Echocardiographic Evaluation of Right Ventricular Function in Patients with Chronic Pre-Capillary Pulmonary Hypertension

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In chronic pre-capillary pulmonary hypertension the right ventricle undergoes extensive remodeling (an increase in volume, a change in shape and an increase in wall thickness) that allows it to maintain an adequate right ventricular (RV) output at rest despite the high afterload. The anatomic characteristics of the pressure overloaded right ventricle have been described using various imaging techniques, including echocardiography and nuclear magnetic resonance [1-4]. However, despite a widespread agreement on the importance of right ventricular function in patients with chronic pulmonary hypertension (both to guide therapy and for risk stratification) the non-invasive assessment of right ventricular morphology and function by means of echocardiography has traditionally been hampered by the complex geometry of this cardiac chamber, so that its evaluation has often been qualitative [5-8].

Recently, two echocardiographic parameters describing right heart performance (the tricuspid annular plane systolic excursion and the Doppler derived flow velocity pattern into the superior vena cava) turned out to be clinically and prognostically useful in advanced heart failure [9-10]. The hemodynamic correlates of these parameters have not been reported in patients with chronic pulmonary hypertension. In addition, there is still a substantial lack of knowledge concerning the relationship between RV morphology and function; in particular, it is still debated whether or not right ventricular hypertrophy might be associated with a better hemodynamic profile and a better prognosis in such patients by permitting a better coupling of the right ventricle with the increased RV wall stress [11-12].

Accordingly, the aim of this prospective study was to define the capability of echocardiography to assess the right heart performance in such patients.

Methods

Patients. Between January 1996 and May 2001, 142 patients were consecutively admitted at our institution because of symptomatic pulmonary hypertension and were diagnosed as having chronic postembolic pulmonary hypertension (n=111: 54 males and 57 females, mean age 51±14 years, 57% in NYHA class III or IV) or primary pulmonary hypertension (n=31: 13 males and 18 females, mean age 45±15 years, 61% in NYHA class III or IV). Patients with a history of drug abuse, HIV infection, chronic obstructive pulmonary disease, interstitial lung disease or collagen vascular disease were not included in this series. Chronic thromboembolic pulmonary hypertension was positively diagnosed when typical pulmonary angiographic findings were present at pulmonary angiography [13, 14]. The diagnosis of primary pulmonary hypertension was done after having ruled out the most representative etiologies of pulmonary hypertension [15]. All patients underwent right heart catheterization and ultrasound examination during the hospitalization period.

Echocardiographic and Doppler Study. A complete M-mode, 2-D and Doppler study was performed using standard parasternal, apical and subcostal approaches, as previously described [16]. The right ventricular end-diastolic diameter and the thickness of the right ventricle free wall were determined in the parasternal view [17]. End-diastolic and end-systolic right ventricular areas were measured in the apical view and the fractional area change was calculated as (end-diastolic area minus end-systolic area) divided by end-diastolic area, x 100. The systolic displacement of the lateral portion of the tricuspid annular plane was measured on the M-mode tracing under the 2D-echo guidance. Tricuspid regurgitation was graded using the jet area method. The diameter of the inferior vena cava was measured from the subcostal approach and its inspiratory collapsibility evaluated [18]. Peak systolic pulmonary artery pressure was calculated by adding a right atrial pressure estimate to the systolic transtricuspid pressure gradient; the right atrial pressure was estimated = 5 mmHg when the inferior vena cava diameter was <20 mm and the collapsibility ≥50%; the estimate was 10 mmHg.
when the inferior vena cava diameter was <20 mm and the collapsibility <50%; the estimate was 20 mmHg when the inferior vena cava diameter was ≥20 mm and the collapsibility <50%. The pulsed Doppler pulmonary flow velocity curve was analyzed to measure the acceleration time and to detect the presence of a mid-systolic notch [19]. The superior vena cava flow velocity curve was recorded from the right supraclavear approach by placing the sample volume in the middle of the stream visualized by color-Doppler format. Peak velocities of the systolic and of the diastolic centripetal waves in superior vena cava and hepatic veins were measured and their ratio calculated. The venous flow velocity pattern was considered normal when the systolic/diastolic ratio was ≥1 and 2; the flow pattern was categorized as "predominant systolic wave" when the ratio was > 2, and as "predominant diastolic wave" when the ratio was < 1 [20]. "Reverse systolic flow" was identified when a retrograde holosystolic wave was present. Left ventricular end-diastolic and end-systolic volumes and left ventricular ejection fraction were calculated using the area-length method. The eccentricity index of the left ventricle was calculated in diastole and in systole. Echocardiographic data were averaged over 3 beats. All Doppler measurements were evaluated in 5 consecutive beats obtained during quiet respiration.

Right heart catheterization. The procedure has been previously described in detail [21]. Briefly, a modified Swan Ganz thermodilution catheter with a rapid response thermistor (93A-431H-7F, American Edwards Laboratories, Irvine CA) was inserted transthoracically via the right internal jugular vein. The thermistor was connected to a dedicated computer (REF-1 Ejection Fraction/Cardiac Output Computer, American Edwards Laboratories) to display on-line the cardiac output and the right ventricular ejection fraction. The following hemodynamic parameters were measured or calculated: systemic blood pressure (arm-cuff sphygmomanometer), right atrial pressure, pulmonary artery (systolic, diastolic and mean) pressure and pulmonary wedge pressure, RV ejection fraction, cardiac output, cardiac index, systemic vascular resistance, pulmonary vascular resistance. All of the thermodilution measurements were obtained in triplicate. On average, the time interval between the ultrasound examination and the right heart catheterization was one day.

Statistical analysis. Data are shown as mean ± SD for continuous variables and absolute or relative frequencies for categorical variables. Group means were compared using the two-tailed t test; group frequencies were compared using the chi-square test.

Linear regression analysis was performed to evaluate the correlations between echocardiographic and hemodynamic parameters.

Cumulative survival was calculated on the basis of Kaplan-Meier estimates; the relative risk of dying and its 95% confidence interval (95%CI) were computed using a Cox model. Cardiac death was the only end-point of survival analysis; lung transplantation and pulmonary thromboendarterectomy were considered as censored observations and the patients were withdrawn from the analysis at the time of intervention. A p value < 0.05 was retained for statistical significance.

Results
Non-invasive estimation of right atrial pressure. Echocardiographic data for estimation of right atrial pressure could be recorded in 112 patients. The flow velocity pattern into the superior vena cava yielded slightly better results than the size and collapsibility of the inferior vena cava.

<table>
<thead>
<tr>
<th>Echocardiographic prediction of right atrial pressure</th>
<th>Doppler equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial pressure (mmHg) = 3.48 + 1.57a + 8.25b</td>
<td>Where a = 1 if the flow pattern is &quot;predominant systolic wave&quot; or 0 in other cases and b = 1 if the flow pattern is &quot;predominant diastolic wave&quot; or &quot;reverse systolic flow&quot; or = 0 in other cases (adjusted R2 = 0.290).</td>
</tr>
</tbody>
</table>

**Echocardiographic prediction of right atrial pressure**

**Two-dimensional equation**

Right atrial pressure (mmHg) = 2.86 + 3.05a + 5.80b

where a = 1 if the inferior vena cava diameter is <20 mm and the collapsibility <50% or = 0 in other cases and b = 1 if the inferior vena cava diameter is ≥20 mm and the collapsibility <50% or = 0 in other cases (adjusted R2 = 0.177).

Non-invasive estimation of pulmonary arterial pressure. The echocardiographic estimate of peak systolic pulmonary artery pressure was feasible in 103 patients.
Non-invasive evaluation of right ventricular performance. The geometry and function of the right ventricle turned out to be related to the hemodynamic severity of pulmonary hypertension. Echocardiographic and hemodynamic indices of right ventricular performance were significantly correlated.

Correlations between mean pulmonary artery pressure and echo parameters of right ventricular morphology and function.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Correlation Coefficient</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV free wall thickness</td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV end-diastolic diameter</td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV end-diastolic area</td>
<td>0.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV fractional area change</td>
<td>-0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TAPSE</td>
<td>-0.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV ejection fraction</td>
<td>-0.47</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Correlations between thermodilution-derived right ventricular ejection fraction and the echo indices of RV function

Thermodilution-derived RVEF and tricuspid annular plane systolic excursion (r=0.51, p<0.001)
Thermodilution-derived RVEF and right ventricular fractional area change (r=0.48, p<0.001).

Hemodynamic correlates of different morphologies of Doppler flow velocity curves into the SVC

<table>
<thead>
<tr>
<th>Flow pattern into the SVC</th>
<th>RAP (mmHg)</th>
<th>RVEF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal (group 1, n=30)</td>
<td>2.5 ±2.7*</td>
<td>2.5 ±2.7*</td>
</tr>
<tr>
<td>predominant systolic wave (group 2, n=69)</td>
<td>26.5±10.3*</td>
<td>26.5±10.3*</td>
</tr>
<tr>
<td>predominant diastolic wave (group 3, n=22)</td>
<td>5.3 ±4.4*</td>
<td>5.3 ±4.4*</td>
</tr>
</tbody>
</table>

The clinical significance of right ventricular hypertrophy

The median right ventricular wall thickness in the whole was 7 mm (range 3-14 mm). Patients were accordingly divided into two groups: those with “severe” hypertrophy (RVWT  7mm) and those with “moderate” hypertrophy (RVWT = 7 mm).

Characteristics of pts with “severe” or “moderate” hypertrophy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RVWT&lt;7 mm</th>
<th>RVWT&gt;7 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class III-IV (%)</td>
<td>48</td>
<td>70</td>
</tr>
<tr>
<td>PAPs (mmHg)</td>
<td>71±20</td>
<td>90±23</td>
</tr>
<tr>
<td>PAPm (mmHg)</td>
<td>42±13</td>
<td>54±14</td>
</tr>
<tr>
<td>PVR (W.U)</td>
<td>9.4±5.4</td>
<td>14.7±5.7</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>2.3±0.7</td>
<td>1.9±0.6</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>22±11</td>
<td>14±7</td>
</tr>
</tbody>
</table>
Discussion

The present study underlines the role of transthoracic echocardiography in the evaluation of the right heart performance in patients with chronic pulmonary hypertension.

Doppler assessment of right sided pressures. The interpretation of the comparison between Doppler-derived hemodynamic variables and direct pressure measurements in the present study requires particular caution. In fact, echocardiography and right heart catheterization were not performed simultaneously; furthermore, standard fluid-filled catheters rather than micromanometer-tipped catheters were used for pressure measurements [22]. Nonetheless, the results of the present study confirm that the non-invasive estimation of right sided pressures from Doppler spectral recordings of the tricuspid regurgitant velocities is feasible in a great percentage of patients with pulmonary hypertension. Echocardiographic data are similar to invasive data if we only look at mean values; however, we must be aware that the wide limits of agreement indicate that clinically significant differences might occur in individual patients. As far as the non-invasive estimation of right atrial pressure is concerned, the study indicates that pulsed Doppler velocimetry into the superior vena cava provides information which is not less valuable than a morphologic analysis of the inferior vena cava, but, in addition, the analysis of the systemic venous return is also useful to estimate right ventricular function as much as in patients with advanced heart failure [10].

Echocardiographic evaluation of right heart performance. Previous studies have described right ventricular enlargement and reduced right ventricular fractional area change as distinctive features in patients with chronic pulmonary hypertension [7,8]. The present study expands those previous observations demonstrating that an in-depth quantitative echocardiographic assessment of right ventricular morphology and function is feasible in such patients using several echo and Doppler parameters. First, the tricuspid annular plane showed a statistically significant correlation with thermodilution-derived right ventricular ejection fraction; future studies should verify its prognostic value in patients with pulmonary hypertension. Second, the pulsed Doppler flow velocity pattern into the superior vena cava turned out to be an indicator of the global right heart performance which is easy to obtain and strongly associated with the hemodynamic profile. Third, the right ventricular free wall thickness could be measured in all patients despite the difficulties in focusing the ultrasonic beam in the near field; it is interesting to notice that the degree of right ventricular hypertrophy was found to be highly variable in the present population. A "severe" RV hypertrophy was associated with a significantly worse right heart hemodynamic profile, and in fact it also indicated poor clinical conditions (worse NYHA class) and poor short-term prognosis.

Conclusion

In patients with chronic pre-capillary pulmonary hypertension, echocardiography not only is useful to estimate pulmonary artery pressures, but it also allows a semi-quantitative assessment of right ventricular geometry and function which is extremely important to evaluate the capability of the right heart to confront with a chronically elevated afterload. Future studies are necessary to establish the prognostic significance of these data.

References