dl; history of chest radiation therapy, collagen vascular disease, or cardiac or lung transplantation; consent for use of patient information for clinical research not available or consent refused. Indications for catheterization based upon referring physician (more than one could be provided) were abstracted from the database.

Patient survival or all-cause mortality status was confirmed through June 30, 2010 (censor date), using Mayo Clinic, Rochester, electronic medical records, Olmsted County, Minnesota, medical record linkage system (Rochester Epidemiology Project) and Social Security mortality index. No patients hospitalized for acute decompensated HF were