Pulmonary Blood Volume Ratio Response to Exercise: A Noninvasive Determination of Exercise-induced Changes in Pulmonary Capillary Wedge Pressure

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SUMMARY To determine if changes in pulmonary capillary wedge pressure could be determined from the pulmonary blood volume (PBV) ratio response on exercise-gated blood pool images, 42 patients had simultaneous exercise-gated blood pool imaging and hemodynamic monitoring during cardiac catheterization. Nine patients were normal and 33 patients had cardiac disease. Changes in the PBV ratio were determined from the 0.5° left anterior oblique end-diastolic frames by placing a region of interest over the left lung. The ratio of exercise/rest counts (PBV ratio) was calculated. The exercise-induced change in mean pulmonary capillary wedge pressure correlated with the PBV ratio (r = 0.72, p < 0.001). Patients were grouped into those with a definite (> 3-mm Hg) exercise-induced decrease, no change or an increase in mean pulmonary capillary wedge pressure in response to exercise. The PBV ratio was 0.929 ± 0.076 (mean ± SD) for the 10 patients with a decrease in wedge pressure, 1.027 ± 0.065 for the eight patients with no change in wedge pressure (p < 0.05), and 1.214 ± 0.131 for the 24 patients with an increase in wedge pressure (p < 0.05). Heart rate and blood pressure response to exercise did not differ for the three groups.

The nine normal subjects had no increase in mean pulmonary capillary wedge pressure with exercise and a normal PBV ratio (mean PBV ratio = 0.92 ± 0.06). Thirteen of the patients with coronary artery disease, 14 with chronic aortic or mitral regurgitation, three with cardiomyopathy (two congestive and one hypertrophic), and one with aortic stenosis and regurgitation had an exercise-induced increase in mean pulmonary capillary wedge pressure and an abnormal PBV ratio. The two patients with mitral stenosis had normal PBV ratios despite exercise-induced increases in mean pulmonary capillary wedge pressure.

We conclude that determination of the PBV ratio from exercise-gated cardiac blood pool images can be used as a noninvasive means of estimating exercise-induced changes in left ventricular filling pressure.

LEFT VENTRICULAR functional reserve with exercise is reflected in a change in left ventricular ejection fraction and pulmonary capillary wedge pressure in the absence of mitral valve disease. Borer and associates reported the value of the gated cardiac blood pool scan at rest and with exercise in detecting inadequate left ventricular functional reserve. We previously reported that exercise-induced changes in the pulmonary blood volume (PBV ratio) could be measured using gated cardiac blood pool scanning. The exercise-to-rest PBV ratio determination demonstrated an exercise-induced increase in patients with coronary artery disease and no change or a decrease in normal persons. Addition of the PBV ratio as a criterion for coronary artery disease significantly increased the percentage of patients with coronary artery disease who have an abnormal response on exercise-gated blood pool scan testing (left ventricular ejection fraction and regional wall motion response). In the present study, gated cardiac blood pool scanning was performed during exercise simultaneously with hemodynamic monitoring to determine if the PBV ratio could be used as a noninvasive means of assessing changes in pulmonary capillary wedge pressure.

Method

Forty-two patients (31 males and 11 females) had simultaneous exercise cardiac gated blood pool imaging and hemodynamic monitoring during diagnostic cardiac catheterization. The average age was 48.2 ± 12.5 years (± SD) (range 16–70 years). At catheterization, nine were normal, 13 had coronary artery disease, 14 had chronic aortic or mitral regurgitation, and six had other types of noncoronary heart disease (two congestive cardiomyopathy, one restrictive cardiomyopathy, two mitral stenosis and one aortic stenosis and regurgitation).

Exercise Imaging And Hemodynamic Monitoring

Patients were in the fasting state. Using local anesthesia, a #7F Swan-Ganz triple-lumen thermocouple catheter was inserted percutaneously through the right brachial vein and positioned within the pulmonary artery such that pulmonary capillary wedge pressure tracings could be obtained upon inflation of the balloon on the catheter tip. Resting 12-lead ECG, heart rate, cuff arterial pressure, pulmonary artery pressure, mean pulmonary capillary wedge pressure, and thermocouple cardiac output were monitored. Pressure transducers were set to zero at the level of the right atrium. Three milligrams of stannous pyrophosphate (Pyrolite, New England Nuclear), followed 20 minutes later by 20 mCi of technetium-99m-labeled pertechnetate, were given intravenously for in vivo...
labeling of red cells.\(^2\) Initial rest imaging was performed in the supine position. Our technique for obtaining gated cardiac blood pool images has been described.\(^2\) At least 200,000 counts were collected in each frame during the rest study in 5–10 minutes. Patients were then exercised in the supine position using a bicycle ergometer. The exercise protocol has been described.\(^2\) Mean pulmonary capillary wedge pressure was recorded continuously during exercise, with the exception of brief periods every 3 minutes, during which pulmonary artery pressure and cardiac output were determined. Multigated cardiac blood pool images were collected in the left anterior oblique position during the final 2 minutes of each 3-minute exercise stage. A mean of 155,000 ± 25,000 (± SD) counts per frame for the blood pool images was obtained during exercise.

Mean pulmonary capillary wedge pressure values at 30-second intervals during the 2-minute gated cardiac blood pool imaging period were averaged to yield a mean value for each 2-minute period.

### Data Analysis

The exercise ECG was considered positive for ischemia if it demonstrated ST-segment depression of at least 1 mm measured 0.08 second from the J point.

Multigated blood pool image ejection fractions were calculated from the left anterior oblique projection at rest and during maximal exercise with a semiautomated edge-detection algorithm by the counts technique using a varying region of interest.\(^4\) Ejection fractions were determined by two independent observers and the values from the two observers were averaged to produce a single ejection fraction. Failure of the ejection fraction to increase by at least 5% during exercise was considered an abnormal response.\(^1\), \(^8\)

The method of determining the exercise PBV ratio has been reported.\(^2\) Briefly, a computer-generated region of interest was placed over the lung fields and lateral to the left ventricle in the 50\(^\circ\) left anterior oblique end-diastolic frame with a light pen at rest and during peak exercise (fig. 1). This region of interest was positioned adjacent to the left border of the descending aorta or the left ventricular myocardium. The region of interest encompassed 40–90 picture elements (16.8–37.8 cm\(^2\) of lung), with 38–110 counts per element. At least 1300 counts were sampled in a lung region of interest. In patients in whom the borders of the descending aorta were unclear, total counts in the region of interest were displayed as a function of time. Fluctuations in counts corresponding to the cardiac cycle were considered evidence of inclusion of the aorta. In such patients, the region of interest was then moved laterally until fluctuations were absent. In this manner, a region of interest for each patient was determined by two independent observers unaware of the cardiac catheterization results. The counts per picture element were corrected for difference in acquisition times for the rest and exercise studies. The PBV ratio was determined by dividing the counts during peak exercise by the counts at rest. The ratios determined by the two observers were averaged to produce a single value for each patient at maximal exercise. One of the observers repeated the PBV ratio determination at least 2 months later for reproducibility. To detect coronary artery disease, a PBV ratio of at least 1.06 was considered significant. This value was derived from the PBV ratio mean plus 2 standard deviations for a previously reported group of control patients.\(^2\)

The exercise-induced change in mean pulmonary capillary wedge pressure was the average value during the final 2 minutes of exercise minus the rest value. A change of at least 3 mm Hg was considered significant for mean pulmonary capillary wedge pressure.

### Statistical Analysis

Differences between groups of patients for mean pulmonary capillary wedge pressure, heart rate, cardiac output, systolic arterial pressure, age, exercise duration, ejection fraction and PBV ratio were analyzed by means of a one-way analysis of variance and the Newman-Keuls multiple-comparison test. All values were expressed as the mean ± SD. Interobserver and intraobserver variances for determination of the PBV ratio were derived from a two-way analysis of variance. The significance of differences in proportions of patients in various subgroups was compared by chi-square analysis. The exercise-induced change in mean pulmonary capillary wedge pressure and the PBV ratio were compared to other exercise measurements using linear-regression analysis.

### Results

The interobserver and intraobserver variances for determination of the PBV ratio were 0.085 and 0.042, respectively.

### Hemodynamic Correlates of the Exercise/Rest PBV Ratio

When the clinical data for the patients grouped into those with an exercise-induced decrease (n = 10), no change greater than 3 mm Hg (n = 8), or an exercise-induced increase (n = 24) in mean pulmonary capillary wedge pressure were compared, there was no

![Figure 1. End-diastolic frames for multigated blood pool images in the left anterior oblique projection. The regions of interest have been included. The pulmonary blood volume ratio was 0.96 in this normal subject.](image-url)
significant difference in the percentage of males, the ages, and the incidence of propranolol or nitrate usage for the three groups. There was more digoxin and diuretic usage in the group that increased pulmonary capillary wedge pressure with exercise (54% and 38%, respectively) compared with the group that decreased pulmonary capillary wedge pressure with exercise (no users) \( (p < 0.05) \). When patients with noncoronary disease were excluded, the frequency of digoxin and diuretic use was still higher in the eight patients with increased pulmonary capillary wedge pressure \( (38\% \text{ and } 38\% \text{, respectively}) \) compared with the nine patients with decreased pulmonary capillary wedge pressure \( (\text{no users}) \) (NS).

The distribution of diagnosis was: decreased pulmonary capillary wedge pressure group — seven normal, two coronary artery disease, one aortic regurgitation; no change pulmonary capillary wedge pressure group — two normal, three coronary artery disease, three aortic or mitral regurgitation; and increased pulmonary capillary wedge pressure group — eight coronary artery disease, 10 aortic or mitral regurgitation, six other noncoronary heart disease. The frequencies of clinical noninvasive indexes of left ventricular function were: decreased pulmonary capillary wedge pressure group — rales 10%, protodiastolic gallop 10%, radiographic evidence of pulmonary vascular redistribution 10%, or increased heart size 20%; no change pulmonary capillary wedge pressure group — rales 13%, protodiastolic gallop 13%, radiographic evidence of pulmonary vascular redistribution 0% or increased heart size 50%; increased pulmonary capillary wedge pressure group — rales 42%, protodiastolic gallop 38%, radiographic evidence of pulmonary vascular redistribution 33% or increased heart size 50%.

Table 1 is a list of the hemodynamic data for the patients based on the mean pulmonary capillary wedge pressure response to exercise. The mean PBV ratio was \( 0.929 \pm 0.076 \) for patients with an exercise-induced decrease in mean pulmonary capillary wedge pressure, \( 1.027 \pm 0.065 \) for those with no change in wedge pressure, and \( 1.214 \pm 0.131 \) for those with an increase in wedge pressure \( (p < 0.01 \text{ between decreased and increased pressure groups}, p < 0.05 \text{ for all other comparisons}) \) (fig. 2). The three groups did not differ significantly in rest, peak exercise, and exercise-induced change in heart rates; rest, peak exercise, and exercise-induced change in peak systolic arterial pressures; rest and peak exercise cardiac outputs; or rest and peak exercise ejection fractions. The exercise-induced change in cardiac output was significantly lower for patients who had an increase in mean pulmonary capillary wedge pressure \( (1.88 \pm 1.85 \text{ l/min}) \) compared with those who had no significant change \( (5.01 \pm 2.76 \text{ l/min}) \) and those who had a decrease in wedge pressure \( (3.75 \pm 1.96 \text{ l/min}) \) \( (p < 0.05) \). The exercise-induced change in ejection fraction was significantly greater for patients who had a decrease in mean pulmonary capillary wedge pressure \( (+5.8 \pm 5.2\%) \) compared with those who had no change \( (-3.3 \pm 6.3\%) \) or an increase \( (-4.3 \pm 11.5\%) \) in wedge pressure \( (p < 0.05) \) (fig. 3).

Linear regression analysis yielded the following relationships: (1) PBV ratio vs exercise-induced change in mean pulmonary capillary wedge pressure \( (r = 0.72) \) (fig. 4); (2) PBV ratio vs exercise-induced change in mean pulmonary capillary wedge pressure (excluding patients with coronary artery disease) \( (r = 0.54) \); (3) PBV ratio vs exercise-induced change in ejection fraction \( (r = 0.39) \); (4) PBV ratio vs exercise-induced change in cardiac output \( (r = -0.37) \); (5)

### Table 1. Hemodynamic Data for Patients Based on Pulmonary Capillary Wedge Pressure Response to Exercise

<table>
<thead>
<tr>
<th></th>
<th>Decrease PCWP (n = 10)</th>
<th>No change PCWP (n = 8)</th>
<th>Increase PCWP (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise duration (min)</strong></td>
<td>10.0 ± 2.8</td>
<td>10.8 ± 4.4</td>
<td>7.3 ± 3.3</td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(beats/min)</td>
<td>Rest</td>
<td>Ex</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>69.2 ± 15.4</td>
<td>119.3 ± 25.2</td>
<td>50.1 ± 28.0</td>
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<tr>
<td></td>
<td>51.1 ± 34.2</td>
<td>119.3 ± 25.2</td>
<td>58.7 ± 67.7</td>
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<tr>
<td><strong>Systolic arterial</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>pressure (mm Hg)</strong></td>
<td>Rest</td>
<td>Ex</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>138.2 ± 29.0</td>
<td>147.8 ± 33.9</td>
<td>117.8 ± 33.9</td>
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<tr>
<td></td>
<td>138.2 ± 29.0</td>
<td>147.8 ± 33.9</td>
<td>117.8 ± 33.9</td>
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<tr>
<td><strong>Cardiac output</strong></td>
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<tr>
<td>(l/min)</td>
<td>Rest</td>
<td>Ex</td>
<td>Rest</td>
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<tr>
<td></td>
<td>5.5 ± 1.98</td>
<td>9.08 ± 2.29</td>
<td>3.75 ± 1.96</td>
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<tr>
<td></td>
<td>5.5 ± 1.98</td>
<td>9.08 ± 2.29</td>
<td>3.75 ± 1.96</td>
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<tr>
<td>**Ejection fraction (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)</td>
<td>Rest</td>
<td>Ex</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>58.6 ± 9.6</td>
<td>64.4 ± 10.7</td>
<td>58.4 ± 5.2</td>
</tr>
<tr>
<td></td>
<td>58.6 ± 9.6</td>
<td>64.4 ± 10.7</td>
<td>58.4 ± 5.2</td>
</tr>
<tr>
<td><strong>PBV ratio</strong></td>
<td>0.929 ± 0.076</td>
<td>* 1.027 ± 0.065</td>
<td>* 1.214 ± 0.131†</td>
</tr>
</tbody>
</table>

Values are mean ± sd.

*\( p < 0.05 \) comparing adjacent groups.

†\( p < 0.05 \) vs "decrease PCWP" group.

‡\( p < 0.05 \) vs "increase PCWP" group.

Abbreviations: PCWP = pulmonary capillary wedge pressure; Decrease PCWP = exercise-induced decrease in PCWP ≥ 3 mm Hg; No change PCWP = exercise-induced change in PCWP < 3 mm Hg; Increase PCWP = exercise-induced increase in PCWP ≥ 3 mm Hg; PBV ratio = pulmonary blood volume ratio; Ex = peak exercise; \( \Delta = \) maximal Ex minus rest value.
Pulmonary Blood Volume Ratio Response to Exercise in Normal Subjects and Patients with Heart Disease

Patients with aortic or mitral regurgitation (mean age 40 ± 14 years) were significantly younger than patients with coronary artery disease (mean age 53 ± 10 years) \( (p < 0.05) \). Patients with coronary artery disease had a significantly higher incidence of a positive electrocardiographic exercise test (nine of 13, 69\%), an abnormal ejection fraction response to exercise (12 of 13, 92\%), and a PBV ratio of 1.06 or greater (11 of 13, 88\%).

PBV ratio vs rest mean pulmonary artery pressure \( (r = 0.20) \); (6) PBV ratio vs exercise-induced increase in mean pulmonary artery pressure \( (r = 0.58) \); (7) PBV ratio vs rest total pulmonary vascular resistance \( (r = 0.21) \); (8) PBV ratio vs exercise-induced increase in total pulmonary vascular resistance \( (r = 0.43) \); (9) exercise-induced change in mean pulmonary capillary wedge pressure vs change in ejection fraction \( (r = -0.21) \); and (10) exercise-induced change in mean pulmonary capillary wedge pressure vs change in cardiac output \( (r = -0.42) \).

In the group of patients that had an increase in mean pulmonary capillary wedge pressure with exercise, there was no significant difference in PBV ratios for (1) patients with a resting mean pulmonary capillary wedge pressure of 12 mm Hg or greater \( (n = 8, \text{mean PBV ratio } 1.187 \pm 0.157) \) vs those with a resting pressure less than 12 mm Hg \( (n = 16, \text{mean PBV ratio } 1.226 \pm 0.119) \); (2) patients with an exercise-induced change in cardiac output of 2 1/min or greater \( (n = 9, \text{mean PBV ratio } 1.175 \pm 0.080) \) vs those with a change in cardiac output less than 2 1/min \( (n = 15, \text{mean PBV ratio } 1.232 \pm 0.168) \); and (3) patients with a resting mean pulmonary artery pressure of 20 mm Hg or greater \( (n = 12, \text{mean PBV ratio } 1.212 \pm 0.173) \) vs those with a resting pressure less than 20 mm Hg \( (n = 12, \text{mean PBV ratio } 1.208 \pm 0.105) \).

The sensitivity of a PBV ratio greater than 1.00 for an exercise-induced increase in mean pulmonary capillary wedge pressure was 96\% (23 of 24). The specificity of a PBV ratio 1.00 or less for an exercise-induced decrease in mean pulmonary capillary wedge pressure was 90\% (nine of 10). When patients with coronary artery disease were excluded, the sensitivity of a PBV ratio greater than 1.00 for an exercise-induced increase in mean pulmonary capillary wedge pressure was 94\% (15 of 16); the specificity of a PBV ratio 1.00 or less for an exercise-induced decrease in mean pulmonary capillary wedge pressure was 88\% (seven of eight).

**FIGURE 2.** Distribution of pulmonary blood volume (PBV) ratios according to the pulmonary capillary wedge pressure response to exercise.

**FIGURE 3.** Distribution of exercise-induced changes in left ventricular ejection fraction (EF) according to the pulmonary capillary wedge pressure response to exercise.
85%) compared with the nine normal patients (none had a positive electrocardiographic exercise test or PBV ratio; three had an abnormal ejection fraction response to exercise) \( (p < 0.05) \). Patients with aortic or mitral valve regurgitation had a significantly higher incidence of an abnormal ejection fraction response to exercise (11 of 14, 79%) and a PBV ratio of 1.06 or greater (12 of 14, 86%) compared with normal patients \( (p < 0.05) \). There were no statistically significant differences between patients with aortic regurgitation and those with mitral regurgitation. The number of patients with cardiomyopathy, mitral stenosis and combined aortic stenosis and regurgitation were too small for statistical comparisons.

Table 2 lists the hemodynamic data for patients according to the clinical diagnosis. The three patients with cardiomyopathy, two with mitral stenosis and one with combined aortic stenosis and regurgitation are not included in this table because of the small numbers. There were no statistically significant differences between patients with aortic regurgitation and those with mitral regurgitation. The PBV ratios for normal persons \( (0.924 \pm 0.061) \) were significantly lower than those for patients with coronary artery disease \( (1.185 \pm 0.191, p < 0.01) \), and for patients with aortic or mitral regurgitation \( (1.168 \pm 0.122, p < 0.01) \) (fig. 5). Patients with coronary artery disease had a shorter exercise duration, higher rest and exercise systolic arterial pressures, a positive increase in mean pulmonary capillary wedge pressure with exercise, and an abnormal ejection fraction response to exercise compared with normal patients \( (p < 0.05) \). Patients with aortic or mitral valve regurgitation had a higher peak exercise heart rate, a higher rest and exercise systolic arterial pressure, a positive increase in mean pulmonary capillary wedge pressure with exercise, and an abnormal ejection fraction response to exercise compared with normal patients \( (p < 0.05) \).

![Figure 4](image_url) **Figure 4.** Linear regression analysis for pulmonary blood volume (PBV) ratio vs exercise-induced changes in pulmonary capillary wedge pressure.

![Figure 5](image_url) **Figure 5.** Distribution of pulmonary blood volume (PBV) ratios according to the diagnosis after cardiac catheterization. CAD = coronary artery disease; AR = aortic regurgitation; MR = mitral regurgitation; CM = cardiomyopathy; MS = mitral stenosis, and AS/AR = combined aortic stenosis and AR.

**Discussion**

**Hemodynamic Correlates of the Exercise/Rest PBV Ratio**

PBV Ratio vs Pulmonary Capillary Wedge Response

This study demonstrates a significant relationship between the mean pulmonary capillary wedge pressure response to exercise and the PBV ratio determined simultaneously using noninvasive gated cardiac blood pool imaging. The mean PBV ratio was lowest (mean 0.929) for patients whose mean pulmonary capillary wedge pressure decreased with exercise, significantly higher (mean 1.027) for those whose wedge pressure did not change with exercise, and highest (mean 1.214) for those whose wedge pressure increased with exercise. Nine of 10 patients (90%) whose wedge pressures decreased with exercise had a PBV ratio of 1.00 or less. Twenty-three of 24 patients (96%) whose wedge pressure increased with exercise had a PBV ratio greater than 1.00. Using linear regression analysis, a significant correlation was demonstrated between the mean pulmonary capillary wedge pressure response to exercise and the PBV ratio \( (r = 0.72) \). The correlation was high despite the wide range of cardiac diagnoses studied. The relationship between wedge pressure changes and PBV ratio is consistent with the observations of Dock and associates and Roy and associates. These investigators used a catheterization technique to demonstrate an increased PBV with elevated left atrial pressures.


**TABLE 2. Hemodynamic Data for Patients Based on Diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Normal (n = 9)</th>
<th>Coronary artery disease (n = 13)</th>
<th>Aortic or mitral regurgitation (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise duration (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>9.4 ± 2.7</td>
<td>*</td>
<td>6.7 ± 2.4</td>
</tr>
<tr>
<td>Ex</td>
<td>120.0 ± 25.8</td>
<td>71.5 ± 11.7</td>
<td>131.1 ± 25.0</td>
</tr>
<tr>
<td>Δ</td>
<td>49.3 ± 29.2</td>
<td>41.6 ± 20.1</td>
<td>141.0 ± 21.5†</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>124.7 ± 7.5</td>
<td>*</td>
<td>134.6 ± 20.1</td>
</tr>
<tr>
<td>Ex</td>
<td>169.7 ± 24.9</td>
<td>172.7 ± 35.0</td>
<td>221.0 ± 43.7†</td>
</tr>
<tr>
<td>Δ</td>
<td>45.1 ± 20.5</td>
<td>38.1 ± 21.9</td>
<td>65.0 ± 30.6</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>5.4 ± 1.5</td>
<td>5.5 ± 1.5</td>
<td>5.2 ± 1.9</td>
</tr>
<tr>
<td>Ex</td>
<td>9.6 ± 2.2</td>
<td>7.4 ± 1.7</td>
<td>9.2 ± 3.7</td>
</tr>
<tr>
<td>Δ</td>
<td>4.3 ± 1.4</td>
<td>1.9 ± 1.8</td>
<td>4.0 ± 3.4</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mm Hg)</td>
<td>7.2 ± 3.0</td>
<td>10.0 ± 6.5</td>
<td>9.9 ± 4.9</td>
</tr>
<tr>
<td>Ex</td>
<td>3.7 ± 2.2</td>
<td>19.6 ± 15.5</td>
<td>17.4 ± 10.0</td>
</tr>
<tr>
<td>Δ</td>
<td>-3.5 ± 1.9</td>
<td>*</td>
<td>9.5 ± 11.6</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>61.7 ± 9.1</td>
<td>49.4 ± 17.3</td>
<td>60.1 ± 12.8</td>
</tr>
<tr>
<td>Ex</td>
<td>65.7 ± 9.9</td>
<td>46.5 ± 14.7</td>
<td>54.4 ± 17.7</td>
</tr>
<tr>
<td>Δ</td>
<td>4.0 ± 6.8</td>
<td>*</td>
<td>-5.7 ± 9.1†</td>
</tr>
<tr>
<td>PBV ratio</td>
<td>0.924 ± 0.061</td>
<td>1.185 ± 0.191</td>
<td>1.168 ± 0.122</td>
</tr>
</tbody>
</table>

*p < 0.05 comparing adjacent groups.  †p < 0.05 compared with normal subjects.  ‡p < 0.01 compared with normal subjects.

Abbreviations: Ex = peak exercise; Δ = difference.

**PBV Ratio vs Cardiac Output, Left Ventricular Ejection Fraction and Rest Pulmonary Artery Pressure**

Although the mean exercise-induced change in cardiac output was lowest for the patients whose mean pulmonary capillary wedge pressures increased with exercise, the change in cardiac output did not appear to be a major determinant of the PBV ratio (r = -0.39). The PBV ratio was also not significantly related to rest mean pulmonary capillary wedge pressure, rest left ventricular ejection fraction, and rest mean pulmonary artery pressure. Although digitalis and diuretic were used more frequently in the patients whose pulmonary capillary wedge pressures increased with exercise, the PBV ratio was not significantly related to digitalis, diuretic or propranolol use.

The less-than-exact linear correlation between mean pulmonary capillary wedge pressure and the PBV ratio (r = 0.72) may be related to a number of factors: (1) Although hemodynamic measurements and gated cardiac blood pool scans were obtained simultaneously during exercise, the gated scans were obtained over 2-minute intervals. Thus, the value for pulmonary capillary wedge pressure corresponding to each PBV ratio value actually represented an averaged value over the 2-minute period. (2) Inaccuracies in the determination of pulmonary capillary wedge pressure are related to patient motion during exercise, respiratory variation, and patient Valsalva during exercise. (3) Because the pulmonary venous system has a limit to its distensibility, a linear relationship between pressure and volume would not be expected. Thus, if the pulmonary blood volume were near maximum at rest, then exercise might result in a large increase in pressure compared to volume. However, this factor probably has only a minor effect on the correlation; we found only a weak relationship between resting pulmonary artery pressure and the PBV ratio. (4) There may be other minor determinants of the PBV ratio, such as total pulmonary vascular resistance, cardiac output and left ventricular ejection fraction. (5) Inaccuracies in the determination of the PBV ratio can arise from technical factors, such as patient motion between or during imaging collections. Care must be taken to avoid including large vascular structures such as the descending aorta in the pulmonary region of interest and to make the exercise and rest image regions of interest as uniform and identically positioned as possible. Regions of interest placed too far lateral to the heart result in fewer counts and reduced statistical reliability.

**PBV Ratio Response to Exercise in Normal Subjects and Patients with Heart Disease**

**Normal PBV Ratio Response to Exercise**

Nine normal subjects had a mean PBV ratio of 0.924; that is, a slight decrease in the PBV with exercise. Only one of nine had a PBV ratio greater than 1.00 (PBV ratio 1.02). This normal PBV ratio was similar to that reported previously by our laboratory for 10 other normal subjects (mean PBV ratio 0.94 ± 0.06).2 Nichols and associates4 used 11C-labeled carbon monoxide inhalation during positron blood pool scanning and demonstrated an exercise-induced decrease in PBV in normal subjects. Levinson et al∗ used an invasive indicator-dilution technique and demonstrated a similar decrease in PBV with exercise.

All normal subjects in the present study demon-
strated a decrease or no change in pulmonary capillary wedge pressure with exercise (range 0–6 mm Hg, mean decrease 3.5 mm Hg). The results of previous studies concerning the effects of exercise on left ventricular filling pressure in the normal heart vary. Ross and associates \(^{10}\) reported that the left ventricular end-diastolic pressure fell with exercise in five of seven normal subjects and increased by 2 mm Hg or less in the other two. Braunwald and associates \(^{11}\) reported no consistent change in left ventricular filling pressure in patients with "nearly normal" hearts. The inconsistent results may have been due to unrecognized left ventricular dysfunction, because all of Braunwald's patients had had some minor cardiac surgery. Vatner and associates \(^{12}\) reported an increase in left ventricular end-diastolic pressure in normal dogs during exercise; however, the degree of exercise was quite severe.

**The PBV Response to Exercise in Patients with Coronary Artery Disease**

This study demonstrated a mean PBV ratio of 1.185 for patients with coronary artery disease; that is, an increase in the PBV with exercise. This value was similar to the mean PBV ratio of 1.14 reported from our laboratory for 37 other patients with coronary artery disease. \(^{2}\) Two of 13 patients with coronary artery disease had a PBV ratio with exercise less than 1.00. The one patient with isolated right coronary artery disease had a normal PBV ratio (0.98). Patients with isolated right coronary artery disease tend to have a normal PBV ratio response to exercise \(^{6}\) for two reasons: There may be only a small amount of left ventricular myocardial ischemia; and right ventricular ischemia could prevent an increase in the PBV ratio by decreasing right ventricular input into the lung. Eight of 13 patients with coronary artery disease had an increase (mean 9.5 mm Hg) in mean pulmonary capillary wedge pressure with exercise.

Nichols and associates, \(^{8}\) using \(^{14}\)C-labeled carbon monoxide with positron imaging, and Austin and associates, \(^{13}\) using the indicator-dilution technique, demonstrated an increase in PBV with exercise in patients with coronary artery disease. This increase in PBV probably occurs because myocardial ischemia leads to a decrease in left ventricular myocardial contractility, \(^{14–16}\) an increase in myocardial stiffness, \(^{17}\) and a decrease in myocardial relaxation. \(^{18}\) These altered mechanics cause an increase in left ventricular end-diastolic pressure and thus, an increase in pulmonary venous pressure. \(^{19–24}\) The increase in pulmonary venous pressure results in an increase in PBV. \(^{6}\)

**PBV Response to Exercise in Patients with Aortic or Mitral Regurgitation**

This study demonstrated a mean PBV ratio of 1.168 for patients with aortic valve regurgitation or mitral valve regurgitation. Thirteen of the 14 patients had a PBV ratio greater than 1.00. Eleven of 14 patients had an exercise-induced increase in mean pulmonary capillary wedge pressure with exercise (mean increase 7.5 mm Hg). However, the response to exercise in this group of patients was extremely variable. One patient had severe chronic aortic regurgitation angiographically, yet a normal ejection fraction response to exercise, a decrease in mean pulmonary capillary wedge pressure with exercise and a normal PBV ratio.

The two patients with congestive cardiomyopathy had PBV ratios of 1.15 and 1.19. One of them had a normal ejection fraction response to exercise. The one patient with restrictive cardiomyopathy (PBV ratio of 1.11) and the one patient with aortic stenosis and regurgitation (PBV ratio of 1.10) had increases in mean pulmonary capillary wedge pressure with exercise and abnormal PBV ratios. However, the ejection fraction response to exercise was normal in both patients. The two patients with mitral stenosis had low PBV ratios (1.04 and 0.99) despite exercise-induced increases in pulmonary capillary wedge pressure. Roy and associates \(^{7}\) used an indicator-dilution technique to demonstrate that the PBV is abnormally large at rest in patients with mitral stenosis. These patients may have less PBV reserve than patients with coronary artery disease or valvular regurgitation. Schreiner and associates measured PBV at rest and during exercise using the indicator-dilution technique in six patients with mitral stenosis. \(^{20}\) Four patients had an increase and two a decrease in PBV during exercise. All six had an increase in left atrial pressure with exercise.

In conclusion, patients with a variety of cardiac diseases demonstrate an increase in the PBV ratio with exercise. A major determinant of the change in PBV ratio is an exercise-induced increase in pulmonary capillary wedge pressure. Thus, determination of the PBV ratio from standard rest and exercise gated blood pool studies can be used as a noninvasive means of estimating exercise-induced changes in left ventricular filling pressures.

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**References**

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