Pulmonary Capillary Wedge Pressure, as Inferred from Lung Areas in Gated Blood-Pool Scintigrams: Concise Communication

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To determine whether the apex-to-base distribution of pulmonary blood volume, as obtained from gated cardiac blood-pool scans, could be used as a noninvasive method to estimate mean pulmonary capillary wedge pressure (PCWP), gated blood-pool scans were analyzed in 77 patients who also had PCWP measurements at cardiac catheterization. Ten of these patients had gated cardiac blood-pool scans and PCWP measurements both at rest and during exercise. The apex-to-base distribution of pulmonary blood volume was determined from the end-systolic frame of the left anterior oblique view by placing equal-sized regions of interest over the apex and base of the right lung. The ratio of apex counts over base counts (A/B ratio) was considered abnormal if greater than unity.

The mean A/B ratio was 1.15 ± 0.27 (1 s.d.) for the 32 studies associated with an abnormal mean PCWP (greater than 12 mm Hg). The mean A/B ratio was 0.85 ± 0.23 for the 55 studies associated with a normal mean PCWP ($p < 0.01$ comparing normal group with abnormal). The sensitivity of the A/B ratio for a mean PCWP >12 mm Hg was 81% (26/32). The specificity of the A/B ratio for a mean PCWP ≯12 mm Hg was 89% (49/55).

Thus, noninvasive determination of the pulmonary apex-to-base ratio from gated cardiac blood-pool scans appears to differentiate subjects with normal and abnormal mean pulmonary capillary wedge pressures.

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The pulmonary capillary wedge pressure (PCWP) reflects the mean left-atrial and pulmonary venous pressures and can therefore, in the absence of mitral valve disease, be used as an indicator of end-diastolic pressure and left-ventricular function. The appearance of the pulmonary vasculature on routine chest radiographs has been related to the PCWP. Interstitial edema, an increase in size of the upper-lobe pulmonary vasculature, pleural effusion, and alveolar edema are some of the radiographic findings consistent with an increase in pulmonary venous pressure (*1*). However, since these radiographic findings do not accurately distinguish patients with normal from those with abnormal PCWP, accurate determination of the PCWP usually requires right-heart catheterization. The purpose of this study was to investigate a noninvasive means of identifying alterations in pulmonary venous pressure by comparing the blood volume in the upper part of the lung with that in the lower part of the lung using conventional gamma blood-pool imaging.

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METHODS

Patient population. Seventy-seven patients ranging in age from 24 to 74 yr (mean 55) had gated cardiac blood-pool scans and right-heart catheterization performed. There were 50 men and 27 women. In ten of

these patients both studies were performed simultaneously, first at rest and then during exercise. In 36 patients, the scans were performed within 24 hr of catheterization. The remaining 31 patients had the gated blood-pool scan performed within 2 wk of the cardiac catheterization, at a time when no change in the patients' clinical status had occurred. The patients had the following diagnoses at cardiac catheterization: 21 had coronary artery disease, four had aortic valve regurgitation, three had aortic valve stenosis, one had mixed aortic valve disease, one had mitral regurgitation, four had mitral stenosis, one had mixed mitral disease, six had primary cardiomyopathy, one had a left-atrial myxoma, two had atrial septal defect, one had a ventricular septal defect, 13 had multivalvular disease, and 19 had no cardiac disease but had undergone cardiac catheterization for chest pain syndromes.

Pulmonary capillary wedge pressure determination. The measurement of the PCWP was performed at the time of cardiac catheterization by passing a balloon-tip catheter to the pulmonary artery before any contrast angiographic studies. The balloon was inflated and the catheter was wedged in the pulmonary artery. The mean PCWP was measured with the patient supine.

Multigated blood-pool studies. Three milligrams of stannous pyrophosphate followed 30 min later by 20 mCi of pertechnetate (Tc-99m) were given intravenously to complete the in-vivo labeling of red cells (*2*). Multigated cardiac blood-pool images were recorded with the patient supine, in the anterior, 50° left anterior oblique (LAO) and 30° left posterior oblique (LPO) positions with a scintillation camera equipped with an all-purpose collimator. The data were stored in a dedicated nuclear medicine computer system. The electrocardiographic physiologic synchronizer was a component of the camera.

For the study at rest, 250,000 counts were collected for each of 32 frames per cardiac cycle during 5–12 min. For the exercised patients, multigated blood-pool images were collected for 3 min during peak exercise with a mean of 150,000 counts per frame.

Scan analysis. Ejection frames were calculated from the multigated blood-pool images in the LAO projection using a varying region of interest (*3*). Ejection fractions were determined by two independent observers who were unaware of the catheterization results, and the two determinations then averaged to produce a single EF for each study.

Gated blood-pool scans were displayed in a cinematic mode and the lung fields carefully observed to identify the vascular sites. A region of interest (ROI) encompassing ten picture elements (approximately 2 cm^2) was then placed over the apical portion of the right lung in the LAO end-systolic frame. This apical ROI was located immediately anterior to the superior vena cava and superior to the right main pulmonary artery, at a level below a line tangential with the upper contour of the aortic arch (Fig. 1). The base ROI was also located in the right lung, horizontally below the inferior aspect of the right pulmonary artery, but leaving an area of separation from the liver. This area was maintained to avoid the inclusion of lung volume below the diaphragm (*4*). The mean number of counts for the 174 regions of interest (87 studies × 2 regions per study) was 545 ± 214 (1 s.d.). Figure 1 shows the regions of interest for one study.

The apex-to-base count ratio (A/B ratio) for the two regions of interest was calculated. The A/B ratio was determined in all 87 studies by one observer, who repeated the A/B determination at least 1 mo after the first determination in 30 randomly selected studies to determine intraobserver variance. The A/B ratio was also determined by three independent observers in 20 randomly selected studies to determine interobserver variance.

We selected the end-systolic image in the LAO view because a preliminary study of 15 patients revealed better separation of normal from abnormal values when this view and frame were used. The anterior view could not be used reliably in women with large breasts or in obese patients, since flagging the basal portion of the right lung resulted in a low count value due to attenuation. The LPO view in most instances did not have enough room posteriorly to allow the placement of the regions of interest over the lung without including structures such as the aorta, the pulmonary artery, or the left atrium.

A value of unity or less was considered normal for the A/B ratio. This value was based on other studies dealing with the distribution of the pulmonary blood flow (*4,5*). A value of 12 mm Hg was considered the upper limit of normal for the mean pulmonary wedge pressure (*6,7*). Left-ventricular EF was considered abnormal if less than 45%, since studies have shown the radionuclide technique to underestimate this EF, as determined by biplane contrast angiography, by about 5% (*3*).

Statistical analysis. All values were expressed as a mean ±1 standard deviation. The mean PCWP, left-

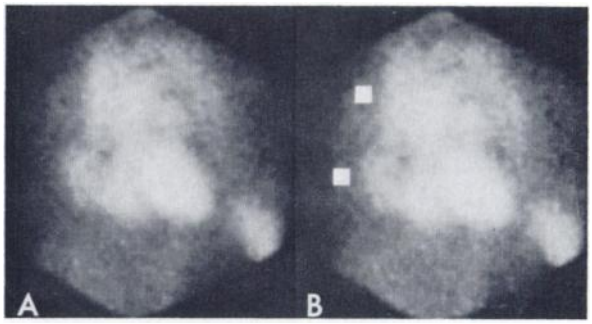

FIG. 1. A: End-systolic frame of multigated blood-pool study (LAO view) from patient with abnormal pulmonary capillary wedge pressure. B: Apex and base regions of interest used to calculate A/B ratio. Here A/B ratio is 1.28.

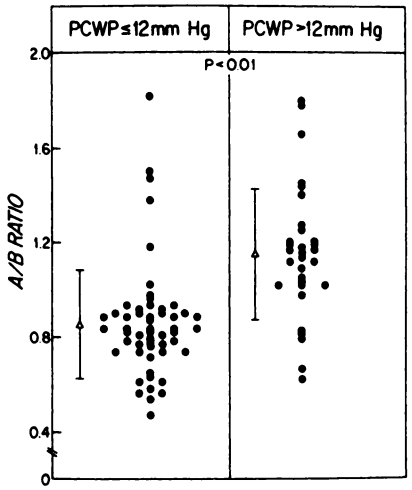

FIG. 2. Distribution of apex-to-base pulmonary blood volume ratios (A/B) for patients with pulmonary capillary wedge pressure (PCWP) ≤12 mm Hg, and for those with PCWP >12 mm Hg. Triangles represent mean and horizontal bars ±1 s.d.

ventricular EF, and A/B ratio were compared using linear regression analysis. Sensitivity was defined as the number of true abnormal responses divided by the total number of studies associated with a mean PCWP >12 mm Hg. Specificity was defined as the number of true normal responses over the total number of studies associated with a mean PCWP ≤12 mm Hg. Proportions of patients in various subgroups were compared by means of chi-square analysis. Differences between groups of patients for the A/B ratio and the left-ventricular EF were analyzed by means of a one-way analysis of variance and the Newman-Keuls multiple comparison test. Interobserver and intraobserver variability for the determinations of A/B ratio and left-ventricular EF were derived from a two-way analysis of variance. The variability was expressed at ±1 s.d.

RESULTS

Thirty-two of the 87 studies (37%) were associated with a mean PCWP >12 mm Hg, while 55 studies (63%) were associated with a normal pressure.

Figure 2 shows the distributions of A/B ratios. For the 32 studies associated with an abnormal PCWP, the mean A/B ratio was 1.15 ± 0.27 (s.d.). Only six of the 32 studies were associated with an A/B ratio ≯1. Thus, the sensitivity of the A/B ratio for a mean PCWP >12 mm Hg was 81% (26/32). The mean A/B ratio was 0.85 ± 0.23 for the 55 studies associated with a normal PCWP ($p<0.01$ compared with abnormal wedge-pressure group). Only six of the 55 studies were associated with an A/B ratio greater than unity. Thus the specificity of the A/B ratio for a normal PCWP was 89% (49/55).

Figure 3 shows the distribution of A/B ratios and mean PCWP. Linear regression analysis yielded a correlation coefficient of r = 0.48, with y = 0.0146x +0.780, where y was the A/B ratio ($p<0.0001$) for the 87 studies.

The intraobserver variability was 0.079 (±1 s.d.) and the interobserver variability was 0.081 (±1 s.d.) for the A/B ratio determination. The interobserver variability was 7.5% (±1 s.d.) for the determinations of left-ventricular EF.

The mean left-ventricular EF was 42.1% ± 15.4 for studies associated with a mean PCWP >12 mm Hg, and 51.6% ± 11.4 for the normal studies ($p<0.01$; Fig. 4). The LVEF had a sensitivity of 65% (21/32) and a specificity of 67% (37/55) for an abnormal mean PCWP. The specificity of the LVEF was significantly lower than that of the A/B ratio for an abnormal mean PCWP.

Results in 77 patients at rest. Excluding ten exercise studies, there were 77 observations at rest. The sensitivity of the A/B ratio for a mean PCWP >12 mm Hg was 81% (21/26) (p = ns compared with analysis for 87 observations). The specificity of the A/B ratio for a normal PCWP was 88% (45/51) (p = ns compared with analysis for 87 observations). Linear regression analysis yielded a weak correlation coefficient between A/B and PCWP: r = 0.48, with y = 0.0162x + 0.7620, where y was the A/B ratio.

Results in 20 observations with simultaneous wedge pressure measurement. The sensitivity of the A/B ratio for a mean PCWP >12 mm Hg was 75% (6/8) for the 20 multigated blood-pool studies where PCWP was determined simultaneously. The specificity of the A/B ratio for a normal PCWP was 91% (11/12) in this group. Linear regression analysis for the A/B ratio versus PCWP yielded a correlation coefficient r = 0.37, with y = 0.0108x +0.8282, where y was the A/B ratio.

The ten studies performed during exercise demonstrated abnormal A/B ratios in five of six patients with a peak PCWP greater than 12 mm Hg during exercise,

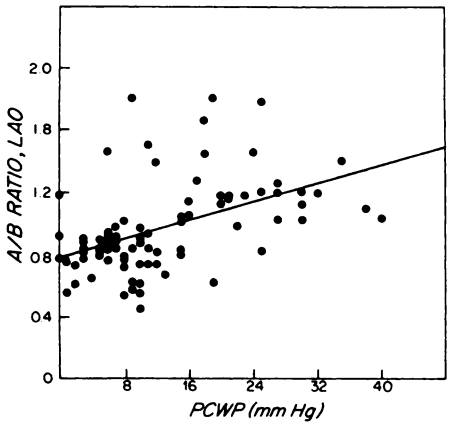

FIG. 3. Linear regression analysis for apex-to-base pulmonary blood volume ratio (A/B) against pulmonary capillary wedge pressure (PCWP) for 87 studies (y = 0.0146x +0.780, where y is the A/B ratio; r = 0.48).

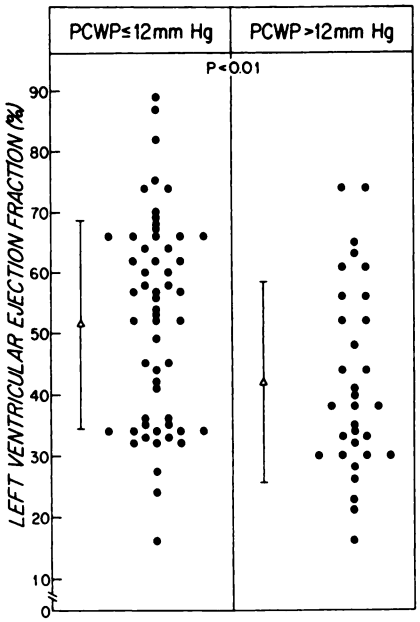

FIG. 4. Distribution of left-ventricular ejection fractions for patients with pulmonary capillary wedge pressure (PCWP) ≤ 12 mm Hg, and for those with PCWP > 12 mm Hg. Triangles represent means and horizontal bars ±1 s.d.

and a normal A/B ratio in all four patients with a peak PCWP ≯ 12 mm Hg during exercise. Linear regression analysis for the A/B ratio versus PCWP yielded a correlation coefficient r = 0.45, with y = 0.0101x +0.8467, where y was the A/B ratio.

DISCUSSION

The present study demonstrates that conventional gated blood-pool imaging can be used to identify alterations in pulmonary venous pressure. Comparison of the blood volume in the uper part of the lung with that in the lower part allows noninvasive differentiation between subjects with normal and abnormal PCWP. By using this labeled-blood technique, the present study yields a mean A/B ratio of 0.85 for supine patients with a normal mean PCWP. Supine patients with an abnormal wedge pressure had a mean A/B ratio of 1.15, suggesting a redistribution of pulmonary blood volume to the upper lung areas.

Our findings show that, in patients with increased pulmonary venous pressure, the abnormally high blood content of the upper lung regions, known to occur in upright subjects, persists in the supine position (*4,8–10*). The mechanism causing these alterations is unclear, but it may be related to focal changes in pulmonary vascular resistance, particularly in the lower lung zones. Dexter (*11*) suggested a reflex arteriolar constriction as the mechanism for the increase in pulmonary vascular resistance in the basal portions of the lung. Using portions of upper and lower lung taken from dogs, who had sudden increases in pulmonary venous pressure, and rapidly frozen, West demonstrated an increase in vascular resistance of both arteries and veins, caused by perivascular edema in the dependent zone of the lungs (*12*). Even though these experiments were performed in vertically suspended lungs, other investigators have found increases in the extravascular lung fluid preferentially in the lower lung zones in patients with diseases of the left heart studied in the supine position (*13*). Whatever the mechanism for increased resistance in the basal parts of the lungs in the presence of elevated pulmonary capillary wedge pressure, our findings suggest that such a mechanism persists in the supine position.

Although the measurement of total pulmonary blood volume in vivo is feasible with the indicator-dilution technique, the regional distribution of this volume cannot be defined with this invasive procedure (*14–16*). Previous noninvasive measurements of blood distribution in the lungs have been made using particles with radioactive labels such as Tc-99m, In-113m, I-131, and Cr-51 (*17–19*). The labeled particles have been mainly macroaggregated albumin and microspheres. They are big enough to be trapped in the pulmonary capillary beds. The regional washout of radioactive gases from the lungs has also been used to determine the distribution of blood flow (*20,21*). However, the microparticle and radioactive-gas techniques determine the distribution of pulmonary-arterial blood flow rather than the distribution of pulmonary blood volume. In the present study, the pulmonary distribution of blood volume was determined using a blood-pool label. This radiotracer technique assumes that the labeled red blood cells are in equilibrium throughout the vasculature, and therefore the measurement of activity in any area of the lung will be proportional to the blood volume in that area (*22*).

There are several possible explanations for the relatively poor correlation (r = 0.48) between PCWP and the A/B ratio. Only 20 of the gated blood-pool studies were performed simultaneously with the wedge pressure measurement. Although none of the patients in this study had a marked clinical episode or a change in diuretic or digitalis therapy in the interval between the gated scan and the cardiac catheterization, some of them may have had a change in PCWP between the two studies. Furthermore, an assumption was made that all tracer material was attached to the red blood cells and that none was contained in the interstitial spaces. Recent work by Froelich et al. (*23*) suggests that in-vivo-labeled red cells do have a significant component of loosely bound technetium, which may have dissociated from the red cells and may have provided increased background in the lungs as it diffused into the extracellular spaces. Finally, because the pulmonary venous system has limited distensibility, one would not expect the volume and pressure relationship to be perfectly linear.

We have previously determined the exercise-induced change in pulmonary blood volume in patients using the

gated blood-pool scan (*24*). Patients with coronary artery disease and an exercise-induced increase in PCWP had an exercise-induced increase in pulmonary blood volume, whereas normal subjects did not. The response of pulmonary blood volume to exercise was found to enhance significantly the diagnostic accuracy of the exercise gated blood-pool study for coronary artery disease. However, the technique used in our previous study could determine only directional changes in PCWP and required two gated blood-pool studies. The A/B ratio determination used in the present study appears to detect an abnormal PCWP using a single gated blood-pool study.

Thus we have observed that the A/B ratio determination appears to distinguish patients with normal ($\leq$12 mm Hg) and abnormal (>12 mm Hg) PCWP. The redistribution of pulmonary blood volume due to increased pulmonary venous pressure previously described in erect subjects seems to persist in the supine position.

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