Right and Left Ventricular Dysfunction in Patients With Severe Pulmonary Disease*

Carmine Dario Vizza, MD; John P. Lynch, MD, FCCP; Laura L. Ochoa, BSN; Gregory Richardson, RN; and Elbert P. Trulock, MD, FCCP

**Objective:** To determine the prevalence of right and left ventricular dysfunction in a prescreened population of patients with severe pulmonary disease, and to analyze the relationship between right and left ventricular function.

**Design:** Retrospective record review of 434 patients with severe pulmonary disease.

**Patients:** Patients with end-stage pulmonary disease, including α₁-antitrypsin deficiency emphysema, COPD, cystic fibrosis (CF), idiopathic pulmonary fibrosis, and pulmonary hypertension (primary and Eisenmenger's syndrome), who were evaluated for lung transplantation between January 1993 and December 1995.

**Measurements:** Pulmonary function tests, arterial blood gases, radionuclide ventriculography, two-dimensional transthoracic echocardiography, pulmonary hemodynamics, coronary angiography.

**Results:** Right ventricular dysfunction (right ventricular ejection fraction [RVEF] <45%) was present in 267 patients (66%), but the prevalence was highest (94%) in patients with pulmonary vascular disease. Among the patients with airway or parenchymal lung disease, the prevalence ranged from 59% in COPD to 66% in CF. In contrast, left ventricular dysfunction (left ventricular ejection fraction [LVEF] <45%) was present in only 6.4%, but it, too, was most common in the group with pulmonary hypertension (19.6%). In the groups with parenchymal or airway disease, the prevalence was 3.6%, and there was no statistical difference among the four diagnoses (α₁-antitrypsin deficiency emphysema; COPD; CF; idiopathic pulmonary fibrosis). LVEF showed a significant correlation with RVEF (r=0.44; p<0.05), and left ventricular dysfunction was associated with the presence of moderate-to-severe tricuspid regurgitation but not with coronary artery disease. In a subset of patients with both right and left ventricular dysfunction who subsequently underwent lung transplantation, RVEF and LVEF increased *pari passu* after transplantation.

**Conclusion:** The prevalence of right ventricular dysfunction is high in patients with end-stage pulmonary disease, but the prevalence of left ventricular dysfunction is relatively low. Left ventricular dysfunction appears to be related to right ventricular dysfunction, perhaps through ventricular interdependence.

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**Key words:** cor pulmonale; end-stage pulmonary disease; left ventricular function; pulmonary hypertension; right ventricular function; ventricular interdependence

**Abbreviations:** AIE=α₁-antitrypsin deficiency emphysema; CF=cystic fibrosis; Dco=diffusing capacity for carbon monoxide; IPF=idiopathic pulmonary fibrosis; LVEF=left ventricular ejection fraction; PH=pulmonary hypertension; RVEF=right ventricular ejection fraction; RVG=radionuclide ventriculography

Although cor pulmonale is not uncommon, the prevalence of right ventricular dysfunction in patients with severe pulmonary disease remains uncertain.1-5 Likewise, the prevalence of left ventricular dysfunction in advanced lung disease is not known, and the concept of left ventricular dysfunc-

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lung transplantation. The purpose was to ascertain the prevalence of ventricular dysfunction among the different lung diseases and to explore the relationship between right and left ventricular impairment.

**Materials and Methods**

**Patients**

The files of 464 patients with end-stage lung disease who had been evaluated for lung transplantation at Barnes-Jewish Hospital between January 1993 and December 1995, were reviewed. The medical records of all referrals were screened before an on-site evaluation, and standard guidelines were used to identify possible candidates for transplantation. Patients with a history of significant coronary artery disease, myocardial infarction, cardiomyopathy, or valvular disease were excluded from further evaluation by the screening process. Potential recipients who were identified in the screening phase were invited to the medical center for a formal evaluation that included a thorough cardiopulmonary assessment, which is detailed below.

Patients were divided into five groups according to their principal diagnosis: α1-antitrypsin deficiency emphysema (A1E, 64 patients), COPD (168 patients), cystic fibrosis (CF, 65 patients), idiopathic pulmonary fibrosis (IPF, 77 patients), and primary pulmonary hypertension or Eisenmenger’s syndrome (PH, 60 patients). Sixteen patients with bronchiectasis, 10 patients with lymphangioleiomyomatosis, and 4 patients with bronchitis oblitas were excluded because their number was small.

**Pulmonary Function Tests**

Pulmonary function tests were done (MedGraphics System 1085; Medical Graphics Corp; St. Paul, Minn) according to American Thoracic Society standards. Thoracic gas volume was measured by plethysmography; total lung capacity and residual volume were calculated by standard formulas. Diffusing capacity for carbon monoxide (DCO) was measured by the single-breath method. All data are reported as a percentage of the predicted normal value. Arterial blood was taken with the patient sitting, breathing room air; pH, Pco2, and Po2 were measured with a blood gas analyzer (Instrumentation Laboratory Model BG3; Lexington, Mass).

**Radionuclide Ventriculography**

The radionuclide studies were performed by the standard technique used by the Mallinckrodt Institute of Radiology at Barnes-Jewish Hospital. Right and left ventricular ejection fractions (RVEF and LVEF, respectively) were measured by gated equilibrium radionuclide ventriculography (RVG) after a peripheral IV injection of 750 MBq 99mTc technetium human serum albumin. An ejection fraction of 45% was considered the lower limit of normal for RVEF and LVEF.

**Echocardiography**

Transthoracic echocardiography was performed in all patients from January 1993 through December 1994. Thereafter, only patients with PH regularly had an echocardiogram. Echocardiograms were deleted from the routine evaluation in patients with other diagnoses because the other standard tests (RVG; cardiac catheterization) provided sufficient information in most cases. Furthermore, in patients with obstructive lung disease, the yield was limited by poor acoustic windows and inconsistent image quality.

Conventional two-dimensional echocardiography equipment was used to obtain standard parasternal, apical, and subcostal views. Pulsed Doppler spectral signals and color-Doppler evaluation of tricuspid regurgitation were studied in the best projections. The degree of tricuspid regurgitation was graded by the area of regurgitant flow (no regurgitation, mild, moderate, moderate-severe, severe). The presence of a right-to-left shunt was evaluated with a color-Doppler examination or with agitated-saline solution echo contrast in the less evident cases. Intrapulmonary shunt was diagnosed by the delayed appearance of agitated-saline solution contrast in the left heart chambers in the absence of an intracardiac shunt.

**Cardiac Catheterization**

Cardiac catheterization was performed within 3 to 5 days of the RVG and echocardiogram without any interval change in medical treatment or clinical conditions. Pressures were measured from the mid-chest position with a fluid-filled catheter and pressure transducer; the average values over three respiratory cycles were recorded. Cardiac output was measured in triplicate by the thermodilution technique (American Edwards Laboratories; Santa Ana, Calif), or, if significant tricuspid regurgitation was present, it was calculated by the Fick method. The value for pulmonary vascular resistance (PVR) was calculated with the formula, 

\[ PVR = \frac{(PAP - WP)}{CO}, \]

where PAP is the mean pulmonary artery pressure, WP is the mean pulmonary wedge pressure, and CO is the cardiac output.

Coronary angiography was done in women >45 years and men >40 years who were considered eligible for lung transplantation after the noninvasive investigations. Coronary artery disease was classified as significant if a luminal narrowing of ≥50% was present in one epicardial vessel. A minimal lesion was defined as a luminal narrowing of 20 to 49% in one epicardial vessel.

**Data Analysis**

Data were expressed as mean±SD. Data from the five groups were evaluated first with a one-way analysis of variance. Variables that showed significant differences were then analyzed with a Neuman-Kuels statistic to determine the differences among the groups. The prevalence of an event between two groups was compared with a χ² test. A least squares linear correlation was used to examine the relationship between RVEF and LVEF. A p value ≤0.05 was deemed statistically significant.

**Results**

**Clinical Variables**

The study included 434 patients, 237 women and 197 men, with a mean age of 45.7±11.6 years (Table 1). The most common diagnosis was COPD; the other four disease groups were similar in size. Not unexpectedly, the characteristics were somewhat different among the five diagnostic groups. Patients with CF were younger, had a lower mean body weight, and had a higher mean hemoglobin concentration than the other groups. Patients with COPD...
were the oldest, and patients with IPF were heavier. Female gender was more prevalent in the groups with PH and COPD.

**Pulmonary Function Tests and Arterial Blood Gases**

The differences among the five groups were consistent with the clinical features of the diseases (Table 2). Patients with PH had nearly normal results of pulmonary function tests; patients with A1E, COPD, and CF showed a severe obstructive pattern; and patients with IPF had a severe restrictive abnormality. Dco was decreased in all groups, but the lowest values were recorded in the groups with A1E, COPD, and IPF.

Comparing the arterial blood gas values among the five groups, patients with PH showed a mild respiratory alkalosis with higher pH, lower Pco2, and higher Po2 than the other groups. Among the four groups with airway or parenchymal disease, those with COPD and CF had a significantly higher Pco2 than the others, but there were no significant differences in Po2.

**Radionuclide Ventriculography**

Radionuclide ventriculography was analyzed in 405 of the 434 patients (Table 3). In 15 patients, the RVG was inadequate because a clear separation between the right atrium and right ventricle could not be obtained, and in 14 patients, data were not available. Significant right ventricular dysfunction, defined as a RVEF <45%, was found in 267 patients

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**Table 1—Profile of Patients***

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>A1E</th>
<th>COPD</th>
<th>CF</th>
<th>IPF</th>
<th>PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>64</td>
<td>168</td>
<td>65</td>
<td>77</td>
<td>60</td>
</tr>
<tr>
<td>Age, yr†</td>
<td>46±7</td>
<td>54±6</td>
<td>29±8</td>
<td>50±10</td>
<td>37±9</td>
</tr>
<tr>
<td>Gender, M:F</td>
<td>33:31</td>
<td>64:104</td>
<td>35:30</td>
<td>51:26</td>
<td>12:48†</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169±10</td>
<td>164±12</td>
<td>165±9</td>
<td>166±12</td>
<td>164±8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>68.6±17.2</td>
<td>65.0±15.3</td>
<td>49.6±11.0</td>
<td>78.5±15.0</td>
<td>69.5±12.5</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.80±0.2</td>
<td>1.70±0.2</td>
<td>1.52±0.2</td>
<td>1.85±0.2</td>
<td>1.75±0.2</td>
</tr>
<tr>
<td>Hgb, g/dL</td>
<td>14.7±1.4</td>
<td>14.0±1.3</td>
<td>13.1±1.8</td>
<td>14.2±1.8</td>
<td>14.0±2.0</td>
</tr>
</tbody>
</table>

*M, male; F, female; BSA, body surface area; Hgb, hemoglobin.

†All groups differ significantly by age (p<0.001).

‡p<0.001, PH vs others.

§p<0.002, COPD vs IPF.

‖p<0.001, CF vs others.

***p<0.001, IPF vs others.

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**Table 2—Pulmonary Function Tests***

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>A1E</th>
<th>COPD</th>
<th>CF</th>
<th>IPF</th>
<th>PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>64</td>
<td>168</td>
<td>65</td>
<td>77</td>
<td>60</td>
</tr>
<tr>
<td>FVC, %†</td>
<td>57±22</td>
<td>55±17</td>
<td>40±13</td>
<td>49±19</td>
<td>93±16</td>
</tr>
<tr>
<td>FEV1, %</td>
<td>19±7</td>
<td>20±6</td>
<td>23±7</td>
<td>50±17</td>
<td>84±20</td>
</tr>
<tr>
<td>TLC, %§</td>
<td>119±59</td>
<td>134±47</td>
<td>99±36</td>
<td>52±23</td>
<td>95±33</td>
</tr>
<tr>
<td>RV, %‡</td>
<td>322±106</td>
<td>292±92</td>
<td>297±108</td>
<td>82±44</td>
<td>129±52</td>
</tr>
<tr>
<td>Dco, %§</td>
<td>35±19</td>
<td>35±17</td>
<td>52±17</td>
<td>32±16</td>
<td>74±24</td>
</tr>
<tr>
<td>PH†</td>
<td>7.42±0.03</td>
<td>7.41±0.03</td>
<td>7.42±0.04</td>
<td>7.42±0.05</td>
<td>7.44±0.03</td>
</tr>
<tr>
<td>Pco2, mm Hg**</td>
<td>41±8</td>
<td>46±11</td>
<td>45±9</td>
<td>40±5</td>
<td>32±5</td>
</tr>
<tr>
<td>Po2, mm Hg‡</td>
<td>60±11</td>
<td>59±12</td>
<td>58±13</td>
<td>57±17</td>
<td>65±14</td>
</tr>
</tbody>
</table>

*TLc=total lung capacity; RV=residual volume.

†p<0.002 among all groups except A1E vs COPD.

‡p<0.001 PH vs others; p<0.002 IPF vs others.

§p<0.002 among all groups except A1E vs COPD and CF vs PH.

¶p<0.002 among all groups except IPF vs PH.

‖p<0.002 PH vs A1E, COPD and IPF; p<0.05 PH vs CF; p<0.02 CF vs A1E, COPD, and IPF.

*p<0.02 PH vs others.

**p<0.02 PH vs others; p<0.02 COPD vs A1E and IPF; p<0.02 CF vs A1E and IPF.

††p<0.02 PH vs others.

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Table 3—Radionuclide Ventriculography*

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>A1E</th>
<th>COPD</th>
<th>CF</th>
<th>IPF</th>
<th>PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>54</td>
<td>158</td>
<td>65</td>
<td>77</td>
<td>51</td>
</tr>
<tr>
<td>RVEF, %</td>
<td>43±10</td>
<td>45±9*</td>
<td>41±9</td>
<td>41±10</td>
<td>27±11*</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60±10</td>
<td>62±9</td>
<td>60±9</td>
<td>61±7</td>
<td>56±11*</td>
</tr>
<tr>
<td>RVEF &lt;45%, No. (%)</td>
<td>33 (61)</td>
<td>93 (59)*</td>
<td>43 (66)</td>
<td>50 (65)</td>
<td>48 (94)*</td>
</tr>
<tr>
<td>LVEF &lt;45%, No. (%)</td>
<td>3 (5.5)</td>
<td>6 (3.8)</td>
<td>2 (3)</td>
<td>5 (6.5)</td>
<td>10 (19.6)*</td>
</tr>
</tbody>
</table>

*p<0.05 COPD vs CF and IPF.
* p<0.001 PH vs others.
* p<0.002 PH vs others.

(66%). Patients with PH had a significantly higher prevalence of right ventricular dysfunction and a much lower RVEF than the other groups. No significant difference in the prevalence of right ventricular dysfunction was detected among the four groups with parenchymal or airway disease, but the mean RVEF was significantly lower in patients with CF and IPF than in patients with COPD.

The overall prevalence of left ventricular dysfunction was 6.4% (26/405). Left ventricular dysfunction was significantly more frequent and the mean LVEF was significantly lower in patients with PH than in the other groups. Patients with parenchymal or airway disease had an overall prevalence of left ventricular dysfunction of 3.6% (13/354) without any significant difference among the four groups.

The relationship between RVEF and LVEF was analyzed, and the data are illustrated in Figure 1. There was a significant correlation between RVEF and LVEF (r=0.44; p<0.05). Ten patients with both right and left ventricular dysfunction subsequently underwent lung transplantation, and their ventricular function was compared before and 12 months after transplantation (Fig 2). The RVEF and LVEF increased *pari passu* in this subset of patients.

Echocardiography

Echocardiograms were done in 337 patients; 95% of the patients who were evaluated before December 1994, when routine use was restricted to patients with pulmonary hypertension, had an echocardiogram (Table 4). Satisfactory examinations were obtained in 221 of the 337 patients as follows: COPD, 61 of 123 (49.5%); A1E, 26 of 54 (48%); CF, 25 of 41 (61%); IPF, 63 of 70 (90%); and PH 46 of 49 (94%). The overall prevalence of moderate or severe
tricuspid regurgitation was 16.4% of these cases, while mild tricuspid regurgitation was present in 56.4%. The group of patients with PH had the highest prevalence of moderate or severe tricuspid regurgitation, and severe tricuspid regurgitation was detected only in patients with IPF or PH. Both RVG and echo-Doppler studies were available in 219 patients. The prevalence of significant, ie, moderate or severe, tricuspid regurgitation was significantly higher in patients with impaired ventricular systolic function by RVG (47% with vs 14% without LVEF <45%, p<0.001; 23% with vs 3% without RVEF <45%; p<0.0001), and the prevalence of left ventricular dysfunction increased with the severity of tricuspid regurgitation (7.7% with mild, 15.7% with moderate, and 22.7% with severe tricuspid regurgitation, respectively).

A right-to-left shunt was discovered in 45 patients, and the highest prevalence was in the PH group. The shunt occurred through a patent foramen ovale in 13 patients with parenchymal or airway disease (COPD, 4; IPF, 9), in 16 of 31 patients with primary PH and in 2 of 4 patients with Eisenmenger’s syndrome (who had previously had an atrial septal defect closed). In 11 patients with Eisenmenger’s syndrome, the shunt was through the primary cardiac defect (atrial septal defect, 8; ventricular septal defect, 2; and patent ductus arteriosus, 1). An intrapulmonary shunt was present in three patients (COPD, one; CF, two).

### Pulmonary Hemodynamics and Coronary Angiography

The PH group had the highest mean right atrial and mean pulmonary artery pressures, the highest pulmonary vascular resistance, and the lowest cardiac index (Table 5). There was no difference in the pulmonary capillary wedge pressure among the five groups. The group with CF had a higher cardiac index than the others, and the group with IPF had a higher pulmonary vascular resistance than the group with COPD.

Coronary angiography was available in 282 patients. The overall prevalence of significant coronary artery disease was only 8.5% (24/282) in this pre-screened population. The prevalence ranged from 2.4% in patients with AIE to 10.5% in those with COPD, but there was no statistical difference in the prevalence among the five disease groups. Furthermore, the prevalence of significant coronary artery

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>AIE</th>
<th>COPD</th>
<th>CF</th>
<th>IPF</th>
<th>PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>54</td>
<td>156</td>
<td>64</td>
<td>77</td>
<td>50</td>
</tr>
<tr>
<td>Mean pressures, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right atrium</td>
<td>8±4</td>
<td>8±4</td>
<td>5±4</td>
<td>6±5</td>
<td>10±6</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>26±7</td>
<td>25±6</td>
<td>28±8</td>
<td>27±12</td>
<td>58±21</td>
</tr>
<tr>
<td>Wedge</td>
<td>12±4</td>
<td>11±4</td>
<td>10±4</td>
<td>10±5</td>
<td>10±5</td>
</tr>
<tr>
<td>PVRI, WU/m²</td>
<td>5.1±2.0</td>
<td>4.4±1.7</td>
<td>4.6±2.3</td>
<td>6.2±5.4</td>
<td>24±11.6</td>
</tr>
<tr>
<td>Cardiac index, L/min/m²</td>
<td>3.0±0.6</td>
<td>3.1±0.7</td>
<td>4.0±0.7</td>
<td>3.0±0.6</td>
<td>2.4±0.8</td>
</tr>
</tbody>
</table>

*PVRI=pulmonary vascular resistance index; WU=Wood units.

†p<0.001, PH vs others.

‡p<0.02, PH vs others.

§p<0.05, IPF vs COPD.
disease was not significantly different between patients with vs without left or right ventricular dysfunction.

**Discussion**

The cardiovascular status of patients with advanced lung disease has not been extensively studied, and the relationship between right ventricular and left ventricular function in this setting remains uncertain. In this study, the prevalence of right and left ventricular dysfunction was determined in a prescreened population with severe pulmonary disease who had been evaluated for lung transplantation. The diseases included the common parenchymal and airway diseases (A1E, COPD, CF, and IPF) and two major pulmonary vascular diseases (primary PH and Eisenmenger’s syndrome). The unique characteristic of these patients is the severity of their disease, and, in this regard, the results offer a perspective of cardiac function in end-stage lung disease.

Not unexpectedly, right ventricular dysfunction (RVEF <45%) was usually present and was much more severe in the patients with pulmonary vascular disease (PH group) than in the patients with parenchymal or airway disease (Table 3). This, of course, correlates with the differences in the hemodynamic profiles between the PH group and the other groups. PH was very severe in the PH group but mild in those with the other diseases (Table 5).

In the groups with parenchymal or airway disease (A1E, COPD, CF, IPF), the prevalence and the degree of right ventricular dysfunction were relatively consistent (Table 3). Although right ventricular dysfunction was present in the majority, the RVEF was only minimally depressed, and the cardiac index was well preserved. Comparing the RVEFs and the hemodynamic parameters among these four groups, there were few relevant differences. The pulmonary vascular resistance was significantly higher in the group with IPF than in the group with COPD; this finding is presumably explained by more extensive vascular involvement in IPF than in COPD. The cardiac index was higher in the CF group than in the COPD group. The reason for this difference is uncertain, but the physiologic effects of younger age and/or chronic infection in the CF group could have had an impact.

In contrast to right ventricular dysfunction, left ventricular dysfunction occurred infrequently. The overall prevalence was only 6%, but because the patients had been prescreened, this probably underestimates the true prevalence in an unselected population. Whereas patients with clinical, radiographic, or physiologic evidence of isolated right ventricular dysfunction were not excluded from an evaluation for transplantation, referrals with known coronary artery disease and/or left ventricular dysfunction were routinely disqualified from further consideration during the screening phase.

Like right ventricular dysfunction, left ventricular dysfunction was most common in the patients with pulmonary vascular disease, and the prevalence was significantly higher in the PH group than in any other group (Table 3). Moreover, there was a significant correlation between LVEF and RVEF (Fig 1). While certainly not conclusive, this relationship between right and left ventricular function suggests ventricular interdependence, whereby right ventricular dilatation can compromise left ventricular function by shifting the interventricular septum. Such an interplay between the ventricles is also supported by the concomitant recovery of both RVEF and LVEF after lung transplantation (Fig 2).

A recent study found left ventricular dysfunction in 32% of patients with COPD who presented with symptomatic deterioration, and the investigators concluded that left ventricular dysfunction was contributing to the patients’ exercise intolerance. However, the results of our study imply that, instead of being an independent factor, left ventricular dysfunction could also be related to cor pulmonale accompanying an exacerbation of COPD. Furthermore, in our study, left ventricular impairment without significant concomitant right ventricular dysfunction was rare, and, in unscreened patients with advanced lung disease, primary cardiovascular disease should be considered when left ventricular dysfunction occurs alone or seems out of proportion to right ventricular dysfunction.

The prevalence of significant coronary artery disease was very low in this study, at least in part because patients with known coronary artery disease were excluded by the preevaluation screening process. The yield of coronary angiography in lung transplant candidates has been similarly low in other studies, and the utility and cost effectiveness of routine angiography remain debatable. Nevertheless, the clinical value of a normal preoperative coronary angiogram cannot be summarily discounted.

Hemodynamic instability is common during the transplant operation and in the early postoperative period, and the risk of myocardial ischemia or infarction would be high if the recipient had significant occlusive disease. Furthermore, preexisting coronary artery disease might be accelerated by systemic hypertension, hypercholesterolemia, hypertriglyceridaemia, and other cardiovascular risk factors that evolve in most lung transplant recipients, and it
could thereby add to intermediate-term morbidity and mortality after transplantation.

The hemodynamic information from right heart catheterization is useful, too. It has prognostic implications\(^{21-23}\) that can be synthesized into the decision about the need for and the timing of transplantation, and it has ramifications for the operation itself, especially the need for cardiopulmonary bypass.\(^{24}\) Thus, in our experience, right and left heart catheterization has been helpful in selecting recipients, planning their operation, and treating them afterwards.

This study has several inherent limitations. Because it is a retrospective review of a prescreened population, the results may be skewed by selection bias and should not be extended to unselected patients without considering this constraint.

The measurement of RVEF by RVG also presents some problems that must be reckoned in the conclusions.\(^{25}\) The gated equilibrium method, which was used in this study, is less accurate than first-pass radionuclide angiography for determining RVEF.\(^{26}\) If the cardiac chambers overlap in the equilibrium technique, the calculated ejection fraction will be erroneously low. Although radionuclide counts were acquired in the projection that gave the best chamber separation, RVEF could have been underestimated by overlap of the right atrium and right ventricle in some cases. Since the reproducibility of the RVEF measurement is no better than \(\pm 3\%\), and the lower limit of normal is sometimes considered 40%,\(^{25}\) instead of 45%, the results of this study could overstate the extent of right ventricular dysfunction, particularly in the groups with a minimally depressed RVEF (Table 3; A1E, COPD, CF, and IPF).

RVEF is a useful gauge of global right ventricular performance, but it must be deciphered carefully. RVEF is affected not only by contractility but also by preload and afterload, and it may be very afterload dependent.\(^{25}\) Hence, a decreased RVEF does not necessarily imply abnormal contractility. In the patients in this study, for example, increased afterload associated with PH is probably the principal cause of right ventricular dysfunction.

Notwithstanding these shortcomings, this study illustrates that significant right ventricular dysfunction occurs frequently in patients with severe primary PH and Eisenmenger's syndrome. However, right ventricular dysfunction is less prevalent and relatively minimal in other end-stage lung diseases. Left ventricular dysfunction is unusual in patients with advanced parenchymal or airway disease when those with known cardiac disease have been eliminated, but it is present in a modest proportion of patients with severe PH and is probably caused by right ventricular overload with septal shift that impairs left ventricular filling.

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