Prediction of Pulmonary Arterial Pressure in Chronic Obstructive Pulmonary Disease by Radionuclide Ventriculography

Pierre Mols, M.D.; Chi-Hoang Huynh, M.D.; Philippe Dechamps, M.D.; Nicole Naeije, M.D.; Marcel Guillaume, Ph.D.; and Hamphrey Ham, M.D., Ph.D.

Pulmonary arterial hypertension represents an important parameter for the assessment of the severity of chronic bronchitis. The measurement of the pulmonary arterial pressure, however, requires invasive techniques of limited routine use because of costs and associated risks. The aim of this study is to evaluate whether the 81mKr right ventricular ejection fraction and parameters derived from equilibrium 99mTc red blood cells' right ventricular curve allow a better estimation of PAP than the 99mTc RVEF. In 41 patients with severe chronic bronchitis, the linear correlation between PAP and 99mTc RVEF was -0.61 (p<0.001). None of the parameters derived from the right ventricular curve was better correlated to PAP than the 99mTc RVEF. In 16 other chronic bronchitis patients, the 81mKr RVEF correlated moderately to PAP. In conclusion, the alternative isotopic methods proposed in this work do not provide a reliable estimation of pulmonary arterial pressure in patients with chronic bronchitis.

C

Chronic obstructive pulmonary disease is one of the chief causes of disability and death in Europe and in the United States. Pulmonary hypertension triggers the development of right ventricular hypertrophy which may lead to right ventricular failure with a high mortality rate. The measurement of PAP requires right heart catheterization. Although this technique is widely available, its routine use is limited by costs and associated risks. Therefore, less invasive methods have been developed to detect and assess the severity of pulmonary hypertension. One of these methods is the determination of RVEF by technetium-99m radionuclide ventriculography. Studies, however, show that the ventricular ejection fraction lacks in specificity and poorly correlates with pulmonary arterial pressure.4,5

During the last few years, however, radionuclide techniques have improved considerably and some curve parameters have shown a better sensitivity than RVEF in assessing pulmonary arterial pressure. An improved method for the evaluation of the RVEF by krypton-81m (81mKr) has also been developed.8,9

The aim of this study was to evaluate whether 81mKr RVEF and parameters derived from equilibrium technetium-99m red blood cells (99mTc RBC) right ventricular curve allow a better estimation of pulmonary arterial pressure.

Material and Methods

Patients

Fifty seven patients with stable and severe chronic obstructive pulmonary disease were subjected to right heart catheterization to measure pulmonary arterial pressure and estimate right ventricular function. There were 53 men and four women (group 1: 64±3 years; group 2: 61±1 years). No patient had any clinical or electrocardiographic evidence of systemic hypertension, valvular heart disease or coronary artery disease. The patients' characteristics and lung function data are given in Table 1. All the patients have given informed consent to the study, which was approved by the Human Investigation Committee of our institution.

Hemodynamic Determination

A triple lumen thermodilution 7F Swan-Ganz catheter was introduced into the right internal jugular vein using the Seldinger technique, and advanced under constant pressure wave and fluoroscopic control.

Table 1—Patients' Characteristics and Lung Function Data

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Age, yr</th>
<th>Male/ Female</th>
<th>FEV1, ml/s</th>
<th>FEV1/FEV10</th>
<th>PaO2, mm Hg</th>
<th>PaCO2, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>16</td>
<td>64±3</td>
<td>16/0</td>
<td>953±122</td>
<td>40±3</td>
<td>64±4</td>
<td>44±2</td>
</tr>
<tr>
<td>Group 2</td>
<td>41</td>
<td>61±1</td>
<td>37/4</td>
<td>912±63</td>
<td>39±6</td>
<td>64±2</td>
<td>43±1</td>
</tr>
</tbody>
</table>

* N, number of patients; values are expressed as mean ± SEM.
oscop ic control in the right pulmonary artery. Pulmonary pressure was measured using a physiologic pressure transducer and recorded on a thermal writing recorder. The zero reference was placed at midchest level and values for pressures were averaged for three successive respiratory cycles. Heart rate was derived from a continuously monitored ECG lead. Cardiac output was measured in triplicate by the thermodilution method using a computer. The following formulae were used for hemodynamic calculations: cardiac index (L/min/m²) = cardiac output (L/min) / body surface area (m²); pulmonary vascular resistance index (dyne×cm⁻⁵×m²) = 80 × (mean pulmonary arterial pressure—pulmonary wedge pressure)/cardiac index.

Right Ventricular Ejection Fraction Techniques

In 16 patients (group 1), RVEF was determined using ⁸¹Kr within the seven days following right heart catheterization. The detailed procedure of the ⁸¹Kr right ventricular study has been described previously. Briefly, the patient was studied supine, in a 30° right anterior oblique projection. The ⁸¹Kr was continuously infused and 16 ECG-gated frames were acquired. Background activity was corrected using ⁹⁹Tc MAA lung perfusion scintigraphy acquired in the same position immediately after the completion of the gated study. End-diastolic and end-systolic right ventricular ROIs were carefully delineated on the background corrected images taking into account isocount lines and the phase and amplitude images of the first and second Fourier harmonics constructed from the original gated data. In 41 patients (group 2), ECG-gated equilibrium ⁹⁹Tc RBC ventriculography was performed simultaneously with right heart catheterization. The patient was studied supine in 45° left anterior oblique projection and 16 ECG-gated frames were acquired. End-diastolic right ventricular ROI was delineated following the limits of the ventricular phase area. For background correction, 50 percent of the maximum activity in the right ventricular area in the end-diastolic frame was subtracted on each pixel of the 16 gated-frames. The end-systolic right ventricular ROI was therefore automatically defined. The RVEF was calculated using the classical end-diastolic minus end-systolic over end-diastolic count rates. A three-harmonics Fourier curve fitting was then applied on the corrected right ventricular volume curve; and the following parameters were calculated (Fig 1): pre-ejection period, ms; time to the first third of the systole, ms; time to peak ejection rate, ms; total ejection time, ms; first third ejection rate, counts⁻¹; peak ejection rate, counts⁻¹; mean ejection rate, counts⁻¹; first third ejection on total ejection, FTE/TE; rapid filling time, ms; slow filling time, ms; time to the first third diastole, ms; time to peak filling rate, ms; total filling time, ms; first third filling rate, counts⁻¹; peak filling rate, counts⁻¹; mean filling rate, counts⁻¹; and first third filling on total filling, FTF/TF.

Study Protocol

In group 1, ⁸¹Kr RVEF was measured at rest and correlated to the pulmonary hemodynamic measurements performed during the same week.

In group 2, ⁹⁹Tc RVEF and the other noninvasive parameters were correlated to pulmonary arterial pressures and resistances measured simultaneously.

Statistics

These consisted of linear, logarithmic and exponential correlations between noninvasive parameters and pulmonary hemodynamics.

RESULTS

The plotting of ⁸¹Kr RVEF and mean pulmonary arterial pressure, presented in Figure 2, shows that both parameters are correlated (r = - 0.75) though not perfectly.

Correlations between curve parameters derived from the ECG-gated right volume curve and mean pulmonary arterial pressure are presented in Table 2. None of these curve parameters correlates better with mean pulmonary arterial pressure than RVEF even when using a logarithmic or exponential correlation
Table 2—Linear Correlation Between Radionuclide and Hemodynamic Parameters.

<table>
<thead>
<tr>
<th></th>
<th>PAP</th>
<th>PAPS</th>
<th>PVRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ejection period</td>
<td>ms</td>
<td>+0.10</td>
<td>+0.05</td>
</tr>
<tr>
<td>Time to peak ejection rate</td>
<td>ms</td>
<td>+0.24*</td>
<td>+0.26*</td>
</tr>
<tr>
<td>Time to first third systole</td>
<td>ms</td>
<td>+0.24*</td>
<td>+0.23*</td>
</tr>
<tr>
<td>Total ejection time</td>
<td>ms</td>
<td>+0.04</td>
<td>+0.09</td>
</tr>
<tr>
<td>First third ejection rate</td>
<td>counts⁻¹</td>
<td>−0.49‡</td>
<td>−0.52‡</td>
</tr>
<tr>
<td>Peak ejection rate</td>
<td>counts⁻¹</td>
<td>−0.29‡</td>
<td>−0.35‡</td>
</tr>
<tr>
<td>Mean ejection rate</td>
<td>counts⁻¹</td>
<td>−0.43‡</td>
<td>−0.46‡</td>
</tr>
<tr>
<td>First third/tot ejection rate</td>
<td>counts⁻¹</td>
<td>+0.17</td>
<td>+0.10</td>
</tr>
<tr>
<td>TPER-PEP*</td>
<td>ms</td>
<td>+0.14</td>
<td>+0.19</td>
</tr>
<tr>
<td>Diastolic phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid filling time</td>
<td>ms</td>
<td>−0.06</td>
<td>−0.04</td>
</tr>
<tr>
<td>Slow filling time</td>
<td>ms</td>
<td>−0.25*</td>
<td>−0.23*</td>
</tr>
<tr>
<td>Time to peak filling rate</td>
<td>ms</td>
<td>+0.01</td>
<td>+0.01</td>
</tr>
<tr>
<td>Time to first third diastole</td>
<td>ms</td>
<td>+0.02</td>
<td>+0.06</td>
</tr>
<tr>
<td>Total filling time</td>
<td>ms</td>
<td>−0.26*</td>
<td>−0.24*</td>
</tr>
<tr>
<td>Peak filling rate</td>
<td>counts⁻¹</td>
<td>−0.13</td>
<td>−0.19</td>
</tr>
<tr>
<td>First third filling rate</td>
<td>counts⁻¹</td>
<td>−0.34‡</td>
<td>−0.35‡</td>
</tr>
<tr>
<td>Mean filling rate</td>
<td>counts⁻¹</td>
<td>−0.23*</td>
<td>−0.27†</td>
</tr>
<tr>
<td>First third to total filling rate</td>
<td></td>
<td>−0.15</td>
<td>−0.19</td>
</tr>
<tr>
<td>RV ejection fraction</td>
<td>%</td>
<td>−0.61‡</td>
<td>−0.63‡</td>
</tr>
</tbody>
</table>

*0 = p<0.05.
†p<0.01.
‡p<0.001.
§TPER-PEP, time to peak ejection—rate pre-ejection period.

instead of a linear correlation. Figures 3 and 4 show the calculated parameters of the systolic and diastolic phases which correlate best with mean pulmonary arterial pressure, respectively first third ejection and filling rate.

The same results have been observed with the systolic pulmonary arterial pressure and the pulmonary vascular resistance index (Table 2).

DISCUSSION

In chronic obstructive pulmonary disease, pulmonary arterial hypertension frequently induces cor pulmonale and symptomatic right congestive heart failure with poor prognosis.1−3 The higher the pulmonary arterial pressure, the worse the prognosis. Therefore, the determination of this parameter seems interesting for both the evaluation and the follow-up of COPD patients. Since measuring pulmonary arterial pressure requires right heart catheterization, a traumatic and expensive procedure, a variety of other techniques have been proposed, including chest roentgenography, echocardiography, radionuclide angiography and others.12−17 Unfortunately, up to now, none of them has yielded accurate estimations of pulmonary arterial pressure.

The most commonly used radionuclide parameter is the RVEF. Indeed, correlations have been found between pulmonary arterial pressure and RVEF, but within both the normal and abnormal range, the variability of estimated pulmonary arterial pressure is important and small changes in RVEF may reflect large variations in pulmonary pressure. Therefore, more reliable radionuclide parameters have been sought. Friedman and Holman6 used regional RVEF

**Figure 3.** Linear correlation between first third ejection rate and mean pulmonary arterial pressure in 41 patients with COPD.

**Figure 4.** Linear correlation between first third filling rate and mean pulmonary arterial pressure in 41 patients with COPD.
during the second half of systole and noted that this improved accuracy in evaluating pulmonary arterial hypertension as compared to the global ejection fraction. However, in their report, accurate and reproducible results were said to require a high degree of proficiency. Marmor et al proposed another index composed by RVEF and right atrial emptying rate. In their hands, this parameter seems to evaluate the severity of pulmonary arterial hypertension very precisely.

We were interested in other radionuclide approaches. First, we used 81mKr radionuclide ventriculography because it solves most of the technical problems posed by classical methods: the surimposition of the heart chambers for equilibrium techniques, the low count rate or low resolution for first pass study, for instance. But the correlation between 81mKr RVEF and pulmonary arterial pressure hardly improved and the range of pulmonary arterial values corresponding to each RVEF was still too large. The use of 81mKr RVEF as an accurate pulmonary arterial pressure predictor index was thus questioned.

Second, the use of right ventricular curve parameters derived from a 99mTc red blood cells ECG gated equilibrium study. Indeed, systolic or diastolic delays, right ventricular ejection or filling speed have not yet been tested as indices evaluating pulmonary arterial pressure. But neither systolic nor diastolic delays could be correlated with pulmonary arterial pressure in our work.

In contrast, Marchandise et al found a correlation between the acceleration time measured by Doppler echocardiography and PAP in patients with COPD. In our study, the time between the onset and peak pulmonary flow velocity is reflected by the difference between time to peak ejection rate and pre-ejection period. This parameter has not allowed an accurate evaluation of pulmonary arterial pressure. The discrepancies between our results and Marchandise's suggest that the measurement of systolic and diastolic delays might be less accurate by the isotopic method than by the Doppler technique. This is probably due to the surimposition of the right auricle and the right ventricle. Moreover, the evaluation of mean pulmonary arterial pressure by parameters derived from a right ventricular equilibrium curve rather than the evaluation of pulmonary arterial pressure values during one heart cycle implies less precise measurements because of chest movements and a variability in duration of the heart cycles.

The speed of right ventricular emptying at different moments of the systolic phase decreases when pulmonary hypertension increases in our work. Since the right ventricular contractility either does not change or increases with deteriorating pulmonary function, the decrease of right ventricular emptying speed might be caused by an increase of RV afterload, and thus, of pulmonary arterial pressure. Unfortunately, in our work, those indices correlate to 20 to 25 percent of measured pulmonary arterial pressure and are of no clinical interest for evaluating pulmonary arterial pressure.

Finally, our findings suggest a slightly negative correlation between pulmonary arterial pressure and right ventricular filling speed during the first third of diastole. This slower early filling speed of the right ventricle is probably to be ascribed to a decreased compliance secondary to both muscular hypertrophy and chamber dilation observed in COPD with pulmonary hypertension.

In conclusion, our findings show that pulmonary hypertension in patients with COPD affects both the systolic and diastolic phase of the right ventricular function. The isotopic methods proposed do not yet provide a reliable estimation of pulmonary arterial pressure in our patients.

REFERENCES

6. Friedman BJ, Holman BL. Scintigraphic prediction of pulmonary arterial systolic pressure by regional right ventricular ejection fraction during the second half of systole. Am J Cardiol 1986; 50:1114-19
18 Stein PD, Sabbah HN, Anbe DT, Marzilli M. Performance of the failing and nonfailing right ventricle of patients with pulmonary hypertension. Am J Cardiol 1979; 44:1050-55

American Board of Internal Medicine, Subspecialty Examination in Pulmonary Disease

The 1990 subspecialty examination in pulmonary disease has been announced by the ABIM. The registration period is January 1-April 1, 1990 and the examination date is November 6, 1990. For information, contact the Registration Section, ABIM, 3624 Market Street, Philadelphia 19104 (800:441-ABIM).