临床研究

右心室扩大，右心室壁增厚，以及多普勒证据提示肺动脉高压

患者有单纯限制性通气障碍

Kalyanam Shivkumar, M.D.; Kumar Ravi, M.D.;
Jerald W. Henry, M.S.; Michael Eichenhorn, M.D., F.C.C.P.;
and Paul D. Stein, M.D., F.C.C.P.

目的

这项研究旨在确定单纯限制性通气障碍的严重程度，导致右心室（RV）扩大，肺动脉高压。二维（2-D）超声心动图，多普勒测量肺动脉血流，以及肺功能测试，在未经选择的患者（17女性，9男性）中进行。RV扩大受限的定义是肺活量（FVC）≥80%预测值，带有正常FEV₁/FVC比值（FEV₁=1 s强迫呼气容积）。患者被分类为RV扩大受限的严重程度：轻度（FVC，65%至80%预测值），中度（FVC，51%至64%预测值），和严重（FVC ≤50%预测值）。RV面积（>20.4 cm²）的增加在10%的患者中与轻度RV扩大受限有关，6%的患者与中度受限有关，2%的患者与重度受限有关。RV壁厚度（>0.5 cm）在10%的男性患者中观察到，这些患者有中度RV扩大受限，3%的男性患者有中度受限，1%的男性患者有重度受限。

受检者

患者患有职业性肺病，可能有轻微或未被发现的右心室异常。本研究旨在确定右心室扩大受限的严重程度，继发于限制性通气障碍。研究的目的是，研究在RV扩大受限严重程度的患者中，限制性通气障碍与RV扩大和肺动脉高压的相关性。

方法

26例患者有单纯限制性通气障碍，定义为肺活量（FVC）≥80%预测值。

*从亨利福特心脏和血管研究所，底特律。

Manuscript收到日期：1993年8月19日；修订日期：1994年3月16日。

Reprint请求：Dr. Stein, Henry Ford Hospital, New Center Pavilion, Rm 1107, 2921 West Grand Blvd, Detroit, MI 48202-2691.

CHEST / 106 / 6 / DECEMBER, 1994 1649

Key words: asbestos; cor pulmonale; pneumoconiosis; pulmonary fibrosis; pulmonary hypertension; restrictive lung disease

和一个正常的FEV₁/FVC比值（FEV₁=1 s强迫呼气容积），由二维（2-D）和M-模式超声心动图，脉冲多普勒超声，以及肺功能测试。

患者特征

26例患者中，15例有无相应的心脏病，7例有心肌梗死（有左心室壁增厚≤1.3 cm和无LV扩大，有正常左心室壁收缩），3例有主动脉瓣狭窄（有正常左心室壁尺寸）。患者被排除，因为左心室侧壁的主动脉瓣狭窄。

超声心动图

所有患者都接受了2-D超声心动图和M-模式研究，包括左心室和右心室，使用 phased-array超声心动图系统（Hewlett-Packard 500）。图像在副膈长轴，副膈短轴，和

1694

CHEST / 106 / 6 / DECEMBER, 1994

http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21704/ on 06/14/2017
Lung tumor
end-diastole.2
if
the
Postthoracotomy
obesity
Morbid
Interstitial lung disease
calculated
as
Scoliosis
spondylitis
Unknown
Surgically induced vertebral fusion posttrauma
1§

*One asbestos, one progressive systemic sclerosis.
†Three patients with interstitial lung disease also had morbid obesity.
§One scoliosis surgically corrected, two uncorrected.
§Also postthoracotomy chest wall restriction.
apical four-chamber views with the patient in the left lateral decubitus position. Images were also obtained in the short axis view at the aortic valve level. All the images were stored on a VHS videotape using a video recorder (Panasonic).

For each study, gain settings and gray scale were optimized to ensure the endocardial borders were clear for planimeterization. Because endocardial definition is influenced by the focal line and center line frequency of the imaging transducer, the highest frequency that allowed adequate penetration was used to optimize the images obtained in each patient.1 Right ventricular area was mapped on the screen after identification of the blood endocardial interface of the right ventricle. The right ventricular area was calculated by planimetry from the apical four-chamber view at end-diastole.3 The end-diastolic frame was identified as the instant of the onset of the electrocardiographic QRS complex or as the video frame at or before the initial systolic coaptation of the mitral valve.1 The right ventricle was considered to be enlarged if the right ventricular area was >20.4 cm².2

Right ventricular wall thickness was measured from the M-mode echocardiographic tracings of the parasternal long axis view. The distance from the epicardium to the endocardium of the right ventricle was taken to be the thickness of the right ventricular free wall. Right ventricular wall thickening was considered to be present when the right ventricular wall was >0.5 cm².

Left ventricular ejection fraction was calculated on the basis of ventricular volumes calculated by the single plane area length method using the apical four-chamber view.1 Left ventricular dimensions in diastole were measured from the apical four-chamber view. Left ventricular wall thickness was measured from the parasternal long axis view.

The pulsed Doppler waveform in the main pulmonary artery was obtained by placing the Doppler sample volume above the pulmonary valve away from the walls of the main pulmonary artery.4 Doppler wave forms were printed on chart paper that also included a continuous electrocardiographic tracing. The acceleration time (ACT) was measured from the onset of pulmonary velocity to the peak of velocity.4 The ejection time (ET) was measured from the onset of the pulmonary velocity to the end of the pulmonary velocity.4 An ACT/ET ratio of <0.32 was considered to be indicative of pulmonary hypertension.4

**Spirometry**

All patients underwent spirometry on the same day as their echocardiographic study. The spirometric tracings were obtained using a benchmark pulmonary function testing system (P.K. Morgan Corp, Andover, Mass) or a pulmonary function testing system (Medical Graphics model 1070, Medical Graphics Corp, St. Paul, Minn). The tracings were obtained with the patients in the sitting position and the best of three tracings was used for analysis. Lung volumes were expressed as percent predicted for the patient's age, height, and sex. An FVC ≤80 percent predicted and a normal FEV₁/FVC ratio were considered indicative of a pure restrictive ventilatory impairment. The patients were grouped according to the FVC percent predicted as follows: mild restriction (FVC, 65 to 80 percent predicted), moderate restriction (FVC, 51 to 64 percent predicted), and severe restriction (FVC ≤50 percent predicted) (Table 2).

**Statistical Analysis**

The strength of the linear relationships was estimated by Pearson correlation coefficients and their 95 percent confidence intervals (CIs). Unpaired Student's t tests were used to compare continuous variables among patients with mild, moderate, and severe restrictive defect. A Bonferroni correction for multiple comparisons was applied. A probability of p<0.01 was considered significant.

---

**Table 1—Underlying Disorders in Patients With Ventilatory Restriction**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial lung disease</td>
<td>9*</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4</td>
</tr>
<tr>
<td>Lung tumor</td>
<td>1</td>
</tr>
<tr>
<td>Morbid obesity</td>
<td>2†</td>
</tr>
<tr>
<td>Respiratory muscle dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Postthoracotomy chest wall restriction</td>
<td>1</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>1</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>3†</td>
</tr>
<tr>
<td>Surgically induced vertebral fusion posttrauma</td>
<td>1§</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
</tr>
</tbody>
</table>

*One asbestos, one progressive systemic sclerosis.
†Three patients with interstitial lung disease also had morbid obesity.
§One scoliosis surgically corrected, two uncorrected.
§Also postthoracotomy chest wall restriction.

---

**Table 2—Age, Cardiac Dimensions, Doppler Evidence of Pulmonary Hypertension, and Spirometric Values According to Severity of Restrictive Lung Impairment**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild (FVC 65-80%) (n=10)</th>
<th>Moderate (FVC 51-64%) (n=12)</th>
<th>Severe (FVC ≤50%) (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>52±11</td>
<td>57±19</td>
<td>76±51</td>
</tr>
<tr>
<td>LVDDd, cm</td>
<td>3.6±0.5</td>
<td>3.9±0.9</td>
<td>3.7±0.9</td>
</tr>
<tr>
<td>EF, %</td>
<td>59±5</td>
<td>59±6</td>
<td>60±7</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.2±0.5</td>
<td>2.0±0.6</td>
<td>1.4±0.4</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>72±4</td>
<td>55±3</td>
<td>43±9</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>86±5</td>
<td>85±5</td>
<td>79±12</td>
</tr>
<tr>
<td>ACT/ET, dimensionless</td>
<td>0.42±0.09</td>
<td>0.29±0.111</td>
<td>0.22±0.04∥</td>
</tr>
<tr>
<td>RV area, cm²</td>
<td>13±3</td>
<td>19±2§</td>
<td>22±4§</td>
</tr>
<tr>
<td>RV wall thickness, cm</td>
<td>0.44±0.04</td>
<td>0.44±0.07</td>
<td>0.45±0.09</td>
</tr>
</tbody>
</table>

*All values are mean±SD. LVDDd=left ventricular diastolic dimension; EF=ejection fraction; FVC=forced vital capacity; RV=right ventricle; LV=left ventricle.
†p<0.01 mild vs severe. p<0.001 mild vs severe.
‡p<0.01, mild vs moderate.
§p<0.001, mild vs moderate.
∥p<0.001, mild vs severe.
RESULTS

Echocardiography

Among all patients with a restrictive ventilatory defect, right ventricular area correlated with the FVC percent predicted (r = −0.90) (95 percent CI, −0.79 to −0.96) (p<0.001) (Fig 1). Among patients with primary restrictive lung disease (n=14), exclusive of patients with dysfunction of the respiratory apparatus, right ventricular area correlated closely with the FVC percent predicted (r = −0.93) (95 percent CI, −0.80 to −0.98) (<0.005). Among patients with a restrictive ventilatory impairment due to a mechanical deformity or dysfunction (n=9), the right ventricular area also correlated closely with the FVC percent predicted (r = −0.89) (95 percent CI, −0.52 to −0.98) (p<0.005).

An increased right ventricular area (>20.4 cm²) was shown only when the FVC was ≤57 percent predicted. Right ventricular area among patients with mild, moderate, and severe restrictive ventilatory impairment was 13±3 cm², 19±2 cm², and 22±4 cm², respectively (p<0.001 mild vs severe and mild vs moderate) (Table 2). None of the patients with a mild restrictive impairment had an increased right ventricular area, 6 of 12 patients (50 percent) with moderate restriction had an increased right ventricular area, and 2 of 4 (50 percent) patients with severe restriction had an increased right ventricular area (Table 3). Right ventricular area correlated with the ACT/ET ratio (r = −0.67) (95 percent CI, −0.38 to −0.84) (p<0.001).

Right ventricular wall thickness did not correlate with the FVC percent predicted (r = 0.14) (95 percent CI, −0.26 to 0.50) (p=NS). Right ventricular wall thickness among patients with mild, moderate, and severe restrictive ventilatory impairment was 0.44±0.04 cm, 0.44±0.07 cm, and 0.45±0.09 cm (all differences NS). Increased right ventricular wall thickness was seen only in patients with an FVC ≤56 percent predicted. None of the patients with a mild restrictive impairment had increased right ventricular wall thickness, 3 of 12 (25 percent) patients with a moderate restrictive defect, and 1 of 4 (25 percent)
patients with a severe restrictive defect had increased right ventricular wall thickness. Right ventricular wall thickness correlated weakly with the ACT/ET ratio \( (r = -0.33) \) (95 percent CI, \(-0.07\) to \(-0.64\) ) \( (p<0.05) \).

The ACT/ET ratio correlated with the FVC percent predicted \( (r=0.73, p<0.001) \) (linear regression) \( (\text{Fig 2}) \). An ACT/ET ratio \(<0.32\), indicative of elevated pulmonary arterial pressures, was shown only if the FVC was \(<60\) percent predicted. The ACT/ET ratios among patients with mild moderate and severe restrictive ventilatory impairment were \(0.42 \pm 0.09, 0.29 \pm 0.11,\) and \(0.22 \pm 0.04\) (Table 2). None of the patients with a mild restrictive defect, \(8\) of \(12\) (66 percent) with a moderate restrictive defect, and \(4\) of \(4\) (100 percent) with a severe restrictive defect had ACT/ET ratios indicative of elevated pulmonary arterial pressures \( (p<0.01 \text{ mild vs moderate and mild vs severe}) \) (Table 3).

**DISCUSSION**

Irrespective of the etiology of interstitial lung disease, there is an accumulation of inflammatory cells that causes further injury and fibrosis.\(^5\) Fibrosis entrap segments of the pulmonary vasculature and infiltrates and compresses the vessels, leading to thrombosis of the vessels and subsequent fibrous organization.\(^6\) The pulmonary vessels may be compressed and obliterated.\(^7\) In pulmonary blood vessels far removed from areas of fibrosis, there are findings consistent with hypoxic pulmonary hypertension with thickening of the arterioles and muscle organization of the vessels.\(^8\) The level of pulmonary artery hypertension usually reflects the severity of hypoxemia.\(^5\) Late in the course of disease, if hypoxemia becomes marked, severe pulmonary hypertension and right-sided heart failure occur.\(^5\)

Disorders causing alveolar hypoventilation due to neuromuscular disorders or chest cage disorders are characterized by hypercarbia and hypoxemia.\(^9\) Hypoxic pulmonary vasoconstriction plays a major role in causing pulmonary artery hypertension.\(^10\) Cor pulmonale is common, and right ventricular failure is a major cause of death.\(^5\)

Previous literature in patients with a restrictive ventilatory impairment does not describe a relationship between the FVC and right ventricular enlargement. There is, however, concern over subtle enlargement of the right ventricle in patients with occupational pleuropulmonary disease. The relationship of right ventricular enlargement to the severity of the ventilatory impairment provides a useful guide for an assessment of the likelihood of cor pulmonale in such patients. The present study shows that patients with a restrictive ventilatory impairment, irrespective of whether it is primary lung disease or due to an impairment of the respiratory apparatus, show a close correlation of the FVC percent predicted with right ventricular enlargement. Right ventricular dilatation occurred only among patients with an FVC \(<57\) percent predicted, and right ventricular thickening occurred only when the FVC was \(<56\) percent.

In patients with diffuse interstitial lung disease, pulmonary arterial diastolic pressure increased hyperbolically as the FVC percent predicted decreased.\(^7\) Pulmonary artery diastolic pressures were normal in patients with an FVC between 50 to 80 percent predicted.\(^7\) Our data showed Doppler evidence of normal pulmonary artery pressure in patients with an FVC >60 percent predicted.

Two-dimensional echocardiographic measurements of the right ventricle have been compared with measurements obtained by ventriculography in 25 patients with normal right ventricles.\(^2\) The normal right ventricular area was \(18.0 \pm 1.2 \text{ cm}^2\). Measurements were also made at autopsy from casts of the normal right ventricles of eight patients. A good correlation was observed \( (r=0.95) \) between the area obtained by 2-D echocardiography of the right ventricular casts and dimensions of the casts measured directly.\(^2\) Right ventricular mass was shown in an autopsy study of 1,500 human hearts to correlate with right ventricular area \( (r=0.78)\).\(^4\)

The ACT/ET ratio has been tested in 20 normal patients. The mean ACT/ET ratio was 0.41 (range, 0.32 to 0.56).\(^11\) An inverse linear relation between the ACT/ET ratio and the pulmonary artery mean pressure \( (r = -0.90) \) was observed in nine patients.\(^12\)

In conclusion, right ventricular dilatation and increased right ventricular wall thickness and Doppler evidence of pulmonary hypertension were seen only in patients with a moderate or severe restrictive ventilatory impairment. These data may be applicable to the clinical assessment of the likelihood of subtle right ventricular enlargement in patients with occupational pleuropulmonary disease.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild (FVC 65-80%)</th>
<th>Moderate (FVC 51-64%)</th>
<th>Severe (FVC ≤50%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV area &gt;20.4 cm²</td>
<td>0/10 (0%)</td>
<td>6/12 (50%)</td>
<td>2/4 (50%)</td>
</tr>
<tr>
<td>RV wall thickness</td>
<td>0/10 (0%)</td>
<td>5/12 (25%)</td>
<td>1/4 (25%)</td>
</tr>
<tr>
<td>ACT/ET &lt;0.32</td>
<td>0/10 (0%)</td>
<td>8/12 (67%)*</td>
<td>4/4 (100%)†</td>
</tr>
</tbody>
</table>

*\(p<0.01\), mild vs moderate.
†\(p<0.01\), mild vs severe.

\[1652\]
REFERENCES

1 Schiller NB. Two-dimensional echocardiographic determination of left ventricular volume, systolic function, and mass: summary and discussion of the 1989 recommendations of the American Society of Echocardiography. Circulation 1991; 84:1280-87


3 Baker BJ, Scovil JA, Kane JJ, Murphy ML. Echocardiographic detection of right ventricular hypertrophy. Am Heart J 1983; 105:611-14


