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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Usefulness of pulmonary capillary wedge pressure as a correlate of left ventricular filling pressures in pulmonary arterial hypertension

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KEYWORDS:
pulmonary arterial hypertension;
right heart catheterization;
pulmonary capillary wedge pressure;
left ventricular end-diastolic pressure;
left ventricular filling pressure

BACKGROUND: Pulmonary arterial hypertension (PAH) is characterized by a pulmonary capillary wedge pressure (PCWP) of ≤15 mm Hg, given a normal left ventricular filling pressure (LVFP). However, recent studies have shown that, in PAH patients, diagnosis based on PCWP can erroneously classify a significant number of patients compared with diagnosis based on left ventricular end-diastolic pressure (LVEDP). Therefore, we sought to compare the diagnostic accuracy of end-expiratory PCWP and LVEDP measurements in patients suspected of having pulmonary hypertension (PH).

METHODS: We reviewed the hemodynamic data from 122 patients suspected of having PH who underwent simultaneous right- and left-side heart catheterizations at a PH referral center from 2006 to 2011.

RESULTS: PH was diagnosed in 105 patients, 79% of whom ($n = 83$) showed a pre-capillary pattern according to the LVEDP measurement. Ninety percent of patients with PCWP ≤15 mm Hg were correctly classified as having pre-capillary PH. However, 39% of patients with a PCWP >15 mm Hg had LVEDP ≤15 mm Hg and would have been erroneously diagnosed with pulmonary venous hypertension based on their PCWP measurements alone. The sensitivity and specificity was 0.89 and 0.64, respectively. A Bland-Altman analysis of the PCWP and LVEDP measurements revealed a mean bias of 0.3 mm Hg with 95% limits of agreement of −7.2 to 7.8 mm Hg.

CONCLUSIONS: A PCWP ≤15 mm Hg was found to be a reliable indicator of normal LVFP in pre-capillary PH patients. When measured properly and analyzed in the clinical context, PCWP is a valuable tool for accurate diagnosis of PAH.

J Heart Lung Transplant 2014;33:157–162

Pulmonary arterial hypertension (PAH) is defined as a mean pulmonary arterial pressure (mPAP) of ≥25 mm Hg at rest and a pulmonary capillary wedge pressure (PCWP) of ≤15 mm Hg,[1] assuming a normal left ventricular filling pressure (LVFP). These hemodynamic values are common to all etiologies of Group 1 pulmonary hypertension (PH) and are indicative of a pre-capillary hemodynamic pattern.[2] Identifying this pattern is essential in correctly evaluating patients suspected of having PAH, as PAH-specific therapies are ineffective for pulmonary venous hypertension caused by left-side heart disease (Group 2 PH), which is characterized by a PCWP of >15 mm Hg,[3] and is indicative of a post-capillary hemodynamic pattern. Importantly, such

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1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2013.10.008

misclassifications can deprive PAH patients of potentially beneficial treatment.

PCWP represents an alternative measure to left ventricular end-diastolic pressure (LVEDP),[4–6] which is the "gold standard" for determining LVFP. However, recent studies have shown that, in PAH patients, PCWP can lead to erroneous PH classification compared with a diagnosis based on LVEDP.[7,8] Many factors can interfere with the accurate measurement of PCWP,[9] including factors related to the measurement techniques themselves[10,11] and patient-specific factors, such as obesity, hypoxemia[12] and ventilation.[13,14] Therefore, it is important to use other tools to confirm the accuracy and reliability of PCWP measurements during right-heart catheterization (RHC). In this context, clinical characteristics are often helpful for distinguishing between PAH patients and patients with PH caused by left-side heart disease.[15,16] Determining the likelihood of each disease may help interpret the RHC results and improve the reliability of PCWP measurements. Although PCWP is a widely used diagnostic measurement, LVEDP is not analyzed in the majority of hemodynamic laboratories. Therefore, we sought to compare the diagnostic accuracy of end-expiratory PCWP and LVEDP in patients suspected of having PH.

Methods

Patients

We reviewed the hemodynamic data from all patients who underwent simultaneous right- and left-side heart catheterizations as part of their evaluations for suspected PH at the Federal University of São Paulo PH referral center between January 2006 and August 2011. According to the institutional protocols in place during this period, all patients suspected of having PH were referred for simultaneous right- and left-side heart catheterizations. All patients followed a standardized diagnostic algorithm in accordance with current PH guidelines,[1,2] prior to RHC indication. Echocardiography, pulmonary function tests, blood-gas analyses, serum brain natriuretic peptide (BNP) levels, human immunodeficiency virus (HIV) serology and other specific tests guided by clinical suspicion were carried out systematically. Based on RHC, patients were stratified according to their hemodynamic pattern, on which the pre-capillary pattern included patients from Groups 1, 3, 4 and 5.

None of the patients had mitral stenosis, or prosthetic mitral valves, or was under mechanical ventilation during the examination. One patient had a prosthetic aortic valve. Patients with unrepaired congenital heart disease were excluded from the analysis. This study was approved by the institutional medical ethics committee.

Hemodynamic measurements

Catheterizations were performed by 6 experienced physicians according to the operational protocols of the hospital's cardiac catheter laboratory. All physicians were under the supervision of the same hemodynamicist (C.M.C.S.). Right- and left-side heart measurements were taken via the right femoral vein and artery, respectively. A 6-French catheter with a terminal balloon was inserted into the pulmonary artery, and a 5-French pigtail catheter was inserted into the aorta. Hemodynamic recordings were taken while placing the catheter in the pulmonary artery, and its progression to the wedge position was guided by fluoroscopic visualization and confirmed by identifying the characteristic waveform. PCWP was measured by determining the average of the *a* wave, which was identified as the atrial systole based on a simultaneous electrocardiogram. Next, the pigtail catheter was advanced into the left ventricle (LV) to measure LVEDP, which was defined as the LV pressure immediately preceding the onset of the ventricular contraction and was measured at the *C* point, representing the rise in the ventricular pressure resulting from atrial contraction.[17]

Zero pressure calibration was performed at the mid-thoracic level with the patient placed in a supine position. Pressure measurements were taken at end-expiration and were the average of at least 3 ventilatory cycles. No patient had a heart rate of >130 beats/min and all were in sinus rhythm. Cardiac output was determined using Fick's method with an estimated oxygen consumption ($125 \times$ body surface area).[18] No patient had cardiac output determined by the thermodilution method. Pulmonary vascular resistance (PVR) was expressed in Wood units (WU).

Statistical analysis

Values are expressed as the mean $\pm$ standard deviation (SD), unless otherwise stated. The diagnostic performance of PCWP vs LVEDP was evaluated using a 2×2 contingency table. Between-group comparisons were performed using one-way analysis of variance (ANOVA). Analyses of sensitivity, specificity, predictive value and likelihood ratio were performed on the PCWP measurements, considering an LVEDP value of ≤ 15 mm Hg as the diagnostic standard. The accuracy of using a PCWP measurement of ≤ 15 mm Hg as the threshold for correctly diagnosing patients with pre-capillary PH was determined by calculating the proportion of patients who would have been reclassified had they been diagnosed based on LVEDP (≤ 15 mm Hg). We used Pearson's correlation coefficient to determine the correlation and Bland-Altman analysis to determine the agreement between the two measurements.[19] $p < 0.05$ was considered significant. Statistical analyses was performed using SPSS software, version 19.0.0 (IBM, Armonk, NY).

Results

Baseline characteristics

A total of 206 patients underwent simultaneous right- and left-side heart catheterizations at our institution between 2006 and 2011. All patients had LVEDP measurements; 69 patients had no PCWP measurements to consult. Fifteen patients had unrepaired congenital heart disease and were excluded from the analysis. There were 122 patients with both LVEDP and PCWP measurements. Among these patients, 105 (86%) were diagnosed with PH, 83 (79%) of whom were diagnosed with a pre-capillary pattern (Figure 1). The different etiologies for PH included idiopathic PAH (IPAH) ($n = 19$), collagen vascular disease ($n = 20$), schistosomiasis ($n = 5$), HIV infection ($n = 4$), portal hypertension ($n = 2$) and congenital heart disease ($n = 18$). Eleven patients had PH because of parenchymal lung diseases, and 16 had chronic thromboembolic disease. Two patients had multifactorial etiologies (chronic renal failure on hemodialysis). Eight patients had left-heart disease as their sole etiology for PH.