A Novel Non-Invasive Method of Estimating Pulmonary Vascular Resistance in Patients With Pulmonary Arterial Hypertension

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Background: The assessment of pulmonary vascular resistance (PVR) plays an important role in the diagnosis and management of pulmonary arterial hypertension (PAH). The main objective of this study was to determine whether the noninvasive index of systolic pulmonary arterial pressure (SPAP) to heart rate (HR) times the right ventricular outflow tract time-velocity integral (TVI_{RVOT}) (SPAP/[HR $\times$ TVI_{RVOT}]) provides clinically useful estimations of PVR in PAH.

Methods: Doppler echocardiography and right-heart catheterization were performed in 51 consecutive patients with established PAH. The ratio of SPAP/(HR $\times$ TVI_{RVOT}) was then correlated with invasive indexed PVR (PVRI) using regression and Bland-Altman analysis. Using receiver operating characteristic curve analysis, a cutoff value for the Doppler equation was generated to identify patients with PVRI $\geq$ 15 Wood units (WU)/m^2.

Results: The mean pulmonary arterial pressure was 52 $\pm$ 15 mm Hg, the mean cardiac index was 2.2 $\pm$ 0.6 L/min/m^2, and the mean PVRI was 20.5 $\pm$ 9.6 WU/m^2. The ratio of SPAP/(HR $\times$ TVI_{RVOT}) correlated very well with invasive PVRI measurements (r = 0.860; 95% confidence interval, 0.759-0.920). A cutoff value of 0.076 provided well-balanced sensitivity (86%) and specificity (82%) to determine PVRI > 15 WU/m^2. A cutoff value of 0.057 increased sensitivity to 97% and decreased specificity to 65%.

Conclusion: The novel index of SPAP/(HR $\times$ TVI_{RVOT}) provides useful estimations of PVRI in patients with PAH. (J Am Soc Echocardiogr 2009;22:523-529.)

Keywords: Pulmonary hypertension, Doppler echocardiography, Hemodynamics, Noninvasive imaging

Over the past 25 years, several studies have demonstrated that Doppler echocardiography provides reliable estimates of systolic pulmonary arterial pressure (SPAP).[1-11] More recently, investigators have proposed simple noninvasive methods of estimating pulmonary vascular resistance (PVR) in patients with heart failure or hypertension. Abbas et al[11] described a simple method of estimating systemic PVR on the basis of the ratio of peak tricuspid regurgitant velocity to the right ventricular (RV) outflow tract (RVOT) time-velocity integral (TVI_{RVOT}). Their novel index provides good estimations of invasive PVR in patients with pulmonary artery catheters in place (mean pulmonary arterial pressure [MPAP], 25 mmHg).[12,13] Scapellato et al[10] described a method of estimating PVR using a ratio of systolic time interval involving the preejection period (PEP), acceleration time (AcT), ejection time, and total systolic time (TT); index = ([PEP/AcT]/TT).

These methods have the advantage of being simple and easily applicable. However, they may not be as reliable in patients with pulmonary arterial hypertension (PAH), and for both of these methods, validation at high values of PVR was limited. The main objective of our study was to investigate whether the index of SPAP/(heart rate [HR] $\times$ TVI_{RVOT}) would provide better estimations of PVR than existing methods.[10,11,13-16] Compared with the method of Abbas et al,[11] the new index would have the advantage of taking into account the contribution of right atrial pressure (RAP) and HR, which may both vary significantly in patients with PAH. The secondary objective of the study was to determine whether estimations of RAP based on inferior vena cava (IVC) size and collapse index are reliable in patients with PAH.

METHODS

After approval of the institutional review board, adult patients with established diagnoses of PAH and scheduled right-heart catheterization as part of their routine care were screened for inclusion in the study. Patients with significant systemic-to-pulmonary shunting (pulmonary output/systemic output > 1.5) or Eisenmenger physiology were excluded. Echocardiography was performed 1 to 3 hours before right-heart catheterization. The physician sonographers (F.H., A.-S.B.) were blinded to the results of the invasive measurements.

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Population

A total of 55 consecutive patients were screened for inclusion in the study, with the subsequent exclusion of 4 patients with Eisenmenger physiology. The final study population included 51 patients with established diagnoses of PAH undergoing right-heart catheterization. The majority of patients were women (n = 35 [69%]), with an average age of 49 ± 11 years. MPAP was 52 ± 15 mm Hg, mean PVR was 11.0 ± 5.1 Wood units (WU), and mean PVR indexed to body surface area (PVRI) was 20.6 ± 9.6 WU/m^2 (Table 1).

Invasive Measurements

A Swan-Ganz catheter was used for pressure and flow measurements. Pulmonary and systemic blood flows were calculated using the Fick method and assumed oxygen consumption (La Farge table). PVR was calculated using the equation PVR = MPAP − pulmonary capillary wedge pressure (PWCP)/pulmonary output. Volume loading was not administered to patients prior to invasive measurements.

Echocardiography

Comprehensive two-dimensional Doppler echocardiography was performed using the Philips iE33 ultrasound system (Philips Medical Systems, Andover, MA) according to guidelines of the American Society of Echocardiography.[17,18] Doppler studies were performed with a combined two-dimensional and Doppler ultrasonograph with a 5-MHz transducer. The sweep speed for Doppler-derived velocity and time interval measurements was 100 to 150 mm/s, and all measures were averaged over ≥5 beats in patients in sinus rhythm and over ≥10 beats for patients with atrial arrhythmias. Maximal Doppler velocities were measured at the peak modal frequency and at a minimal insonation angle. Doppler gain was also carefully adjusted to avoid the overestimation of maximal velocities.

PVRI was estimated using 4 different methods. The first method is based on the novel index of SPAP/(HR × TVI_{RVOT}). RV systolic pressure was estimated using the transtricuspid regurgitation gradient according to the modified Bernoulli equation and the estimated RAP. In the absence of a significant transpulmonary systolic gradient (<5 mm Hg), SPAP was approximated by RV systolic pressure. TVI_{RVOT} (in centimeters) was obtained by placing a 1-mm to 2-mm pulsed-wave Doppler sample volume in the proximal RVOT just before the pulmonary valve when imaged from the parasternal short-axis view. The sample volume was placed so that the minimal closing but not opening click of the pulmonary valve was visualized.

The second method is based on the ratio of peak tricuspid regurgitant velocity to TVI_{RVOT}, as described by Abbas et al.[11] The third method corresponds to the arithmetic method described by Selimovic et al,[7] in which PVR was derived from individual estimations according to the formula PVR = (PAP_{mean} − PCWP)/cardiac output. Because PCWP is generally <15 mm Hg in patients with PAH, PCWP was assumed to be 10 mm Hg in the study population.[1] MPAP was derived from the estimated SPAP and diastolic pulmonary arterial pressure (DPAP) according to the formula MPAP = DPAP + 1/3(SPAP − DPAP). DPAP estimations were based on the measurement of the tricuspid regurgitation gradient at the time of pulmonary valve opening (DPAP = 4[tricuspid gradient at the time of pulmonary valve opening]^2 + estimated RAP). At the time of pulmonary valve opening, RV end-diastolic pressure and pulmonary diastolic pressure are equal. The timing of pulmonary valve opening was determined as the time from the beginning of the QRS complex to the onset of systolic pulmonary flow (on pulsed-wave Doppler). This time interval was then superimposed onto the velocity spectrum of the transtricuspid regurgitation signal (Figure 1). To be considered representative, the RR interval difference between the pulmonary and tricuspid signals had to be <10%. Cardiac output was calculated as the product of HR and stroke volume. Stroke volume was calculated as the product of the cross-sectional area and the velocity-time integral of the left ventricular outflow tract. In the absence of shunt physiology or aortic regurgitation, systemic flow was considered equivalent to effective pulmonary flow. Cardiac output was not derived from the RVOT, because accurate measurements of the RVOT are difficult to obtain in adults.

The fourth method is based on the study of Scapellato et al,[10] in which PVR was estimated using the ratio of systolic time interval involving PEP, AcT, ejection time, and TT; index = ([PEP/AcT]/TT). PEP was defined as the distance between the onset of tricuspid regurgitation and the onset of pulmonary systolic flow. In the presence of elevated SPAP and PVR, tricuspid regurgitation may well continue after the premature closure of the pulmonary valve (ie, the premature

Table 1 Clinical characteristics of study patients

Characteristic	Value
Age (y)	49 ± 11
Women/men	35 (69%)/16 (31%)
Etiology of PAH	
Idiopathic	24 (47%)
Stimulant associated	13 (25%)
Connective tissue disease	8 (16%)
Portopulmonary	6 (12%)
NYHA class	
I	1
II	6
III	40
IV	4
Rhythm	
Sinus rhythm	49 (96%)
Atrial arrhythmia	2 (4%)
SPAP (mm Hg)	85 ± 24
MPAP (mm Hg)	52 ± 15
PCWP (mm Hg)	9 ± 4
RAP (mm Hg)	8 ± 5
Cardiac output (L/min)	4.2 ± 1.2
Cardiac index (L/min/m^2)	2.2 ± 0.6
PVRI (WU/m^2)	20.5 ± 9.6
PVR (WU)	11.0 ± 5.1
RV end-diastolic area (cm^2)	33 ± 11
RV fractional area change (%)	27 ± 10
Tricuspid annular plane systolic excursion (cm)	1.9 ± 0.5
TR	
None	3
Mild	21
Moderate	19
Severe (3-4+)	8
PR	
None	15
Mild	30
Moderate	6
Severe	0
LVEF (%)	59 ± 8
NT-BNP (pg/mL)	870 ± 920

LVEF, Left ventricular ejection fraction; *NT-BNP*, N terminal B-type natriuretic peptide; *NYHA*, New York Heart Association; *PR*, pulmonary regurgitation; *TR*, tricuspid regurgitation.