A Simple Method for Noninvasive Estimation of Pulmonary Vascular Resistance

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OBJECTIVES

We sought to test whether the ratio of peak tricuspid regurgitant velocity (TRV, ms) to the right ventricular outflow tract time-velocity integral (TVI RVOT, cm) obtained by Doppler echocardiography (TRV/TVI RVOT) provides a clinically reliable method to determine pulmonary vascular resistance (PVR).

BACKGROUND

Pulmonary vascular resistance is an important hemodynamic variable used in the management of patients with cardiovascular and pulmonary disease. Right-heart catheterization, with its associated disadvantages, is required to determine PVR. However, a reliable noninvasive method is unavailable.

METHODS

Simultaneous Doppler echocardiographic examination and right-heart catheterization were performed in 44 patients. The ratio of TRV/TVI RVOT was then correlated with invasive PVR measurements using regression analysis. An equation was modeled to calculate PVR in Wood units (WU) using echocardiography, and the results were compared with invasive PVR measurements using the Bland-Altman analysis. Using receiver-operating characteristics curve analysis, a cutoff value for the Doppler equation was generated to determine PVR >2WU.

RESULTS

As calculated by Doppler echocardiography, TRV/TVI RVOT correlated well (r = 0.929, 95% confidence interval 0.87 to 0.96) with invasive PVR measurements. The Bland-Altman analysis between PVR obtained invasively and that by echocardiography, using the equation: PVR = TRV/TVI RVOT × 10 + 0.16, showed satisfactory limits of agreement (mean 0 ± 0.41). A TRV/TVI RVOT cutoff value of 0.175 had a sensitivity of 77% and a specificity of 81% to determine PVR >2WU.

CONCLUSIONS

Doppler echocardiography may provide a reliable, noninvasive method to determine PVR. (J Am Coll Cardiol 2003;41:1021–7) © 2003 by the American College of Cardiology Foundation

Pulmonary vascular resistance (PVR) is a hemodynamic variable that contributes to the management of patients with advanced cardiovascular and pulmonary conditions. It is used to evaluate the response to pharmacologic therapy in patients with congestive heart failure (1). Also, PVR is an essential component of heart- and liver-transplant candidate evaluation (2) and in predicting both early and late clinical outcomes (3,4). Moreover, PVR is an important variable in deciding the surgical outcome of patients with congenital heart disease (5). Pulmonary vascular resistance is calculated invasively by the ratio of transpulmonary pressure gradient (Δp) to transpulmonary flow (Qp) (6).

Doppler echocardiography has significantly impacted clinical medicine by its ability to determine intracardiac hemodynamics noninvasively. Since flow and pressure variables can be measured, we hypothesized that a measure of PVR might be accurately obtained by Doppler-derived variables.

METHODS

This study was approved by the Institutional Review Board. A sample of 44 patients who had a pulmonary artery catheter in place was evaluated. Each subject provided written, informed consent. The patients’ demographic and clinical characteristics are shown in Table 1. Doppler and invasive measurements were obtained within 45 min of each other. Tricuspid regurgitation grade >2+, as determined by Doppler echocardiography, was exclusionary.

Invasive measurements. A Swan-Ganz catheter was used for hemodynamic measurements. Pulmonary capillary wedge pressure (PCWP), pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure, and mean pulmonary artery pressure (MPAP) were measured.

Cardiac output was calculated by thermodilution as a mean of three consecutive measurements not varying by more than 10%.

The PVR in Wood units (WU) was calculated using the equation:

\[ PVR = \frac{MPAP - PCWP}{\text{cardiac output}} \]

Doppler measurements. Doppler echocardiography was performed using the GE Vivid FiVe (GEMS, Milwaukee,
Abbreviations and Acronyms

- CI = confidence interval
- ICC = intraclass correlation coefficient
- MPAP = mean pulmonary artery pressure
- PASP = pulmonary artery systolic pressure
- PCWP = pulmonary capillary wedge pressure
- PVR = pulmonary vascular resistance
- PVR\textsubscript{CATH} = invasive pulmonary vascular resistance
- PVR\textsubscript{ECHO} = pulmonary vascular resistance calculated by echocardiography
- Q\textsubscript{p} = transpulmonary flow
- Δp = transpulmonary pressure gradient
- RAP = right atrial pressure
- TRV = peak tricuspid regurgitant velocity
- TVI\textsubscript{RVOT} = right ventricular outflow tract time-velocity integral
- WU = Wood units

Wisconsin) or Acuson Sequoia (Acuson, Mountain View, California) ultrasound systems.

The right ventricular outflow tract time-velocity integral (TVI\textsubscript{RVOT}) (cm) was obtained by placing a 1- to 2-mm pulsed wave Doppler sample volume in the proximal right ventricular outflow tract just within the pulmonary valve when imaged from the parasternal short-axis view. The sample volume was placed so that the closing but not opening click of the pulmonary valve was visualized. Pulsed wave Doppler was used rather than continuous wave Doppler to eliminate cases with increased pulmonary velocities secondary to either pulmonary valve or peripheral pulmonary artery stenosis.

Continuous wave Doppler was used to determine the peak tricuspid regurgitant velocity (TRV) (m/s). The highest velocity obtained from multiple views was used. Agitated saline was used to enhance suboptimal Doppler signals (7). In patients with atrial fibrillation (n = 3), the average of five measurements were used. The TRV/TVI\textsubscript{RVOT} ratio was then calculated (Figs. 1A, 1B, 2A, and 2B).

Individuals in whom both invasive measurements and Doppler variables were obtained were blinded to each other’s calculations.

**Statistical analysis.** SAS version 8.0 software was used for statistical computations (SAS Institute Inc., Cary, North Carolina). Linear regression analysis was generated between invasive PVR (WU) (PVR\textsubscript{CATH}) and TRV/TVI\textsubscript{RVOT}, and Pearson’s correlation coefficient was obtained. A regression equation was derived in which a value for PVR (WU) was modeled based on TRV/TVI\textsubscript{RVOT} (PVR\textsubscript{ECHO}). Furthermore, a plot of PVR\textsubscript{ECHO} compared with PVR\textsubscript{CATH} was generated using the Bland-Altman analysis.

Using receiver-operating characteristics curves, a dichotomized PVR was analyzed based on TRV/TVI\textsubscript{RVOT}. A logistic model was generated, and a cutoff value for TRV/TVI\textsubscript{RVOT} with balanced sensitivity and specificity values was obtained to predict elevated PVR values (PVR > 2 WU). Confidence intervals were calculated for the sensitivity and specificity values by using the exact binomial method. Another cutoff value was then generated to determine a higher specificity of predicting PVR > 2 WU.

Twenty percent of the Doppler images were re-evaluated to quantify the intra- and interobserver reliability by calculating the intraclass correlation coefficient (ICC = σ\textsuperscript{2}\textsubscript{patients}/[σ\textsuperscript{2}\textsubscript{patients} + σ\textsuperscript{2}\textsubscript{error}]). Confidence intervals for the ICC were calculated using the method of Shrout and Fleiss (8).

**RESULTS**

Thirteen of our patients had increased right atrial pressure (RAP) (>8 mm Hg), whereas 20 had elevated mean left atrial pressure (PCWP > 12 mm Hg).

The linear regression analysis between PVR\textsubscript{CATH} and TRV/TVI\textsubscript{RVOT} revealed a good correlation (r = 0.93, 95% confidence interval [CI] 0.87 to 0.96) for all patients (Fig. 3). The equation derived from the linear regression was:

\[\text{PVR}_{\text{ECHO}} = 0.1618 + 10.006 \times \text{TRV/TVI}_{\text{RVOT}} + \text{error}\]

Patients with elevated PCWP and RAP were evenly distributed among the patient population (Fig. 4).

Using the Bland-Altman analysis, PVR\textsubscript{ECHO} measurements derived from this equation showed satisfactory limits of agreement with PVR\textsubscript{CATH} (Fig. 5), with a mean value of 0.0 ± 0.41 (SD). The PVR\textsubscript{ECHO} and PVR\textsubscript{CATH} values were well within one standard deviation (Figs. 1 and 2).

The area under the receiver-operating characteristics curve was calculated at 0.916 (Fig. 6). A TRV/TVI\textsubscript{RVOT} cutoff value of 0.175 provided the best-balanced sensitivity (77%; 95% CI 46% to 96%) and specificity (81%; 95% CI 63% to 93%) to determine PVR > 2 WU.

A TRV/TVI\textsubscript{RVOT} cutoff value of 0.2 provided a spe-
Figure 1. Images showing peak tricuspid regurgitant velocity (TRV) and right ventricular outflow time-velocity integral (TVI_{RVOT}) in a patient with normal pulmonary vascular resistance (PVR). (A) TRV is 2.86 m/s. (B) TVI_{RVOT} is 20.8 cm. The ratio of TRV/TVI_{RVOT} = 2.86/20.8 = 0.1375. PVRECHO = 0.1375 × 10 + 0.16 = 1.53 Woods units (WU). This patient’s invasive PVR measurement was within 0.4 WU of the echocardiographic value (PVRCATH = 1.3 WU). PVRECHO = PVR in WU calculated based on the linear regression equation in which a value for PVR in WU was modeled based on TRV/TVI_{RVOT}, PVRCATH = invasive PVR.

Figure 2. Images showing TRV and TVI_{RVOT} in a patient with elevated PVR. (A) TRV is 3.64 m/s. (B) TVI_{RVOT} shows a clear deceleration of pulmonary flow before the pulmonic valve closure click and is calculated at 6.3 cm. The ratio of TRV/TVI_{RVOT} = 3.64/6.3 = 0.56. PVRECHO = 0.56 × 10 + 0.16 = 5.76 WU. This patient’s invasive PVR measurement is also within 0.4 WU of the echocardiographic value (PVRCATH = 6.0 WU). Abbreviations as in Figure 1.
Figure 3. Linear regression analysis between $\text{PVR}_{\text{CATH}}$ and $\text{TRV/TVI}_{\text{RVOT}}$. The circle highlights the PVR cutoff value of 2 WU ($r = 0.929$, 95% confidence interval 0.87 to 0.96). Abbreviations as in Figure 1.

Figure 4. Linear regression analysis between $\text{PVR}_{\text{CATH}}$ and $\text{TRV/TVI}_{\text{RVOT}}$. The correlation remained robust among all groups of patients. Patients with normal left atrial pressure (LAP) and right atrial pressure (RAP) (open squares), elevated LAP and RAP (solid squares), elevated LAP and normal RAP (solid triangles), and elevated RAP and normal LAP (open triangles) were evenly distributed among the study population. Abbreviations as in Figure 1.
Figure 5. Bland-Altman analysis showing the limits of agreement between $PVR_{ECHO}$ and $PVR_{CATH}$. Abbreviations as in Figure 1.

Figure 6. Receiver-operating characteristics curve. A $TRV/TVI_{RVOT}$ cutoff value of 0.175 provided the best-balanced sensitivity (77%) and specificity (81%) to determine patients with a $PVR$ value $>2$ WU. (Area under the curve = 0.916.) Abbreviations as in Figure 1.
Doppler parameters to evaluate PVR (11,15–PVR. The ICC and CI for inter- and intraobserver reliabilities were 0.99 (95% CI 0.95 to 1.0) and 0.99 (95% CI 0.98 to 1.0), respectively.

DISCUSSION

Pulmonary vascular resistance is directly related to \( \Delta p \) and inversely related to \( Q_p \) (6). Thus, TRV and TVI\(_{RVOT} \) can be used as correlates of \( \Delta p \) and \( Q_p \), respectively (9,10). As PVR increases, changes in TVI\(_{RVOT} \) and TRV occur in opposite directions (9,11). In accordance with the Bernoulli equation, TRV will increase as the PASP increases (9,12,13). However, both hyperdynamic flow states and true pulmonary vascular disease can elevate PASP; therefore, a measure of \( Q_p \) is crucial. As PVR increases, there is earlier and enhanced reflection of the pressure wave propagated from the RVOT into the pulmonary trunk. This is reflected by a conformational change in TVI\(_{RVOT} \), where mid-systolic notching and premature deceleration of pulmonary flow occur, leading to a decreased right ventricular ejection time (11,14–17). The Doppler-derived ratio of TRV/TVI\(_{RVOT} \) was hence hypothesized as a good correlate of PVR.

Previous investigators have described the use of various Doppler parameters to evaluate PVR (11,15–23). These efforts have focused primarily on the timing of events such as right ventricular pre-ejection and ejection times, acceleration time of the RVOT velocity, and flow propagation velocities. These studies support the notion that a conformational change in TVI\(_{RVOT} \) occurs with increasing PVR. However, these methods require obtaining additional information than routinely acquired with less robust test characteristics.

Based on our results, we propose a simplified equation for noninvasive calculation of PVR:

\[
PVR(WU) = 10 \times \text{TRV/TVI}_{RVOT}
\]

We also propose that in patients with increased PASP on Doppler echocardiography and TRV/TVI\(_{RVOT} >0.2 \), an elevated PVR is suggested, and these patients may require further invasive workup. However, in patients with TRV/TVI\(_{RVOT} <0.2 \), PVR values are likely to be normal, even in the presence of Doppler evidence of increased PASP.

Study limitations. Proper alignment of the ultrasound beam is a crucial factor to ensure adequate determination of TRV and TVI\(_{RVOT} \).

Detection of TRV is crucial. The TRV signal could not be obtained in only one patient and was excluded. Agitated saline and ultrasound contrast agents can also enhance the Doppler signal when needed (7).

A correction for heart rate in TVI\(_{RVOT} \) was not made, as all patients had a heart rate between 60 and 100 beats/min.

Heart rate correction may be required for extreme variations.

Possible confounding hemodynamic variables that were not included in our Doppler equation include correlates of RAP and PCWP. Patients in whom the results of this study may be beneficial will likely have elevated RAP and PCWP. However, despite the presence of these patients in our study, the correlation remained robust (Fig. 4).

Thermoludation was used to calculate cardiac output, which may be inaccurate in the presence of moderate or severe tricuspid regurgitation; thus, those patients were excluded. Further studies will be needed to determine the applicability of this formula to those groups of patients in whom the Fick method was used for calculation of cardiac output.

Anatomic variations of the right-heart structures may interfere with Doppler variables. Further studies will be needed to determine the applicability of this formula to patients with congenital heart disease, shunts, or pulmonary artery dilation who were not included in our study.

Conclusions. Noninvasive determination of PVR is possible using variables that are routinely obtained by Doppler echocardiography. Increased PASP may be secondary to increased transpulmonary flow or abnormal PVR. Patients with TRV/TVI\(_{RVOT} <0.2 \) are likely to have low PVR values (<2 WU), and pulmonary vascular disease may be excluded despite increased PASP by Doppler.

We propose that the term “increased pulmonary pressures” may be preferred to describe all patients with increased PASP. However, the term “pulmonary hypertension” may be more appropriately used in patients who also have increased PVR.

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