**Echocardiography Can Identify Patients With Increased Pulmonary Vascular Resistance by Assessing Pressure Reflection in the Pulmonary Circulation**

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**Background**—Pulmonary hypertension is a frequent finding in patients with cardiopulmonary disorders. It is important to recognize pulmonary hypertension due to increased pulmonary vascular resistance (PVR), as this affects treatment and prognosis. Patients with increased PVR have an increased pulmonary pressure reflection. We hypothesized that pressure reflection can be described by echocardiography and that variables related to pressure reflection can identify patients with increased PVR.

**Methods and Results**—The study comprised 98 patients investigated within 24 hours of right heart catheterization and 20 control subjects. The pressure reflection variables were obtained by pulsed Doppler in the pulmonary artery and continuous Doppler of tricuspid regurgitation. We selected 3 variables related to pressure reflection: the interval from valve opening to peak velocity in the pulmonary artery (AcT, ms), the interval between pulmonary artery peak velocity and peak tricuspid velocity (tPV-PP, ms), and the right ventricular pressure increase after peak velocity in the pulmonary artery (augmented pressure, AP, mm Hg). The correlation between simultaneous catheter- and echocardiography-determined AP was strong (n=11005, R=0.83). The AcT, tPV-PP, and AP in patients with a PVR of >3 Woods units (n=71) was (mean±SD) 77±16 ms, 119±36 ms, and 22±12 mm Hg, respectively, and differed from patients with a PVR of ≤3 Woods units (n=27, P<0.0001), 111±32 ms, 39±54 ms, and 3±4 mm Hg, and from controls, 153±32 ms, −19±45 ms, and 0 mm Hg, respectively (P<0.0001). The AcT, tPV-PP, and AP values were not correlated with capillary wedge pressure (R=0.08–0.16). The areas under the receiver operator characteristic curve (95% CI) for AcT, tPV-PP, and AP were 0.87 (0.82 to 0.95), 0.94 (0.89 to 0.99), and 0.98 (0.95 to 1.0), respectively.

**Conclusions**—In this study, we describe a novel echocardiography method for assessing pressure reflection in the pulmonary circulation. This method can be used to identify patients with pulmonary hypertension due to increased PVR.

**Key Words:** echocardiography ■ pulmonary hypertension ■ pulmonary vascular resistance

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Pulmonary hypertension is a frequent finding in patients who undergo Doppler echocardiography. Most of these patients have left heart disease (LHD) with pulmonary hypertension secondary to an increase in left ventricular filling pressure but normal pulmonary vascular resistance (PVR). Pulmonary vascular disease with increased resistance to flow leads to pulmonary hypertension, with a poor prognosis owing to right ventricular failure.1 There are many different pathogenic pathways that might cause an increase in resistance in the pulmonary circulation: pulmonary artery hypertension (PAH), pulmonary hypertension associated with lung disease, and chronic thrombotic embolism (CTEPH). It is important to distinguish patients with pulmonary hypertension due to increased PVR from those with pulmonary hypertension due to increased left ventricular filling pressure without increased PVR, as this affects both treatment and prognosis.2

**Clinical Perspective on p 432**

Low pulmonary artery (PA) mean pressure, low peripheral resistance, and high compliance in the central large arteries characterize the normal pulmonary circulation, and together this causes little reflection of the pressure wave. The shape of the pressure wave in the normal pulmonary circulation is similar to that of the flow wave.3 From previous invasive studies in patients without increased PVR, we know that peak flow and peak pressure normally coincide, and there is no increase in pressure after peak flow.4,5 On the other hand, in patients with pulmonary hypertension due to increased PVR, augmented pressure (AP) after peak flow due to an earlier and
more pronounced pressure reflection has been observed. The increase in pressure after peak flow imposes a wasted pressure effort on the right ventricle. This phenomenon has been studied invasively and by Doppler echocardiography in patients with pulmonary embolism. However, to the best of our knowledge, there are no studies that have used Doppler echocardiography for a comprehensive description of pressure reflection, the effects of pressure reflection on PA flow, and the right ventricle pressure profile. In the present study, we hypothesize that pressure reflection and its effect on the right ventricle pressure profile can be described noninvasively by Doppler echocardiography. Furthermore, we investigate whether these variables associated with pressure reflection can be used to identify patients with increased PVR.

**Methods**

**Study Population**

The study comprised 98 patients who underwent Doppler echocardiography and right heart catheterization. The inclusion criteria were (1) regular cardiac rhythm, (2) right heart catheterization within 24 hours of Doppler echocardiography, (3) pulsed Doppler registration in the PA, and (4) tricuspid regurgitation that enabled assessment of right ventricular peak systolic pressure (RVPS) by Doppler echocardiography. The pressure reflection variables were also studied in healthy control subjects (n=20) without hypertension or diabetes mellitus and with normal standard echocardiography findings. Forty patients had LHD (mean±SD left ventricular ejection fraction, 36±18%), 42 patients had PAH, and 16 patients had CTEPH. In the PAH group, 27 cases were idiopathic, 8 were associated with a connective tissue disorder, and 4 were associated with portal hypertension. Some of the investigations were follow-up catheterizations of patients on treatment. The diagnosis of PAH or CTEPH was based on the baseline diagnostic investigation, not the level of PA pressure or PVR on follow-up. Nineteen catheter investigations performed simultaneously with Doppler echocardiography were used to investigate the agreement between catheter and Doppler echocardiography findings.

Informed consent was obtained from all patients participating in the investigations with simultaneous Doppler and pressure measurements, and the ethics committee at the University of Gothenburg approved the study.

**Pressure Reflection: Theoretical Considerations**

In the normal pulmonary arterial tree, the pressure and flow waves generated by the right ventricle are almost completely dampened, and the pressure and flow waves therefore have a similar contour. In the normal right ventricular outflow tract, there is no obstruction to flow or pressure gradient. The waveform of the systolic portion of the right ventricular pressure curve is therefore similar to the PA pressure curve. Changes in pulmonary precapillary properties, such as reduced compliance and increased resistance, cause a reflection of the pressure and flow waves, with marked changes in wave contours (Figure 1). The reflected pressure wave adds to the forward traveling pressure and flow waves, with marked changes in wave contours. The reflected pressure wave adds to the forward traveling pressure and flow waves, and the corresponding reflected flow wave is subtracted. The reflected pressure wave adds to the forward wave, and the corresponding reflected flow wave is subtracted. Pressure reflection influence the timing of peak velocity (AcT), the increase in pressure from peak velocity to peak pressure (augmented pressure).

Diastolic diameter was obtained from M-mode recordings. The left ventricular ejection fraction was measured either from the M-mode data with Simpson’s method or by visual inspection. Mitral and pulmonary vein flow was recorded by pulsed Doppler from the tip of the valve or the upper right pulmonary vein orifice. All Doppler echocardiography measurements were performed off-line with a sweep speed of 100 to 200 mm/s, and the investigator was blinded to the results of the catheterization investigation. All patients were examined in several nonstandard projections guided by color Doppler. Most frequently, the highest velocity was obtained in a projection showing the right ventricle in a position between a standard apical 4-chamber view and a parasternal view. Pulmonary flow velocity was recorded by placing a 5-mm pulsed-wave Doppler sample volume in the right ventricular outflow tract at the level of the pulmonary valve.

The timing of the pulmonary valve opening, the peak velocity, and closing were determined as the time from the QRS complex (most often, the R-wave) and the onset (a-b), peak velocity (a-c), and ending (a-d) of systolic flow in the PA registered by pulsed-wave Doppler (Figure 2). The time interval (a-c) was superimposed onto the velocity spectrum of the tricuspid regurgitant jet to calculate the right ventricular pressure corresponding to the peak velocity in the
pulmonary artery (RVPV; Figure 2). The velocity across the tricuspid valve at this time interval was measured, and the pressure gradients between the right ventricle and right atrium were calculated (pressure gradient = 4 × velocity^2). The mean right atrial pressure was estimated from the vena cava inferior dimension and collapsibility index with inspiration. The timing of the right ventricular peak systolic pressure (RVSP) was determined as the time from the QRS to peak velocity of the regurgitant jet (a-d). The right ventricular ejection time was calculated as [(a-b)-(a-d)]. The time from peak pressure in the right ventricle to peak velocity in the pulmonary artery (tPV-PP) was calculated as [(a-c)-(a-c)]. The time from onset of flow in the pulmonary artery to peak velocity (acceleration time, AcT) was calculated from [(a-c)-(a-b)]. The AP in the right ventricle from peak velocity in the PA RVSP was calculated as RVSP−RVPV (Figure 2). The augmentation index was calculated as AP/RVSP×100.

Hemodynamic Measurements
A Swan-Ganz catheter (7F, Baxter Healthcare, Edwards Critical Care Division, Deerfield, Ill) was introduced through the right internal jugular vein under fluoroscopic guidance with the Seldinger technique. Pressures and cardiac output were obtained after 10 minutes of rest. All patients were awake and breathing spontaneously. In patients with simultaneous catheter and Doppler echocardiography registrations, the right ventricular pressure corresponding to the peak velocity (ie, RVPV) was measured by superimposing the time interval from onset of flow in the PA until peak velocity (AcT), as assessed by pulsed Doppler on the right ventricular pressure curve. Onset of flow was defined as the point on the right ventricular pressure curve corresponding to PA diastolic pressure. PA compliance was calculated as stroke volume/pulse pressure (PA systolic − PA diastolic pressure).

Statistical Methods
Continuous variables with a normal distribution are expressed as mean±SD and median (range) when the distribution is not normal. The degree of linear relation between catheter measurements and Doppler echocardiography was assessed by the correlation coefficient (R). The magnitude of differences between 2 variables was assessed by Bland-Altman analyses, calculating the mean difference ± SD. To compare multiple groups, we used a 1-way ANOVA when the distribution was normal or the Kruskal-Wallis test when the distribution was not normal. In cases where the null hypothesis was rejected (probability value <0.05 considered statistically significant), we continued with a post hoc analysis by using the independent-sample t test or Mann-Whitney test where appropriate. We then performed comparisons between 3 groups, and the probability value considered significant was 0.016, according to the Bonferroni adjustment. The receiver operator characteristic (ROC) curve for the detection of increased PVR defined as >3 Woods units (WU) with the area under the curve (95% CI) was determined for the 3 pressure reflection variables. To evaluate the diagnostic ability of the 3 variables, we compared the 95% CIs for the area under the curve. To determine clinically useful cutoff levels for the different variables, we selected from the ROC analysis the value corresponding to the best combination of sensitivity and specificity. To evaluate the interindividual variability, measurements were made by 2 different investigators on the same Doppler echocardiography recording (n=14). The variability was described by the coefficient of variation, which was expressed as the mean value of differences (group variability) or the SD of differences (individual variability) divided by the mean value of 2 measurements.
The authors had full access to and take full responsibility for the integrity of the data. All the authors have read and agree to the manuscript as written.

## Results

### Patient Characteristics

The mean ± SD (range) age in the total patient group was 55 ± 14 (19–78) years, and the percentage of females was 55%. Mild tricuspid regurgitation was present in 60%, moderate regurgitation in 29%, and moderately severe regurgitation in 11%. Table 1 summarizes the hemodynamic data from right heart catheterization. Patients with PAH and CTEPH had more pronounced pulmonary hypertension compared with LHD patients. Thirty-eight percent of patients with LHD had increased pulmonary capillary wedge pressure (PCWP >12 mm Hg), whereas patients with PAH and CTEPH had a normal PCWP in overall terms. Patients with PAH and CTEPH had reduced compliance compared with those with LHD. Compared with those with PAH and CTEPH, patients with LHD had reduced left ventricular ejection fraction, increased diastolic volume, a disturbed mitral and pulmonary vein flow pattern, and a dilated left atrium, indicating increased left ventricular filling pressure.

### Comparison Between Catheter and Doppler Echocardiography Findings

Table 2 shows the results of catheter pressure measurements and simultaneously obtained estimations from Doppler echocardiography. There was a strong, linear correlation between estimated and measured right atrial pressure, RVSP, and RVPV. In absolute terms, there was a small yet significant difference between catheter-measured and Doppler echocardiography–estimated AP. Furthermore, there was no difference between catheter- and nonsimultaneous Doppler-estimated RVSP in the study population (65 ± 27 vs 66 ± 26 mm Hg, P = 0.52). The correlation was strong (R = 0.90), but the limits of agreement were relatively wide (mean ± SD difference, 0.5 ± 12 mm Hg).

### Pressure Reflection in Controls and Patients With and Without Increased PVR

The difference in RR interval between pulsed Doppler recordings in the PA and continuous-wave Doppler in the tricuspid valve was 0.4 ± 4%. Table 3 shows Doppler findings in controls and patients with and without increased PVR. There was no difference in age between controls and patients with and without increased PVR. In the majority of controls, we observed peak velocity in the PA after the peak velocity in the tricuspid regurgitant jet (15/20, 75%), or else the peak velocity in the PA was equal to peak pressure in the right

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**Table 1. Data From Right Heart Catheterization and Doppler Echocardiography**

<table>
<thead>
<tr>
<th>Variable</th>
<th>LHD (n=40)</th>
<th>PAH (n=42)</th>
<th>CTEPH (n=16)</th>
<th>Overall P Value</th>
<th>LHD vs PAH</th>
<th>LHD vs CTEPH</th>
<th>PAH vs CTEPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index, (L/min)/m²</td>
<td>2.3 ± 0.7</td>
<td>2.7 ± 0.8</td>
<td>2.3 ± 0.5</td>
<td>0.046</td>
<td>0.06</td>
<td>1.00</td>
<td>0.27</td>
</tr>
<tr>
<td>RAP, mm Hg</td>
<td>9 (1–25)</td>
<td>6 (0–21)</td>
<td>5 (0–20)</td>
<td>0.064</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASP, mm Hg</td>
<td>48 ± 17</td>
<td>82 ± 26</td>
<td>81 ± 20</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>1.00</td>
</tr>
<tr>
<td>PAMP, mm Hg</td>
<td>31 ± 11</td>
<td>52 ± 17</td>
<td>45 ± 12</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.002</td>
<td>0.08</td>
</tr>
<tr>
<td>PADP, mm Hg</td>
<td>20 ± 7</td>
<td>32 ± 13</td>
<td>26 ± 7</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>19 (3–34)</td>
<td>8 (2–19)</td>
<td>9 (2–25)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.80</td>
</tr>
<tr>
<td>PVR, WU</td>
<td>2.5 (0.4–13)</td>
<td>8.9 (2.8–23)</td>
<td>8.9 (2.8–13.7)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.52</td>
</tr>
<tr>
<td>SV/PP, ml/mm Hg</td>
<td>2.0 (0.6–7.6)</td>
<td>1.1 (0.6–4.4)</td>
<td>1.0 (0.6–2.9)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Values are mean ± SD for variables with a normal distribution and median (range) for variables with a nonparametric distribution. RAP indicates right atrial pressure; PASP, PA systolic pressure; PAMP, PA mean pressure; PADP, PA diastolic pressure; SV, stroke volume; PP, pulse pressure; LVEF, left ventricular ejection fraction; LA, left atrium; E/A, ratio between early and late mitral filling velocity; and S/D, ratio between systolic and diastolic pulmonary vein velocity. Other abbreviations are as defined in text.

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**Table 2. Comparison Between Catheter and Simultaneous Doppler Echocardiography**

<table>
<thead>
<tr>
<th>Variable, mm Hg (n=19)</th>
<th>RAP</th>
<th>RVSP</th>
<th>RVPV</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter</td>
<td>9 ± 6</td>
<td>76 ± 20</td>
<td>49 ± 13</td>
<td>27 ± 10</td>
</tr>
<tr>
<td>Simultaneous Doppler</td>
<td>9 ± 5</td>
<td>73 ± 17</td>
<td>50 ± 12</td>
<td>23 ± 9</td>
</tr>
<tr>
<td>Mean difference ± SD</td>
<td>1 ± 3</td>
<td>2 ± 9</td>
<td>-1 ± 8</td>
<td>4 ± 6</td>
</tr>
<tr>
<td>Correlation coefficient (R)</td>
<td>0.84</td>
<td>0.89</td>
<td>0.82</td>
<td>0.83</td>
</tr>
<tr>
<td>P value</td>
<td>0.21</td>
<td>0.27</td>
<td>0.49</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Values are mean ± SD. RAP, mean right atrial pressure. Other abbreviations are as defined in text.
ventricle. As a result, most control subjects did not have any AP after peak velocity (18/20, 90%). Compared with controls, patients with increased PVR had significantly shorter AcT, longer tPV-PP, and more pronounced AP. In patients without increased PVR, AcT, tPV-PP, and AP differed significantly from controls and from patients with increased PVR. Figure 3 shows the right ventricular pressure recording, pulsed-wave Doppler from the PA, and the tricuspid continuous-wave Doppler in a patient without increased PVR and a patient with PAH. In the patient without increased PVR (left), the peak velocity in the PA coincides with peak velocity in the tricuspid jet. The pressure reflection variables in patients with LHD differed significantly from those in controls (Figure 4). Compared with those with PAH, patients with CTEPH had shorter AcT, and the tPV-PP tended to be longer and the AP more pronounced (Figure 4). The AcT, tPV-PP, and AP values in patients with LHD and a PVR >3 WU (n=15) were 82±20 ms, 102±37 ms, and 13±9 mm Hg, respectively, and these differed from the values of patients with LHD and a PVR ≤3 WU (n=25, P=0.0001; 113±32 ms, 36±54 ms, and 3±4 mm Hg, respectively).

### Determinants of PA Pressure Reflection

Table 4 shows the results of a correlation analysis of a relation between the different variables describing the pressure reflection (AcT, tPV-PP, AP) and possible determinants (cardiac index, PCWP, compliance, PVR). There was a weak correlation between cardiac index and AcT. PCWP was not correlated with any of the pressure reflection variables. Pulmonary arterial compliance and PVR showed a moderate correlation with the pressure reflection variables (R range of 0.43 to 0.68).

### Pressure Reflection Variables and Increased PVR

Figure 5 shows the ROC curves for the pressure reflection variables. All 3 variables had large areas under the ROC curve. The 95% CI for AcT did not overlap with that corresponding to AP but it did with tPV-PP. The cutoff values that gave the best combined sensitivity and specificity were <103 ms for AcT, >89 ms for tPV-PP, and >8 mm Hg for AP. Table 5 shows diagnostic performance when these cutoff values were used.

### Interobserver Variability

The respective interobserver group variability for measurements made on the same recording was 4%, 3%, 6%, 8%, and 9% for RVPS, RVPV, AcT, tPV-PP, and AP. The corresponding interobserver individual variability was 4%, 7%, 7%, 9%, and 13%.

### Discussion

In the present study, we used the pressure reflection phenomenon assessed by Doppler echocardiography to identify patients with pulmonary hypertension due to increased PVR and pulmonary vascular disease. Importantly, noninvasive estimation of pressure reflection and pressure augmentation in the pulmonary circulation is easy to perform and is not obtained during routine cardiac catheterization.

Several previous reports have shown a close agreement between catheter and Doppler echocardiography during simultaneous measurements of PA systolic pressure. The direct, noninvasive estimation of PVR has not previously been possible. Some investigators have used Doppler echocardiography methods indirectly related to PVR in patients with heart failure. The ratio between peak tricuspid regurgitant velocity (a surrogate for PA mean pressure) and the right ventricular outflow tract time-velocity integral (a surrogate for cardiac output) showed good agreement with catheter-derived PVR. This ratio is, however, more an estimate of total pulmonary resistance (PA mean pressure/cardiac output) than PVR, and it is therefore conceivable that the variable cannot be used to identify patients with an increased transpulmonary gradient. Characteristic changes of the flow profile in the PA due to pressure reflection with a notch after peak velocity (see Figure 2) have been described in patients with pulmonary embolism. In the presence of a notch, we should suspect increased PVR, but absence of the notch has a low predictive value. In patients with PAH, we have shown in a recent study that PVR can be calculated with a strong correlation (R=0.93) between catheter and Doppler methods. These results were obtained in a group of patients with normal PCWP and a relatively high PA mean pressure.
In patients with LHD and less severe pulmonary hypertension, we anticipated that the uncertainty in PCWP and cardiac output assessments would make the direct estimation of PVR less precise. Patients with pulmonary vascular disease have increased pressure reflection due to increased PVR, reduced compliance, or a combination of the 2, leading to pressure augmentation in late systole. In the present study, we found that the Doppler echocardiography variables were able to identify these patients with a high degree of accuracy. The proposed variables are easy to obtain and not influenced by PCWP. This implies that these variables are able to identify patients with a combination of increased PVR and increased PCWP.

Pulmonary hypertension is characterized by an increase in right ventricular afterload. The right ventricle initially adapts to the pressure overload, but the cause of death is most often right ventricular failure. Right ventricular afterload in patients with pulmonary vascular disease and pulmonary hypertension is most frequently defined with a PVR that reflects the load in relation to steady flow. Blood flow is pulsatile, however, and a more comprehensive description of right ventricular afterload should include variables that assess the load in relation to pulsatile flow. Wave reflection arises from any discontinuation in caliber or change in elastic properties. The observed pressure reflection is a composite parameter that contains information on precapillary pathologic changes in the pulmonary vascular bed, consistent with the moderate correlation with PVR in the present study. The 3 Doppler echocardiography variables were able to discriminate patients with increased PVR from those without. However, in patients with a PVR ≥3 WU, these variables differed significantly from controls, indicating that although PVR was not elevated, they had some degree of pressure reflection. The underlying pathophysiologic explanation of this observation or the clinical importance of this finding is unclear. Importantly, we are able to conclude that, by combining information from the flow profile in the PA and the tricuspid regurgitant jet, we can obtain important information on right ventricular afterload due to pulmonary vascular impedance. Today, it is part of clinical routine to assess PA systolic pressure with Doppler echocardiography, and pulmonary hypertension is a frequent finding.18 The majority of these patients have pulmonary hypertension due to systolic or diastolic LHD or valvular heart disease and normal PVR. It is important to recognize when LHD is associated with increased PVR. In patients who are candidates for left ventricular assist or heart transplant, right heart catheterization should be performed to confirm the finding and to assess the severity and reversibility of the increased PVR. In some LHD patients undergoing optimal treatment and a normalized or only slightly elevated PCWP, residual pulmonary hypertension and increased PVR might indicate that PAH-specific therapy could be beneficial.2 The diagnosis of PAH is known to be difficult, and diagnostic delay is a problem.19,20 In PAH patients, even a mild elevation of PA pressure with normal right ventricular function is often associated with extensive pulmonary vascular damage.21 The suspicion of pulmonary vascular disease in patients with pulmonary hypertension should therefore be high to detect the disease in an earlier phase. In every patient with pulmonary hypertension, the investigator should also make a statement about the likelihood of increased PVR. In a recently published diagnostic algorithm aiming at earlier detection of PAH, the first question when pulmonary hypertension has been diagnosed by Doppler echocardiography is whether the patient has pulmonary hypertension due to

![Figure 3. Right ventricular pressure curves (top), pulsed Doppler from the PA (middle), and continuous-wave Doppler (bottom) from an individual without increased PVR (left) and a patient with increased PVR due to PAH (right). In the individual with normal PVR (1.2 WU), the AcT is long (186 ms), and the peak flow in the PA (c-d) coincides with the RVPS. The RVPS (**) was 41 mm Hg measured by Doppler and 29 mm Hg measured by catheter. In the patient with increased PVR (14.3 WU), the AcT is short (66 ms), the peak flow in the PA is earlier than the RVPS (tPV-PP=91 ms), and there is marked augmentation in pressure. The AP measured by both catheter and Doppler was 17 mm Hg. The catheter RVPS was 69 mm Hg, whereas the Doppler RVPS was 67 mm Hg.](http://circimaging.ahajournals.org/)

In patients with LHD and less severe pulmonary hypertension, we anticipated that the uncertainty in PCWP and cardiac output assessments would make the direct estimation of PVR less precise. Patients with pulmonary vascular disease have increased pressure reflection due to increased PVR, reduced compliance, or a combination of the 2, leading to pressure augmentation in late systole. In the present study, we found that the Doppler echocardiography variables were able to identify these patients with a high degree of accuracy. The proposed variables are easy to obtain and not influenced by PCWP. This implies that these variables are able to identify patients with a combination of increased PVR and increased PCWP.

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LHD. In clinical practice, this is often difficult to determine, in particular among patients with a normal left ventricular ejection fraction and normal valve function. Normal filling pressure at rest does not exclude left ventricular systolic and diastolic dysfunction, and the relation between Doppler echocardiography variables and filling pressure is no more than moderate. Today, with the opportunity to treat PAH, many patients with pulmonary hypertension and inconclusive Doppler echocardiography results in terms of wedge pressure are referred for invasive evaluation. A noninvasive method with a high negative predictive value would therefore be of interest, as it can reduce the need for catheterization.

Study Limitations
The patients included in the study were those undergoing diagnostic right heart catheterization. The percentage of patients with pulmonary hypertension, increased PVR, and increased PCWP was therefore high, and we can expect this population to differ from the patient population investigated with Doppler echocardiography. Theoretically, this could have a particular impact on our assessment of positive and negative predictive values.

In the present study, we have shown that the pressure reflection variables can be used to identify patients with increased PVR. However, the linear relation between these
variables and PVR was only moderate (R range of 0.43 to 0.68), and therefore we cannot directly estimate the PVR.

In the World Health Organization classification of pulmonary hypertension, there are 5 different subgroups. The most important subgroups are represented in the present study (PAH, LVD, and CTEPH), but we do not have data on patients with pulmonary hypertension associated with lung disease or hypoxemia. Pulmonary hypertension in patients with lung disease is due to multiple factors, including the loss of small vessels due to emphysema or fibrosis, intimal thickening, and vasoconstriction secondary to alveolar hypoxia. From these pathophysiologic mechanisms, we can expect increased pressure reflection. The new proposed method for diagnosing pressure reflection and thereby pulmonary vascular disease might be a useful tool, but further studies are needed in patients with lung disease.

To what extent these pressure reflection variables are influenced by treatment can be used to monitor changes, improvement, or worsening has not been studied. Furthermore, the potential prognostic information from pressure reflection variables is unknown. The possible confounding effects of right ventricular failure or the presence of severe thickening, and vasoconstriction secondary to alveolar hypoxia. From these pathophysiologic mechanisms, we can expect increased pressure reflection. The new proposed method for diagnosing pressure reflection and thereby pulmonary vascular disease might be a useful tool, but further studies are needed in patients with lung disease.

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Table 4. Relation Between Variables Describing Pressure Reflection and Possible Determinants

<table>
<thead>
<tr>
<th>Variable</th>
<th>AcT</th>
<th>tPV-PP</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>P</td>
<td>Value</td>
<td>R</td>
</tr>
<tr>
<td>Cardiac index</td>
<td>0.28</td>
<td>0.004</td>
<td>0.06</td>
</tr>
<tr>
<td>PCWP</td>
<td>0.16</td>
<td>0.12</td>
<td>0.08</td>
</tr>
<tr>
<td>SV/PP</td>
<td>0.68</td>
<td>&lt;0.0001</td>
<td>0.50</td>
</tr>
<tr>
<td>PVR</td>
<td>0.54</td>
<td>&lt;0.0001</td>
<td>0.43</td>
</tr>
</tbody>
</table>

See Tables 1 and 3 and text for explanation of abbreviations.

Table 5. Diagnostic Performance of Pressure Reflection Variables

<table>
<thead>
<tr>
<th>Variable (Cutoff Value)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT (&lt;103 ms)</td>
<td>94 (86–98)</td>
<td>74 (60–86)</td>
<td>90</td>
<td>85</td>
</tr>
<tr>
<td>tPV-PP (&gt;89 ms)</td>
<td>87 (77–94)</td>
<td>89 (77–96)</td>
<td>82</td>
<td>92</td>
</tr>
<tr>
<td>AP (&gt;8 mm Hg)</td>
<td>90 (81–96)</td>
<td>94 (82–99)</td>
<td>86</td>
<td>95</td>
</tr>
</tbody>
</table>

NPV indicates negative predictive value; PPV, positive predictive value. Other abbreviations are as defined in text.

In the present study, we identified patients with LHD and both increased PVR and increased PCWP. This is an important and promising ability of the pressure reflection variables. However, we have not studied patients with mixed diseases with increased PCWP (secondary to coronary artery disease) and increased PVR due pulmonary vascular disease (PAH, lung disease). Therefore, further studies are needed to evaluate the possible use of these Doppler echocardiography variables.

Conclusions

In the present study, we found that the effects of pressure reflection in the pulmonary arterial tree on the right ventricular pressure waveform can be described by a new Doppler echocardiography method. Importantly, these easily obtainable Doppler echocardiography variables can be used to identify patients with increased PVR.

Disclosures

None.

References

Pulmonary hypertension is a frequent finding in patients investigated with Doppler echocardiography. Most of these patients have left heart disease with pulmonary hypertension secondary to an increase in the left ventricular filling pressure with normal pulmonary vascular resistance. Pulmonary vascular disease with increased resistance to flow leads to pulmonary hypertension with a poor prognosis due to right ventricular failure. Diagnostic delay is a well-known problem in patients with pulmonary hypertension due to pulmonary vascular disease. It is important to distinguish patients with pulmonary hypertension due to increased pulmonary vascular resistance from those with pulmonary hypertension due to increased left ventricular filling pressure without increased resistance, as this affects both treatment and prognosis. Low pulmonary artery mean pressure, low peripheral resistance and high compliance in the central large arteries characterize the normal pulmonary circulation and together this causes little reflection of the pressure wave. In the present study, we hypothesized that pressure reflection and its effect on the right ventricle pressure profile can be described noninvasively by using Doppler echocardiography. Further, we tested the hypothesis that variables associated with pressure reflection can be used to identify patients with increased pulmonary vascular resistance. We found that Doppler echocardiography can be used to describe pressure reflection in the pulmonary circulation and, importantly, the method can be used to identify patients with increased pulmonary vascular resistance.
Echocardiography Can Identify Patients With Increased Pulmonary Vascular Resistance
by Assessing Pressure Reflection in the Pulmonary Circulation
Odd Bech-Hanssen, Fredrik Lindgren, Nedim Selimovic and Bengt Rundqvist

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