Echocardiography based estimation of pulmonary vascular resistance in patients with pulmonary hypertension: a simultaneous Doppler echocardiography and cardiac catheterization study

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Aims

Pulmonary vascular resistance (PVR) is an important measurement for the diagnosis of patients with pulmonary hypertension (PH) but needs accurate determination of mean pulmonary artery pressure (PAMP). We aimed to test the accuracy of a Doppler-derived measurement of PVR, using the conventional invasive equation in patients with PH.

Methods and results

We investigated 30 patients undergoing right heart catheterization (RHC), mean age 62 ± 13 years, 21 females, with different diseases; idiopathic pulmonary arterial hypertension (PAH) (n = 5), associated PAH (n = 16), chronic thromboembolic PH (n = 6), interstitial lung disease (n = 2), and after closure of an atrial septal defect (n = 1). Patients with impaired left ventricular systolic function (EF < 50%) or elevated pulmonary capillary wedge pressure (PCWP > 15 mmHg on RHC) were excluded. We used the formula: PAMP = PASPecho × 0.61 + 2 mmHg, where PASPecho is the peak tricuspid regurgitation pressure drop + 10 or 7 mmHg. Pulmonary vascular resistance was then calculated as PAMP echo - PCWP/cardiac output. Pulmonary capillary wedge pressure was estimated at 10 mmHg in all cases. The Doppler-derived estimation of PVR echo was achievable in 90% of patients, in whom accurate calculation of PAMP was obtainable. Pulmonary vascular resistance echo individual values strongly correlated with those from RHC (r = 0.85, P < 0.001 and r = 0.87, P < 0.001 for the two estimated values for right atrial pressure, respectively). The regression equation using this formula was PVRrhc = 0.95 × PVRecho - 0.29, and the regression line was close to identity. The Bland–Altman plot showed a good agreement between PVR echo and PVRrhc values, with a mean difference of −0.66 ± 2.1 Wood unit.

Conclusion

The proposed Doppler-derived formula for estimating PVR based on the conventionally used invasive equation strongly correlates with invasive gold standard measures.

Keywords

Doppler echocardiography • Pulmonary vascular resistance • Right heart catheterization

Introduction

Estimation of pulmonary artery pressure (PAP) is important in refining the diagnosis, optimizing follow-up after treatment and predicting prognosis in patients with pulmonary hypertension (PH). ¹ Although non-invasive estimation of PAP by Doppler echocardiography is well established in clinical practice,² it does not account for variations in the flow.³ A more accurate measurement

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of PH is thus needed. Pulmonary vascular resistance (PVR) reflects better the disease process; hence its measurement should account for most accurate disease assessment. Furthermore, PVR is known as a strong predictor for reduced exercise capacity in thromboembolic patients after thrombendarterectomy. Right heart catheterization (RHC) is the gold standard investigation for determining pulmonary haemodynamics including vascular resistance, but its routine use is limited by its invasive nature and incurring cost. Other non-invasive resting5–9 and exercise10 methods have been proposed but with limited accuracy.11 The aim of this study was therefore to test a new Doppler-derived method, based on conventional invasive measurement in estimating PVR in patients with PH.

Methods

We investigated 30 patients with PH of different aetiologies, undergoing diagnostic and follow-up RHC of a mean age 62 ± 13 years and 21 were females. The aetiology of PH was classified according to guidelines12 as: (i) idiopathic PAH (n = 5), (ii) associated PAH (n = 16), (iii) chronic thromboembolic type of PH (n = 6), (iv) PH due to lung disease (n = 2), and (v) closed atrial septal defect (n = 1). Patients were excluded from the study if they had signs of impaired left ventricular (LV) systolic function, as reduced ejection fraction (EF < 50%) or elevated mean pulmonary capillary wedge pressure (PCWP > 15 mmHg on RHC).

Right heart catheterization

Venous access was obtained by inserting an introducer in a medial cubital vein or in the femoral vein. A retrograde catheterization was then performed using a Swan-Ganz® Standard Thermodilution Catheter (Edwards Lifesciences). Mean right atrial pressure (RAP), systemic and end-diastolic right ventricular pressures, pulmonary artery systolic, mean and diastolic pressures (PASP, PAMP and PADP, respectively), and PCWP were measured. Blood samples for estimation of oxygen saturation were drawn from the superior and inferior caval veins, as well as right atrium, and that from the pulmonary and femoral arteries were used for screening for intra-cardiac shunts. Cardiac output was determined by thermodilution. Pulmonary vascular resistance was calculated from the equation PAMP – PCWP (trans-pulmonary gradient) divided by CO.

Echocardiographic examination

Echocardiographic examination was performed using a Vivid 7 system (GE Medical Systems, Horten, Norway) equipped with an adult 1.5–4.3 MHz phased array transducer. Standard views from the parasternal long and short axis and apical four-chamber views were used.13 Flow velocities were obtained using pulsed and continuous wave Doppler techniques as proposed by the American Society of Echocardiography.14,15 Stroke volume and COecho measurements were made at the level of the LV outflow tract because of the known limitations of acquiring accurate respective measurements from the right ventricular outflow tract (RVOT).15,16 Pulmonary artery flow was measured by placing the pulsed wave Doppler sample volume at the centre of the transpulmonary valve jet, obtained from the short-axis view. Retrograde systolic tricuspid flow was obtained from either parasternal right ventricular inflow view or apical four-chamber view for measuring peak tricuspid pressure drop using continuous wave Doppler. Right ventricular long-axis function (strain) was studied using speckle tracking echocardiography technique (STE). All Doppler recordings were made at a sweep speed of 50–100 mm/s with a superimposed ECG (lead II). Off-line analysis was made using a commercially available software system (General Electric, EchoPac version 5.0.1, Waukesha, Wisconsin, US) and mean of three consecutive tracings were calculated. The study protocol was approved by the Regional Ethics Committee of Umeå (DNPI 07–092M) and all subjects signed an informed consent.

Measurements

Pulmonary vascular resistance was estimated using our proposed equation: $PVR = \frac{PAMP_{echo} \times CO_{echo}}{PCWP}$ where $PAMP_{echo}$ is calculated as PASPecho $\times$ 0.61 $+ 2$ mmHg, according to Chemla et al.,17 with $PASP_{echo} = peak$ tricuspid systolic retrograde pressure drop $+ 10$ and $7$ mmHg (two proposed estimated values for RAP). Pulmonary capillary wedge pressure of $10$ mmHg was also estimated for all cases. These results were compared with other previously published methods:

(i) $PAMP – PCWP/CO_{echo}$; where $PAMP$ was calculated as PADP $+ 0.33$ (PASP-PADP) and PADP which was calculated as $4 \times$ (tricuspid systolic pressure drop at the time of pulmonary valve opening)$^2$ + estimated RAP of $10$.6

(ii) The ratio of tricuspid peak pressure drop/RV outflow tract velocity time integral.5

(iii) PASP($HR \times RVOT$ velocity time integral).18

We also measured RV systolic deformation (strain) at the basal, mid-cavity and apical segments using STE.9

Statistical analysis

Normally distributed continuous data were expressed as mean ± standard deviation. Relationships between variables were tested using Pearson’s correlation. Partial correlations were made to control for age, sex and type of PH. The Bland–Altman test was used to evaluate the mean difference ± 2SD, between echocardiography and RHC. The statistical software package (PASW Statistics version 18) was used for all calculations.

Results

Clinical characteristics are shown in Table 1. The majority of patients were females and had PH, in most cases associated with connective tissue disease.

Relationships between invasive and new Doppler-derived measure of pulmonary vascular resistance

The new method (Lindqvist) was feasible in 90% of the cases and the results obtained correlated closely with PVRecho $\times 0.85$, $P < 0.001$) with a regression equation of $0.95 \times PVRecho - 0.29$ and the regression line close to identity (Figure 1A). The Bland–Altman plot showed an excellent agreement between PVRecho and PVRecho, with a bias of $-0.66 \pm 2.1$ (Figure 1B). The sensitivity and specificity of the method for identifying patients with PVR > 3 WU were 100 and 63%, respectively, and negative and positive predictive values were 100 and 86%, respectively (Table 2). Using an estimated RAP of 7 mmHg resulted in a stronger correlation ($r = 0.87, P < 0.001$) with a regression equation of $1 \times PVRecho - 0.08$ (Figure 1C). The Bland–Altman plot showed an even tighter agreement between PVRecho and PVRecho with a bias of $-0.10 \pm 2.0$ (Figure 1D). The sensitivity and specificity of the method for identifying patients with PVR > 3 WU were 95 and
The linear regression equation was \( r = 0.74 \), \( P < 0.001 \) in predicting \( \text{PVR}_{\text{rhc}} \). The regression equation was \( 22.5 \times \text{PVRecho} + 21.0 \) WU. The sensitivity and specificity using a cut-off value of \( < 0.04 \) for identifying patients with elevated PVR was 94 and 100%, respectively, and the negative and positive predictive values were 88 and 100%, respectively (Table 2).

Assessment of RV strain function using STE at mid-segment showed an acceptable feasibility of 77% but only modest correlation with \( \text{PVR}_{\text{rhc}} \) (\( r = 0.59, P < 0.001 \)). The regression equation was \( \text{PVR}_{\text{rhc}} = \text{RV strain} \times 0.20 + 2 \) (Figure 2D). The Bland–Altman analysis showed a low agreement between \( \text{PVRecho} \) and \( \text{PVR}_{\text{rhc}} \), bias of \( 6.4 \pm 4.1 \) WU. The sensitivity and specificity using a cut-off value of \( < -20\% \) for identifying patients with elevated PVR was 88 and 63%, respectively, and the negative and positive predictive values were 71 and 82%, respectively (Table 2).

The correlations between Doppler echocardiography and RHC were not influenced by age, sex, or aetiology of PH.

### Findings

This study shows that our Doppler-derived equation for estimating PVR proved very accurate in identifying patients with raised PVR. In the patient’s group, as a whole, results of individual patients strongly correlated with the respective catheter-based measurements of PVR as well as CO. Finally, this correlation was not influenced by age, sex, or type of PH.

### Data interpretation

Right heart catheterization has been the gold standard method for confirming the diagnosis of PH, providing accurate measurements of PAP and pulmonary vascular resistance. However, the method is limited to be used in the regular follow-up of patients because of its invasive nature and potential risks, despite being rare. Doppler echocardiography has become the investigation of choice for studying cardiac structure and function as well as estimating intra-cardiac and transvalvular pressures. Doppler echocardiography has particularly revolutionized our cardiology practice for assessing PAP non-invasively. Retrograde transtricuspid pressure drop using continuous wave Doppler is a solid routine estimate of peak PAP in most patients undergoing echocardiographic examination. It has, however, certain limitations particularly when RAP rises, right ventricular systolic function drops and tricuspid regurgitation becomes severe. In addition, the known limitation of pulmonary pressure measurements, which reflects the pulmonary circulation status, makes assessment of pulmonary vascular resistance a serious need for optimal patient management.

A number of Doppler echocardiographic measurements and equations for estimating PVR have been proposed and proved to have at least one of the four measures of accuracy: sensitivity, specificity, positive, or negative predictive values. However,
Figure 1  Linear correlation (A) and the Bland–Altman plot (B) comparing invasive pulmonary vascular resistance right heart catherization (PVRrhc) and pulmonary vascular resistance from the new method (M1) using estimated right atrial pressure (RAP) of 10 mmHg. Additionally the correlation (C) and the Bland–Altman plot (D) comparing invasive pulmonary vascular resistance right heart catherization and pulmonary vascular resistance from the new method (M1) using estimated right atrial pressure of 7 mmHg.

Table 2  Diagnostic accuracy using different Doppler echocardiographic methods in estimating pulmonary vascular resistance

<table>
<thead>
<tr>
<th>Echocardiographic variables</th>
<th>Cut-off analysis</th>
<th>Bland–Altman analysis</th>
<th>Feasibility (%)</th>
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<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>PPV</td>
</tr>
<tr>
<td>PVR (Lindqvist et al., RAP 10 mmHg) (WU &gt; 3)</td>
<td>100 63</td>
<td>86 100</td>
<td>–0.66 ± 2.1</td>
</tr>
<tr>
<td>PVR (Lindqvist et al., RAP 7 mmHg) (WU &gt; 3)</td>
<td>95 75</td>
<td>90 86</td>
<td>–0.10 ± 2.0</td>
</tr>
<tr>
<td>PVR (Selimovic et al.) (WU &gt; 3)</td>
<td>100 14</td>
<td>66 100</td>
<td>–1.8 ± 2.9</td>
</tr>
<tr>
<td>TRVpeak/VTIrvot (Abbas et al.), (&gt;0.175)</td>
<td>88 86</td>
<td>94 75</td>
<td>6.1 ± 4.0</td>
</tr>
<tr>
<td>PASP/HR × VTImax (Haddad et al.), (&lt;0.04)</td>
<td>94 100</td>
<td>100 88</td>
<td>6.4 ± 4.1</td>
</tr>
<tr>
<td>RV Strain (STE), mid, % (&lt; – 20)</td>
<td>88 63</td>
<td>82 71</td>
<td>21.0 ± 7.6</td>
</tr>
</tbody>
</table>

PVR, pulmonary vascular resistance; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; TRV, tricuspid regurgitation velocity; VTI, velocity time integral; rvot, right ventricular outflow tract; RV, right ventricular; STE, speckle tracking echocardiography; PPV, positive predictive value; NPV, negative predictive value; HR, heart rate.
direct comparison of our proposed equation showed high feasibility and significantly higher specificity and accuracy in identifying patients with raised pulmonary vascular resistance of >3 WU compared with previously published methods. Several factors can explain the higher accuracy of our method. We acquired our Doppler echocardiographic recordings at the same time of the direct invasive measurements, virtually simultaneously; therefore we limited potential variations in pressure and flow. We also did not factor for Doppler time measurements, which are generally dictated by the cycle length as well as the functional status of the right ventricular myocardium. Furthermore, our method used the same equation conventionally used during RHC to calculate PVR, thus comparing similar ingredients. In addition, we adhered to estimating PAMP using the same equation proposed by Aduen et al. and Chemla et al.\(^{19,20}\), which has been well investigated. To our knowledge, this calculation of PAMP has not been previously used in the estimation of PVR. Finally, we did not include exact estimations of RAP or PCWP but instead a constant value of ‘10 or 7’ for RAP and ‘10’ for PCWP, having excluded patients with potential causes for raised atrial pressures. The reason behind this approach was the serious inaccuracies previously reported from using exact estimations of atrial pressures in patients with preserved LV ejection fraction.\(^{21–24}\)

It seems, therefore, that we have succeeded in avoiding potential sources of under or overestimation of PVR using Doppler echocardiographic measurements. Furthermore, using 10 mmHg for RAP has been shown accurate in estimating pulmonary artery systolic pressures.\(^{25}\) The correlation between our estimated values of the PVR and those obtained directly from RHC showed a value of \(r = 0.85\) and \(r = 0.87\) and gave a sensitivity and negative predictive values of 100% for both using 10 mmHg for RAP and 95 and 86%, respectively, using an RAP of 7 mmHg. This supports the proposed equation as a very viable non-invasive method for monitoring patients with pulmonary vascular disease.

**Clinical application**

We have proposed a simple Doppler-derived model for estimating PVR which is based on the invasive concept and

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![Figure 2](https://example.com/figure2.png)

**Figure 2** Linear correlation plots between methods proposed by Selimovic et al. (A), Haddad et al. (B), Abbas et al. (C) and RV strain method (D) comparing invasive pulmonary vascular resistance right heart catherization and simultaneous pulmonary vascular resistance from Doppler echocardiography.
proved to have excellent accuracy, high sensitivity and negative predictive value for monitoring patients with raised PVR. The sensitivity of this method in differentiating raised pulmonary pressures secondary to raised left atrial pressure remains to be determined.

**Limitations**

We intentionally excluded patients with poor LV function and those with raised left atrial pressure in order to obtain a pure form of raised PVR rather than values potentially clouded by left-side cardiac disease. Likewise, we excluded patients with severe tricuspid and aortic regurgitation as potential causes of inaccurate stroke volume measurement. Thus, our findings need to be re-tested in such groups of patients. None of our patients had more than moderate tricuspid regurgitation, making our equation potentially limited.

**Conclusion**

The proposed catheter based non-invasive formula for estimating PVR using Doppler-derived measurements strongly correlates with invasive gold standard measures and has high accuracy in identifying patients with raised pulmonary vascular resistance.

**Conflict of interest:** none declared.

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**References**


