Noninvasive Evaluation of Pulmonary Artery Pressure During Exercise by Saline-Enhanced Doppler Echocardiography in Chronic Pulmonary Disease

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To determine the feasibility of noninvasive determination of right ventricular systolic pressure (RVSP) during a graded-exercise protocol, saline contrast-enhanced Doppler echocardiography of tricuspid insufficiency was performed in 36 patients with chronic lung disease and 12 normal controls. In the patients with chronic pulmonary disease, symptom-limited, incremental supine bicycle exercise and pulse oximetry were performed on and off high-flow oxygen. Technically adequate Doppler studies were initially obtained in 20 patients (56%) at rest and 14 (39%) on exercise; these numbers increased to 33 (92%) and 32 (89%), respectively, after enhancement with agitated saline (both p<0.001). In 10 patients with chronic lung disease who had simultaneous hemodynamic monitoring during exercise, the correlation between Doppler and catheter measurements of pulmonary artery systolic pressure was close (r=0.98). Among controls, RVSP increased from 22±4 at rest (mean±SD) to 31±7 mm Hg at peak exercise. In patients with chronic lung disease, RVSP increased from 46±20 to 83±30 mm Hg (both p<0.001 vs. controls). Despite normal resting values for RVSP in 28% of study patients, nearly all showed abnormal increases in RVSP during supine bicycle exercise. Increases in RVSP during exercise were greatest in patients who showed oxyhemoglobin desaturation. The short-term administration of oxygen significantly blunted the increase in RVSP during exercise. Saline contrast-enhanced Doppler evaluation of tricuspid insufficiency seems a potentially valuable noninvasive method of determining the exercise response of RVSP in patients with chronic pulmonary disease. (Circulation 1989;79:863–871)

Pulmonary hypertension is a complication of chronic lung disease that is associated with augmented morbidity and mortality.1-4 Therefore, identifying pulmonary hypertension at rest or in response to exercise is important for diagnostic, prognostic, and therapeutic purposes. The measurement of pulmonary artery pressure during exercise in patients with chronic lung disease has been accomplished only with invasive techniques involving right heart catheterization.5-8 In patients with chronic obstructive pulmonary disease, exercise often provokes elevations of pulmonary artery pressure, pulmonary capillary wedge pressure, and right ventricular end-diastolic pressure.5-8

Doppler echocardiography offers an accurate noninvasive approach to determining right ventricular systolic pressure (RVSP) at rest.9 In patients with chronic pulmonary disease, we used saline contrast-enhanced Doppler of tricuspid insufficiency to determine the exercise response of RVSP while the patients were on and off oxygen. The study was performed to determine 1) the feasibility and accuracy of noninvasive determination of RVSP during exercise in patients with chronic lung disease, 2) the
relation between RVSP and arterial hypoxemia during exercise, and 3) the effect of short-term supplemental oxygen therapy on these indexes.

Methods

Patient Population

The protocol was approved by the Committee for Human Research at the University of California, San Francisco. The patient population consisted of 12 control patients (aged 27–68 years, 11 male) with no history of cardiopulmonary disease and 36 patients with moderate-to-severe chronic pulmonary disease (aged 32–80 years, 21 male) from the Fort Miley Veterans Hospital or the University of California, San Francisco, who consented to participate in the study. Pulmonary diagnoses were based on the results of clinical evaluation, chest radiography, and pulmonary function testing. Etiologies of pulmonary disease included chronic obstructive pulmonary disease in 23 patients, interstitial lung disease in eight (sarcoidosis in four, idiopathic in three, radiation-induced in one), primary pulmonary hypertension in two, thromboembolic disease in two, and scleroderma with pulmonary vascular disease in one.

Pulmonary function tests, resting arterial blood gas, and hemoglobin were performed on all patients within 1 week of the study. Total lung capacity was measured by a nitrogen washout technique at the Fort Miley Veterans Hospital and by a helium dilution method at the University of California; diffusing capacity was measured by a single-breath carbon monoxide method and corrected for hemoglobin. We excluded patients with known coronary artery disease, congestive heart failure, and vascular, orthopedic or neurologic problems of the lower extremities that precluded bicycle exercise. In addition, two patients were excluded after baseline echocardiography showed evidence of a previous inferior wall myocardial infarction in one patient and moderate left ventricular dysfunction with diffuse hypokinesis in another. Evaluations were scheduled when patients were clinically stable; testing was postponed when clinical exacerbations of symptoms occurred within the previous 4 weeks.

Oximetry

An N-10 or N-200 (R wave–gated) pulse oximeter (Nellcor, Hayward, California) with continuous readout was placed on the index finger of the right hand. The right hand was gently immobilized to prevent motion artifact during bicycle exercise. The lowest value for arterial saturation during each stage of exercise was recorded. Arterial desaturation during exercise was defined as a 4% or greater decrease from baseline levels of oxyhemoglobin saturation to less than 90% saturation.

Exercise Protocol

Exercise studies were performed at 9:00 AM. Patients were instructed to eat a light breakfast on the morning of testing and to take their usual prescribed medications. Of the 36 study patients, 33 exercised on room air and oxygen (23 patients on 10 l/min by nasal cannula and 10 patients on 40% oxygen). The order of testing on room air or oxygen was randomized. Before each exercise test, patients breathed the chosen gas for at least 15 minutes. Between tests, patients rested for 40 minutes. The first 10 patients were aware of which gas they were breathing; for the final 23 patients, testing was conducted in a double-blinded fashion.

A variable-load supine bicycle ergometer (Engineering Dynamics Corporation Model 8420, Lowell, Massachusetts) was used for all testing with the ergometer table tilted to 20° (patient’s left side down) to obtain the echocardiographic apical view. Patients pedalled at a constant speed, beginning at a workload of 10 W and increasing by 10 W every 2-minute stage until reaching dyspnea or symptom-limiting fatigue. Heart rate, cuff blood pressure, minimum oxyhemoglobin saturation, and maximum tricuspid insufficiency velocity (see below) were recorded at rest, at each stage of exercise, and after 4 minutes of recovery. Continuous lead 2 electrocardiogram was monitored throughout exercise. The duration of exercise on and off oxygen and the limiting symptoms were recorded in each patient.

Control patients exercised on room air only, beginning at 25 W and increasing by 25 W every 2 minutes. Control patients exercised to symptom-limiting fatigue or to a maximum workload of 200 W. The same indexes as noted above were recorded at rest, at each stage of exercise, and during recovery.

Echocardiography

With a 3.5-MHz transducer for imaging and a 2.5-MHz transducer for Doppler (Irex Meridian, Ramsey, New Jersey), a complete resting two-dimensional echocardiogram, including imaging and Doppler echocardiograms in all standard views, and subcostal imaging of the inferior vena cava was performed just before exercise.

Ratios of right to left ventricular end-diastolic sizes in the apical four-chamber view (RV/LV size) were determined with a phantom-calibrated computerized light-pen (Diasonics, Milpitas, California) by a single-plane area-length method. Tracings were made during held inspiration, when right ventricular sizes were the largest. From previous work, the mean value for the ratio of RV/LV size in normal adults is 0.6 ± 0.1.

Right atrial pressure was estimated at rest by the response of the inferior vena cava to deep inspiration and was assumed to be constant throughout exercise. With the trailing-edge to leading-edge technique, maximum inferior vena cava diameters before inspiration and minimum diameters after inspiration were measured in the subcostal view within the first 2 cm of the entrance to the right atrium. When the diameter of the inferior vena cava (measured at rest with the legs raised onto the bicycle pedals)
decreased by less than 50% after deep inspiration, right atrial pressure was defined to be 15 mm Hg; when the diameter decreased by more than 50%, right atrial pressure was defined to be 5 mm Hg.\textsuperscript{16,17} All patients except one showed greater than a 50% decrease in vena cava diameter at rest.

Intravenous injections of 2 to 3 ml agitated isotonic saline (contrast) were performed at rest, at each stage of exercise, and at recovery. Saline was agitated with two syringes mounted on a three-way stop-cock and injected directly into an antecubital vein through a 20-gauge catheter. Contrast media was injected to delineate the right ventricular cavity, to enhance the tricuspid insufficiency Doppler signal, and to detect right-to-left shunting through a patent foramen ovale.

Doppler evaluation of the tricuspid valve was performed in the apical four-chamber view. The regurgitant jet was localized in the pulsed mode, then maximized and measured in the continuous wave mode at a sweep speed of 75 mm/sec. By a modification of the Bernoulli formula,\textsuperscript{18} the maximum transtricuspid gradient (in mm Hg) was estimated as the product of 4 and the square of the maximum tricuspid insufficiency velocity ($\Delta P = 4V^2$). RVSP was computed as the sum of the transtricuspid gradient and right atrial pressure (RVSP $= 4V^2 +$ right atrial pressure).\textsuperscript{9}

Throughout exercise, continuous full-screen monitoring of tricuspid insufficiency at a sweep speed of 75 mm/sec was performed. During each 2-minute stage of incremental exercise, agitated saline was injected intravenously to enhance the Doppler signal. We considered tricuspid insufficiency envelopes to be technically adequate when signals were pansystolic and showed well-defined borders. After videotape review, the maximum tricuspid insufficiency velocity was assigned to the highest coherent boundary on the spectral wave form.\textsuperscript{9} Maximum velocities recorded at rest, at each stage of exercise, and during recovery permitted the calculation of the transtricuspid gradient and RVSP throughout the test (Figure 1).

To ensure accurate transducer position throughout exercise, the location of the continuous wave Doppler cursor was checked intermittently by two-dimensional imaging. Tricuspid insufficiency was distinguished from aortic outflow or mitral regurgitation by 1) the location of the Doppler cursor within the boundaries of the right heart, 2) the characteristic high-pitched audio signal, 3) the characteristic sound and appearance of contrast enhancement of the tricuspid insufficiency profile (left heart Doppler signals will not show contrast enhancement in the absence of a right-to-left intracardiac shunt), and 4) the comparison to the contours of the resting Doppler envelopes.

**Invasive Testing**

Of the 36 patients with chronic pulmonary disease in the study, 10 had flow-directed pulmonary artery catheters, and 10 had radial or brachial arterial catheters in place at the time of exercise testing; these catheters had been inserted for reasons unrelated to this study.

Etiologies of chronic pulmonary disease in the 10 patients who exercised with flow-directed pulmonary artery catheters in place were obstructive disease in five, primary pulmonary hypertension in two, thromboembolic disease in two, and interstitial disease in one. In these 10 patients, Doppler estimation of RVSP during exercise was correlated with simultaneous determination of pulmonary artery systolic pressure by catheter. Correct placement of the pulmonary artery catheter was confirmed by pressure tracings and chest radiograph. Zero reference was midthorax at 20° leftward tilt on the exercise ergometer. Measurements of RVSP and pulmonary artery systolic pressure by two experienced, independent observers were compared for the average of five consecutive, simultaneous heart beats that showed technically superior Doppler signals at rest, at the end of each stage of exercise, and at 2–4 minutes of recovery.

To correlate the values for calculated and measured oxyhemoglobin saturation, arterial blood gases were drawn at rest and at peak exercise. Calculated oxyhemoglobin saturation was derived from arterial oxygen tension with Severinghaus equations\textsuperscript{19}; measured oxyhemoglobin saturation was determined by pulse oximetry.

**Data Analysis**

For all variables, the mean rest value was compared with the mean exercise value by the paired $t$
TABLE 1. Pulmonary Function Data in Patients With Chronic Obstructive and Interstitial Pulmonary Disease

<table>
<thead>
<tr>
<th></th>
<th>Obstructive disease</th>
<th>Interstitial disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>23</td>
<td>8</td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>1.0±0.5 (35)</td>
<td>1.7±0.8 (73)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.8±1.1 (73)</td>
<td>2.0±0.8 (64)</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0.36±0.15</td>
<td>0.85±0.31</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>6.9±1.0 (107)</td>
<td>4.1±0.1 (74)</td>
</tr>
<tr>
<td>DLCO (ml/min/mm Hg)</td>
<td>21±13 (71)</td>
<td>16±6 (63)</td>
</tr>
<tr>
<td>PaO2 (mm Hg)</td>
<td>67±8</td>
<td>64±21</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>42±10</td>
<td>44±8</td>
</tr>
<tr>
<td>Hemoglobin (g)</td>
<td>16.5±1.5</td>
<td>16.4±2.3</td>
</tr>
</tbody>
</table>

Data are mean±SD. Numbers in parentheses are average percentages of predicted values.

FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FEV1/FVC, ratio of forced expiratory volume in 1 second to forced vital capacity; TLC, total lung capacity; DLCO, diffusing capacity for carbon monoxide; PaO2, arterial oxygen tension on room air; PaCO2, arterial carbon dioxide tension on room air.

test. Data on patients with chronic lung disease were compared with data on controls by analysis of variance. In patients with chronic lung disease, values for RVSP at rest and at peak exercise that exceeded control means by more than 2 SD were considered abnormally elevated.

Exercise data on room air were compared with data on oxygen by the paired t test. Because exercise duration was usually greater on oxygen than on room air, comparisons were made at identical workloads: at rest (0%), 20%, 40%, 60%, 80%, and 100% of peak workload on room air, and at 4 minutes of recovery.

Patients were subdivided into subgroups based on 1) the presence or absence of pulmonary hypertension at rest, or 2) the presence or absence of oxyhemoglobin desaturation with exercise. Analysis of variance was performed separately on the data from these subgroups. Correlations among pulmonary function and exercise data were determined with least-squares linear regression analysis. Data are listed as mean±SD. The null hypothesis was rejected at the 5% level.

Results

Pulmonary Function Tests

Results of pulmonary function testing in the 23 patients with chronic obstructive pulmonary disease and in eight with interstitial lung disease are shown in Table 1. At the time of testing, no patient had a resting arterial oxygen tension below 55 mm Hg.

Technical Adequacy of Two-Dimensional and Doppler Echocardiography

Of the 36 two-dimensional echocardiograms in study patients at rest, 33 (92%) had apical four-chamber views of sufficient quality to permit the measurement of RV/LV size.

Of the Doppler echocardiograms, technically adequate tricuspid insufficiency Doppler signals were initially obtained in only 20 patients (56%) at rest and 14 (39%) while exercising. After contrast enhancement of the Doppler signals (Figures 2A and 2B), these numbers increased to 33 (92%) and 32 (89%), respectively (both p<0.001). In the remaining patients, inability to clearly detect tricuspid insufficiency precluded calculation of RVSP at rest or exercise, despite multiple attempts at contrast enhancement in various echocardiographic windows. Technically adequate Doppler signals were initially obtained in seven of the 12 control patients at rest and 5 of 12 on exercise; after contrast enhancement, these numbers increased to 11 (p=NS) and 11 (p<0.05), respectively.

Contrast studies at rest after Valsalva maneuver revealed right-to-left shunting through a patent foramen ovale in two patients; both also showed shunting at peak exercise. No other patient showed shunting either at rest or at peak exercise.

Limiting Symptoms

Of the 36 study patients, 26 stopped exercise because of dyspnea and 10 because of leg fatigue. No patient had chest pain, ischemic electrocardiographic changes, or significant arrhythmias.

Correlation of Noninvasive and Invasive Data

The correlation between RVSP by contrast-enhanced Doppler and pulmonary artery systolic pressure by pulmonary artery flotation catheter at rest and exercise in 10 patients (30 simultaneous measurement points) was close (r=0.98, p<0.0001, Figure 3). Doppler tended to slightly underestimate pulmonary artery systolic pressure as measured by catheter, especially at peak exercise (RVSPDoppler = 0.88×pulmonary artery systolic pressurecatheter + 4, Figure 3). Mean right atrial pressure by Swan-Ganz catheter rose from 7±4 at rest to 14±7 mm Hg at peak exercise (p<0.01).

The correlation between calculated and measured values for oxyhemoglobin saturation at rest and peak exercise in 10 patients (20 simultaneous measurement points) was also close (r=0.97, p<0.0001, Saturationmeasured = 1.00×Saturationcalculated + 1.4).

Exercise Performance of Controls

Exercise data on room air for control patients are presented in Table 2. Mean RVSP at control patients was 22±4 mm Hg (range, 15–29 mm Hg); mean RVSP at peak exercise was 31±7 mm Hg (range, 25–44 mm Hg). The upper limits of normal values for RVSP at rest and exercise were defined as two standard deviations greater than control means; these were 30 and 45 mm Hg, respectively.

Exercise Performance of Patients on Room Air

For the 32 patients with technically adequate Doppler studies of tricuspid insufficiency at rest and exercise, mean room air RVSP at rest was 46±20 and increased to 83±30 mm Hg at peak exercise (p<0.001). Patients exercised 9.2±5.8 minutes to a workload of 44±27 W. Mean heart rate increased by
38 beats/min, systolic blood pressure increased by 47 mm Hg, and oxyhemoglobin saturation decreased by 13% to a mean nadir of 84±11% (Table 2).

**Exercise Performance of Patients on Oxygen**

Although the duration of exercise was greater on oxygen than on room air in all but three patients (p<0.01), differences in exercise time were often small. Increases in workload, heart rate, and systolic blood pressure were not significantly different on room air and oxygen (Table 2).

Although RVSP at peak exercise on oxygen was not significantly lower than RVSP at peak exercise on room air, RVSP on oxygen was significantly lower when matched for equivalent workloads. The differences between mean values for RVSP on oxygen and room air increased as workload progressed and became significant at 80% and 100% of peak exercise (Figure 4).

**Comparison of Patients With and Without Resting Pulmonary Hypertension**

Of the 32 patients with technically adequate tricuspid insufficiency Doppler signals at rest and exercise, nine (28%) had normal resting values for RVSP on room air (≤30 mm Hg, group A), and 23 (72%) had resting pulmonary hypertension (group B). During exercise, RVSP rose from 26±4 to 56±16 mm Hg in group A and from 59±17 to 93±30 mm Hg in the group B (Figure 5). The increase in RVSP with exercise was similar between the two groups but greater than in control patients (p<0.05). At peak exercise on room air, RVSP in seven of nine patients in group A increased to abnormal levels (>45 mm Hg, Figure 5). Compared with group A patients, those in group B had significantly higher mean values for resting arterial oxygen tension (77±9 vs. 64±8 mm Hg) and lower values for hemoglobin (15.4±1.1 vs. 16.9±1.9 g) and RV/LV size ratio (0.5±0.2 vs. 1.2±1.0, all p<0.05).

**Comparison of Patients With and Without Exercise Desaturation**

Twenty-two patients (61%) showed oxyhemoglobin desaturation on room air exercise (decrease in saturation by more than 4% to less than 90%
satisfaction). Compared with the patients who had desaturation with exercise on room air, those who showed desaturation had lower values for diffusing capacity and arterial oxygen tension and had higher values for RV/LV size ratio, RVSP at rest, RVSP at peak exercise, and increase in RVSP with exercise (Table 3). Differences in duration of exercise, workload, heart rate, and systolic blood pressure on room air were not significant (Table 3).

**Correlations Among Pulmonary Function and Exercise Data**

Significant correlations did not occur between pulmonary function indexes and RV/LV size ratio, RVSP at rest, RVSP at peak exercise, or increase in RVSP with exercise. However, modest correlations occurred between RV/LV and RVSP at rest (r=0.59) or exercise (r=0.69, both p<0.001) and between RVSP at rest and peak exercise (r=0.77, p<0.0001).

**Discussion**

**Measurement of Right Ventricular Systolic Pressure (RVSP) During Exercise**

We have shown the potential value of the noninvasive measurement of RVSP as an estimate of pulmonary artery pressure at rest and during exercise in patients with chronic lung disease. Despite the technical limitations of standard echocardiography and Doppler in these patients, saline contrast enhancement of tricuspid insufficiency permits the

**TABLE 2. Results of Exercise Testing on Room Air and Oxygen**

<table>
<thead>
<tr>
<th>Chronic pulmonary disease</th>
<th>Room air</th>
<th>Oxygen</th>
<th>Oxygen equivalent</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak workload (W)</td>
<td>44±27</td>
<td>56±30</td>
<td>. . .</td>
<td>158±49</td>
</tr>
<tr>
<td>Change in heart rate (beats/min)</td>
<td>38±20</td>
<td>40±21</td>
<td>34±14</td>
<td>75±28</td>
</tr>
<tr>
<td>Change in SBP (mm Hg)</td>
<td>47±29</td>
<td>43±22</td>
<td>39±21</td>
<td>66±29</td>
</tr>
<tr>
<td>RVSP rest (mm Hg)</td>
<td>48±19</td>
<td>44±19</td>
<td>. . .</td>
<td>22±4</td>
</tr>
<tr>
<td>RVSP peak exercise (mm Hg)</td>
<td>86±29</td>
<td>78±28</td>
<td>66±18*</td>
<td>31±7</td>
</tr>
<tr>
<td>Change in RVSP (mm Hg)</td>
<td>39±20</td>
<td>35±16</td>
<td>26±13*</td>
<td>11±6</td>
</tr>
<tr>
<td>Nadir oxyhemoglobin saturation (%)</td>
<td>84±11</td>
<td>93±6*</td>
<td>92±4*</td>
<td>96±3</td>
</tr>
</tbody>
</table>

Data are mean±SD. Oxygen equivalent, data on oxygen at equivalent workload to peak exercise on room air; SBP, systolic blood pressure; RVSP, right ventricular systolic pressure by Doppler.

*p<0.05 vs. chronic pulmonary disease on room air. All entries in first three columns differ significantly from controls except nadir of oxyhemoglobin saturation on oxygen or oxygen equiv.
determination of RVSP in a high percentage of patients. Intravenous injection of agitated isotonic saline has been previously used to enhance right-heart Doppler signals at rest with no adverse consequences.15,20–22 During exercise, we chose to perform continuous Doppler evaluation of the tricuspid valve alone, because we found that attempts to record signals from more than one valve impaired the ability to gather high-quality data.

In this study, RVSP determined by Doppler at rest and exercise compared favorably with simultaneous hemodynamic measurements. In patients with chronic lung disease in whom were placed indwelling flow-directed pulmonary artery catheters, pulmonary arterial systolic pressures were used as a close approximation of right ventricular systolic pressures. No patient had known pulmonary valve disease. Because the catheter may, itself, cause tricuspid insufficiency, we cannot exclude the possibility that the catheter improved the quality of the Doppler envelope in these patients. Although RVSP by contrast-enhanced Doppler showed an excellent correlation with pulmonary artery systolic pressure by catheter, Doppler underestimated catheter values by an average of 12%. This underestimation tended to be greater at peak exercise than at rest and may reflect 1) technical difficulty in aligning the ultrasound beam parallel to the tricuspid insufficiency jet near peak exercise because of tachypnea and tachycardia, and 2) the error encountered in assigning a constant value to right atrial pressure throughout exercise (in the patients with indwelling catheters, mean right atrial pressure increased from 7 to 14 mm Hg during exercise). The latter problem could be improved in future studies by allowing for an increase in right atrial pressure with exercise.

Table 3. Comparison of Patients With and Without Oxyhemoglobin Desaturation at Rest and During Exercise on Room Air

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>22</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLCO (ml/min/mm Hg)</td>
<td>10.0±4.7 (47)</td>
<td>17.3±6.4* (75)</td>
</tr>
<tr>
<td>PaO2 (mm Hg)</td>
<td>63±8</td>
<td>76±8*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>40±11</td>
<td>39±4</td>
</tr>
<tr>
<td>Hemoglobin (g)</td>
<td>16.9±1.9</td>
<td>15.8±1.5</td>
</tr>
<tr>
<td>Echo/Doppler at rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV/LV size ratio</td>
<td>1.26±1.11</td>
<td>0.51±0.22*</td>
</tr>
<tr>
<td>Rest RVSP (mm Hg)</td>
<td>56±1</td>
<td>32±12*</td>
</tr>
<tr>
<td>Echo/Doppler at peak exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise duration (min)</td>
<td>8.1±4.4</td>
<td>10.9±7.8</td>
</tr>
<tr>
<td>Workload (W)</td>
<td>38±18</td>
<td>54±35</td>
</tr>
<tr>
<td>Increase heart rate (beats/min)</td>
<td>38±16</td>
<td>39±25</td>
</tr>
<tr>
<td>Increase SBP (mm Hg)</td>
<td>43±30</td>
<td>53±27</td>
</tr>
<tr>
<td>Nadir oxyhemoglobin sat (%)</td>
<td>79±11</td>
<td>91±4*</td>
</tr>
<tr>
<td>Peak RVSP (mm Hg)</td>
<td>98±30</td>
<td>61±10*</td>
</tr>
<tr>
<td>Increase in RVSP (mm Hg)</td>
<td>44±23</td>
<td>31±12*</td>
</tr>
</tbody>
</table>

Data are mean±SD. Numbers in parentheses are average percentage of predicted values.

DLCO, diffusing capacity; PaO2, arterial oxygen tension; PaCO2, arterial carbon dioxide tension; RV/LV, ratio of right to left ventricular size in apical four-chamber view by single-plane area-length method; RVSP, right ventricular systolic pressure by Doppler; SBP, systolic blood pressure.

*p<0.05 vs. patients with desaturation.
patients with chronic lung disease who have a normal resting RVSP and right ventricular size, yet who have abnormal increases in RVSP with exercise.

Effect of Short-term Oxygen Administration on Right Ventricular Systolic Pressure During Exercise

The graded exercise protocol used in this study has been advocated as a relatively safe and reliable means of ascertaining the maximum workload in patients limited by respiratory symptoms. Patients were exercised on and off high-flow oxygen. To avoid either a consistent training effect or a pulmonary vasodilating effect of a first exercise test, the order of exercise testing on room air or oxygen in this study was randomized. In addition, testing was conducted in a double-blinded fashion regarding the gas breathed in most studies. Oxygen was chosen over other pulmonary vasodilators because of its safety and possible therapeutic utility; high flow rates were administered in an attempt to prevent the development of arterial hypoxemia during exercise.

Although the short-term administration of high-flow oxygen increased exercise duration in most patients, mean heart rate and cuff systolic blood pressure were not significantly different during exercise on room air and oxygen. At identical peak workloads, the increase in RVSP during exercise was significantly blunted on oxygen compared with room air. Although the patients in this study did not have resting hypoxemia, our findings are similar to those of a recent hemodynamic report of hypoxic patients with chronic obstructive pulmonary disease, in whom short-term oxygen administration resulted in a small but significant decrease in mean pulmonary artery pressure at peak exercise.

In patients with chronic pulmonary disease, the abnormal increase in pulmonary artery pressure during exercise has been attributed to destruction of the pulmonary capillary bed, resulting in limitation of pulmonary vascular reserve. In addition to fixed pulmonary vascular disease, reactive pulmonary vasoconstriction due to exercise-induced hypoxia may contribute to elevations in pulmonary pressure. The short-term administration of oxygen corrects hypoxemia and may also improve ventilatory muscle function, alleviate right ventricular ischemia, and decrease right ventricular afterload. Because cardiac output and pulmonary vascular resistance were not measured in most study patients, the relative contributions of each of these factors to the decrease in exercise RVSP on oxygen cannot be estimated. However, data from the Nocturnal Oxygen Therapy Trial Group showed that exercise on oxygen compared with room air was associated with a decrease in mean pulmonary vascular resistance at peak exercise with little change in cardiac output.

Oxyhemoglobin Saturation

Similar to data in previously reported studies, the patients who had desaturation had significantly lower values for diffusing capacity and resting oxygen tension than those who did not have desaturation. In addition, patients who had desaturation had larger right ventricles and higher values for RVSP at rest and peak exercise than patients who did not have desaturation. Right-to-left shunting through a patent foramen ovale at rest or exercise was present in only two patients (one desaturated) and thus was not an important factor in the development of arterial hypoxemia during exercise.

The development of pulmonary hypertension in chronic lung disease may be related to repetitive episodes of transient hypoxic vasoconstriction. We have previously shown that only 21% of patients with severe chronic obstructive pulmonary disease who are not hypoxic at rest undergo desaturation during sleep and that the degree of right ventricular enlargement and pulmonary hypertension in these patients is not greater than in those who do not undergo desaturation. In comparison, 61% of patients in the present study showed oxyhemoglobin desaturation during exercise. Unlike the results of the sleep study, the patients in this study who had desaturation during exercise had significantly larger right ventricles and higher pulmonary pressures at rest and peak exercise than those who did not have desaturation.

Summary

We have shown that saline contrast-enhanced Doppler is potentially valuable for the noninvasive estimation of pulmonary artery pressure during exercise in patients with chronic lung disease. Patients who showed arterial oxyhemoglobin desaturation during exercise had larger right ventricles and higher pulmonary pressures at rest and exercise than patients who did not show desaturation. Despite normal resting values for RVSP in 28% of patients in the study, nearly all showed abnormal increases in RVSP during supine bicycle exercise. In addition, the short-term administration of oxygen blunted the increase in RVSP during exercise.

Acknowledgment

We are indebted to Nellcor (Hayward, California) for providing the pulse oximeters used in the study and to the technicians in the echocardiography laboratory for their invaluable assistance.

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KEY WORDS  • Doppler  • echocardiography  • emphysema  • exercise  • pulmonary hypertension  • tricuspid insufficiency  • contrast
Noninvasive evaluation of pulmonary artery pressure during exercise by saline-enhanced Doppler echocardiography in chronic pulmonary disease.
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