CHEST

A Simple Derived Prediction Score for the Identification of an Elevated Pulmonary Artery Wedge Pressure Using Precatheterization Clinical Data in Patients Referred to a Pulmonary Hypertension Center

Stefan E. Richter, MD; Kari E. Roberts, MD; Ioana R. Preston, MD; and Nicholas S. Hill, MD

BACKGROUND: One of the foremost diagnostic challenges in clinical pulmonary hypertension is discriminating between pulmonary arterial hypertension (group 1) and heart failure with preserved ejection fraction (group 2.2). Group 2.2 is defined as a normal left ventricular ejection fraction (> 50%) and a pulmonary arterial wedge pressure (PAWP) > 15 mm Hg. We aimed to determine whether patient history, demographics, and noninvasive measures could predict PAWP before to right heart catheterization.

METHODS: Data were prospectively collected on 350 consecutive patients at a single tertiary care medical center; of these patients, 151 met criteria for entry into our study (88 in group 1 and 63 in group 2.2). Data included historical features, demographics, and results of a transthoracic echocardiogram. A multivariate regression model was developed to predict PAWP > 15 mm Hg.

RESULTS: Univariate predictors of PAWP > 15 mm Hg included older age, higher BMI and weight, systemic systolic BP and pulse pressure, more features of the metabolic syndrome, presence of hypertension and left atrial enlargement, absence of right ventricular enlargement, and lower glomerular filtration rate and 6-min walk distance. The optimal model for predicting PAWP > 15 mm Hg was composed of age (> 68 years), BMI (> 30 kg/m^2), absence of right ventricular enlargement, and presence of left atrial enlargement (area under the curve, 0.779).

CONCLUSIONS: Clinical characteristics obtained before diagnostic right heart catheterization accurately predict the probability of elevation of PAWP > 15 mm Hg in patients with preserved ejection fraction. These combined clinical characteristics can be used a priori to predict the likelihood of group 2.2 pulmonary hypertension. CHEST 2016; 149(5):1261-1268

KEY WORDS: epidemiology (pulmonary); heart failure; pulmonary arterial hypertension; research-clinical

ABBREVIATIONS: 6MWD = 6-min walk distance; DPG = diastolic pressure gradient; EGFR = estimated glomerular filtration rate; HFpEF = heart failure with preserved ejection fraction; LA = left atrium/left atrial; LVEF = left ventricular ejection fraction; mPAP = mean pulmonary arterial pressure; PAH = pulmonary arterial hypertension; PAWP = pulmonary arterial wedge pressure; PH = pulmonary hypertension; PH-HFpEF = pulmonary hypertension in heart failure with preserved ejection fraction; RHC = right heart catheterization; RV = right ventricular; TPG = transpulmonary gradient

AFFILIATIONS: From the Division of Pulmonary and Critical Care Medicine, Department of Medicine (Dr Richter), University of California, Los Angeles, Los Angeles, CA; and the Division of Pulmonary, Critical Care, and Sleep Medicine (Drs Roberts, Preston, and Hill), Tufts Medical Center, Boston, MA.

Heart failure with a preserved ejection fraction (HFpEF), defined as a pulmonary artery wedge pressure of > 15 mm Hg with a left ventricular ejection fraction (LVEF) on echocardiogram > 50%,[1-4] has become increasingly prevalent.[5-7] The combination of HFpEF with pulmonary hypertension (PH), defined as a mean pulmonary artery pressure (mPAP) ≥ 25 mm Hg (PH-HFpEF), imparts a worse prognosis than HFpEF without PH and is classified as group 2.2 PH. Considering the prognostic implications of proper phenotyping of patients with PH, the lack of specific pharmacotherapies for patients with PH-HFpEF, and the potential harm if therapies approved for group 1 pulmonary arterial hypertension (PAH) are prescribed for patients with PH-HFpEF,[8,9] it is critically important to have accurate clinical tools to differentiate between group 1 and 2 patients. Furthermore, the lack of consistency of definitions for group 2 PH and the inaccuracy of PAWP measurements[10,11] intensify the need for ways to phenotype these patients consistently.

Because PAWP is currently the standard measurement for differentiating PAH from PH-HFpEF, we sought to derive a prediction score for PAWP > 15 mm Hg. Several other studies[12-17] have examined the relationship between demographic, echocardiographic, and hemodynamic characteristics of patients with various types of PH. Those studies have either not attempted prediction algorithms,[12] focused on patients with PAH compared with patients with only mild elevations in PAWP[13] or those with PH-HFpEF with elevated transpulmonary gradient (TPG),[14,15] or looked only at cardiac imaging as a predictor of PAWP.[16,17] In addition, many of those studies included patients who were receiving therapy at the time of data collection.[13-15,17] We used our contemporary PH registry of prospectively and consecutively enrolled treatment-naive subjects at a single center to identify the clinical phenotype associated with PAWP > 15 mm Hg.

Methods

Study Design

This was a prospective cohort of consecutive patients undergoing diagnostic right heart catheterization (RHC) for evaluation of PH at Tufts Medical Center between 2001 and January 2013. The study was conducted in accordance with the amended Declaration of Helsinki. All subjects provided written informed consent and the study was approved by Tufts institutional review board No. 7347.

Study Groups and Inclusion and Exclusion Criteria

All members of the cohort were included if they had an LVEF of >50%, had not had PH-specific treatment at the time of diagnostic catheterization, and had an mPAP ≥ 25 mm Hg. They were excluded if they met criteria for group 3 (chronic lung disease), group 4 (chronic thromboembolic disease), or group 5 (heterogeneous conditions) PH.[1,2,4,12] Also excluded were those with an echocardiogram demonstrating significant valvular disease other than tricuspid regurgitation, left ventricular inflow or outflow obstruction, or renal failure requiring dialysis.

For the primary analysis, patients were divided into two groups according to PAWP at the time of RHC: ≤ 15 mm Hg (PAH) and PAWP > 15 mm Hg (PH-HFpEF).[1-4,18] Because the goal of the study was to predict PAWP > 15 mm Hg, no further subdivisions were made within the PAWP > 15 mm Hg group regarding the presence of combined (ie, diastolic pressure gradient [DPG] ≥ 7 mm Hg) or isolated (DPG < 7) group 2.2 PH.[7]

Patient Characteristics and Diagnostic Testing

All patients underwent baseline RHC by one of three operators (N. S. H., I. R. P., or K. E. R.), as previously described.[19] Demographics, comorbidities, and smoking history were recorded and 6-min walk distance (6MWD) and data from the transthoracic echocardiogram, serum creatinine, and brain natriuretic peptide were included if they were obtained within 6 months, 3 months, and 24 h of the RHC, respectively.

Transthoracic echocardiograms were interpreted per guidelines published by the American Society of Echocardiography.[20] Right ventricular (RV) enlargement was scored primarily qualitatively but it was considered to be present when it was at least as large as the left ventricle or when any two RV measurements were moderately above normal (during diastole, basal RV diameter > 3.3 cm, mid-RV diameter > 3.7 cm, or base to apex length > 8.5 cm). RV dysfunction was scored when the fractional change in area was < 32% or the tricuspid annular plane systolic excursion was < 1.5 cm combined with qualitative assessment. Left atrial (LA) enlargement was scored when the LA area at the end of ventricular systole was > 20 cm^2 and RA enlargement was scored when the RA appeared to be enlarged on the apical four-chamber view, typically correlating to a minor-axis dimension of >4.5 cm.

Estimated glomerular filtration rate (EGFR) was calculated using the Modified Diet in Renal Disease equation.[21] The following definitions were applied: overweight (BMI ≥ 25), obese (BMI ≥ 30),[22] chronic kidney disease (EGFR < 60), and metabolic syndrome points (one point each for obesity, hypertension, hyperlipidemia, and diabetes).

Statistical Analysis

Continuous data were reported as mean ± SD if normally distributed or as median (interquartile range) if data were nonnormally distributed as evidenced by substantial differences between medians and means. Categorical variables were reported as frequency (%). Between-group differences were assessed using χ^2 tests, analysis of variance, two-

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CORRESPONDENCE TO: Stefan E. Richter, MD, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of California, Los Angeles Center for Health Sciences #37-131, 10833 Le Conte Ave, Los Angeles, CA 90095; e-mail: srichter@mednet.ucla.edu

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