Comparison of Ejection Fraction and Pulmonary Blood Volume Ratio as Markers of Left Ventricular Function Change After Coronary Angioplasty

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Exercise-induced increases in pulmonary blood volume ratio have been shown to be a sensitive marker of coronary artery disease, and correlate well with exercise-induced increases in left ventricular filling pressure. To compare the impact of single vessel coronary disease on left ventricular systolic function (ejection fraction) versus diastolic filling pressure (pulmonary blood volume) before and after intervention, serial supine exercise gated blood pool scans were performed before and after coronary angioplasty in 32 patients with isolated left anterior descending coronary artery disease. By applying previously established criteria of abnormal ejection fraction (rest <50% or failure to rise by 5% with exercise) and pulmonary blood volume ratio (>1.06), 66% of the patients were found to have abnormal responses before angioplasty by ejection fraction compared with 81% abnormal responses by pulmonary blood volume ratio ($p = 0.15$). After angioplasty, the proportion of patients with abnormal ejection fraction (59%) was essentially unchanged, whereas only 38% continued to have an abnormal pulmonary blood volume ratio ($p < 0.01$ compared with before angioplasty). The mean pulmonary blood volume ratio also decreased significantly from 1.15 ± 0.10 before angioplasty to 1.02 ± 0.15 after angioplasty ($p < 0.001$).

It is concluded that in single vessel coronary artery disease: 1) pulmonary blood volume ratio is abnormal at least as frequently as is ejection fraction; 2) in contrast to ejection fraction, pulmonary blood volume ratio improves significantly after successful angioplasty; and 3) pulmonary blood volume ratio may be a more sensitive indicator of changes in ventricular function after an intervention in single vessel coronary disease.

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Patients with single vessel coronary artery disease may demonstrate both abnormal systolic function and abnormal diastolic filling pressure during exercise (1,2). However, the relative incidence of these changes and the improvement in left ventricular function after revascularization are less well understood. Previous work from our laboratory (3) has demonstrated that the change in relative pulmonary blood volume from rest to exercise is a sensitive indicator of left ventricular dysfunction. This variable also correlates well with exercise-induced elevation in left ventricular filling pressure (4).

To analyze the impact of single vessel coronary disease on left ventricular function and to assess the potential changes after revascularization, serial gated blood pool scans were acquired in 32 patients before and after percutaneous transluminal coronary angioplasty. Our specific goal in the study was to determine in isolated left anterior descending coronary artery disease whether pulmonary blood volume ratio (a reflector of left ventricular diastolic filling pressure) is as sensitive an indicator of left ventricular dysfunction as is ejection fraction (a reflector of left ventricular systolic function). In addition, we sought to determine which variable is more sensitive in indicating the improvement in ventricular function after successful revascularization by coronary angioplasty.

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Methods

Study patients. Thirty-two consecutive patients with isolated left anterior descending coronary artery disease who underwent successful percutaneous transluminal coronary angioplasty at our hospital were studied. There were 24 male and 8 female patients, with a mean age (±SD) of 52 ± 9 years. All patients were symptomatic with chest pain: 21 had classical and 11 had atypical angina.

Any patient with a history of myocardial infarction with either Q waves on the electrocardiogram or wall motion abnormalities at rest on the radionuclide ventriculogram, was excluded from the study. Patients were also excluded if they had unstable angina, chronic congestive heart failure, recent myocardial infarction, previous cardiac surgery, multivessel coronary artery disease, other heart disease or serious systemic illness. All patients were in sufficiently stable condition to undergo exercise testing within 1 week before and 2 weeks after coronary angioplasty.

The patients were receiving a variety of antianginal medications, including beta-adrenergic blocking agent (14 patients), long-acting nitrates (16 patients) and calcium channel blockers (12 patients). Medications were not discontinued before exercise testing, but the patients were maintained on the same medical regimen, with the addition of antiplatelet agents, for at least 3 months after angioplasty.

Coronary angiography. The coronary arteriograms were performed in all patients several weeks before angioplasty using the Judkins or Sones technique. Multiple views of the coronary artery tree were visualized with intracoronary injections of Renografin-76. The arteriograms were reviewed by two experienced observers and lesions of greater than 50% luminal reduction were considered to be hemodynamically significant. All patients in this study had at least a 50% narrowing in either the proximal or the mid-left anterior descending coronary artery, with no significant stenoses elsewhere. Coronary arteriography was repeated immediately before angioplasty in each case to confirm the persistence of the original lesion and to exclude the development of new stenoses during the interim period.

Coronary angioplasty. Angioplasty was performed in all patients by introducing a balloon-tipped dilating catheter (USCI, Meditech of Advanced Catheter Systems) across the coronary stenosis over a guide wire. The balloon was inflated three or four times for 30 to 60 seconds each at a pressure of 5 to 10 atm. Angioplasty was considered successful if there was a significant reduction in severity of stenosis with a minimal 20% increase in angiographic luminal diameter (previously published National Heart, Lung, and Blood Institute criterion) (5). However, in all patients this conservative criterion was comfortably exceeded and the average stenosis decreased from 84 ± 9 to 26 ± 16% ($p < 0.0001$). The translesional pressure gradient was also measured before and after angioplasty, and decreased from 51 ± 12 to 18 ± 8 mm Hg ($p < 0.00001$).

Gated blood pool image acquisition. Rest and exercise gated blood pool scans were acquired 1 week before and repeated within 2 weeks after angioplasty. The gated blood pool scans were acquired according to a previously published protocol (6). Briefly, after modified in vivo labeling of the patient's red blood cells with 740 MBq (20 mCi) of technetium-99m pertechnetate, gated blood pool scans were recorded with the patient in the supine position using the anterior and 45° left anterior oblique views for 200,000 counts/image field at 14 frames/RR interval. Supine bicycle exercise was then carried out starting at 25 W of work load, continued at 25 W incremental stages every 3 minutes until the onset of exhaustion, chest pain, arrhythmias or greater than 3 mm ST segment depression. The exercise gated blood pool scans were acquired for at least 2 minutes during each stage of exercise after stabilization of the heart rate.

Ejection fraction. This variable was calculated by a commercially available semiautomated edge detection method, using a count-based algorithm. The ejection fraction response was considered normal if the ejection fraction was greater than 50% at rest and increased by at least 5% with exercise (7).

Gated blood pool scan analysis. *Pulmonary blood volume ratio.* The calculation for this variable was derived using a previously reported technique employing the end-diastolic frame in the 45° left anterior oblique view (3). A pulmonary region of interest was manually placed immediately lateral and superior to the main blood pool activity in the left ventricle, avoiding the left atrium and descending aorta (Fig. 1). A time-activity curve was constructed for the assigned region of interest in each case to ensure that it was not inadvertently overlying a vascular structure. The pulmonary blood volume ratio was then calculated as the average count per pixel from the designated region of interest from the exercise image divided by counts from the rest image, after correction for different framing intervals. The upper limit of normal (1.06) was determined from previous studies in our laboratory (3).

Regional wall motion. The gated blood pool scans were reviewed by three unbiased observers using previously reported criteria (7). Briefly, each view was divided into three myocardial segments. The wall motion in each segment was graded on a scale from −1 to 3 (−1 = dyskinesia, 0 = akinesia, 1,2 = severe and mild hypokinesia, respectively, and 3 = normal), and the results were averaged (7). An average score of 2 or less at rest was considered abnormal for any myocardial segment, and a fall of 1.0 or more in average score during exercise was considered a significant exercise-induced deterioration.

Ethical considerations. The procedures were fully explained to the patients before the study, and informed con-

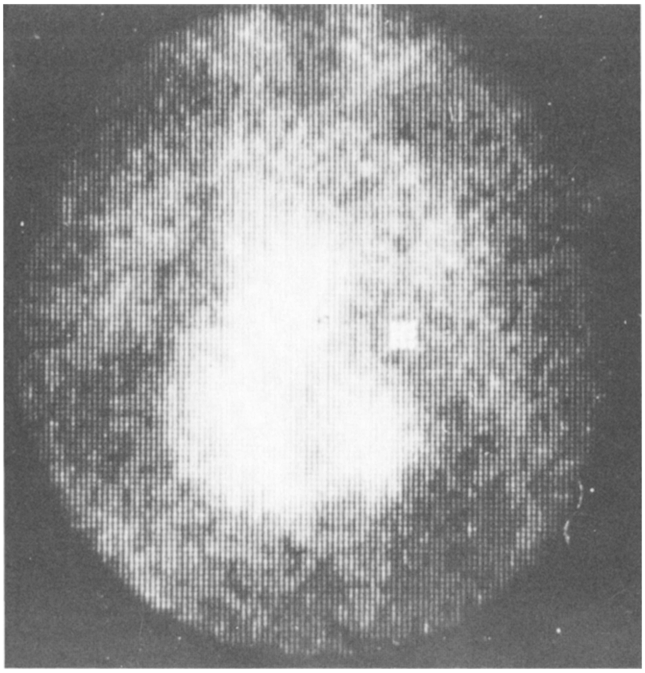

Figure 1. The manually outlined pulmonary regions of interest for the calculation of pulmonary blood volume ratio.

sent was obtained. The protocol was approved by the Subcommittee on Human Studies of the Committee on Research at the Massachusetts General Hospital. The radiation exposure was calculated to be 0.29 rem to the whole body and 1.95 rem to the spleen for each gated blood pool scan.

Statistical analysis. All values were expressed as mean ± SD. Comparison of ejection fraction and pulmonary blood volume ratio before and after angioplasty was done by paired *t* testing. A p value of less than 0.05 was considered significant. Comparison of different attributes of the high versus normal pulmonary blood volume ratio groups was done by analysis of variance and Neuman-Keuls multiple range testing.

Results

Ejection fraction response. Before angioplasty, 21 patients (66%) were found to have an abnormal ejection fraction response to exercise. In 5 of these, ejection fraction was abnormal at rest and in 16 it failed to increase by at least 5% at peak exercise. The mean ejection fraction was 0.62 ± 0.08 at rest and 0.62 ± 0.10 with exercise (Fig. 2A). After angioplasty 17 patients (53%) still had an abnormal ejection fraction response (p = NS compared with before angioplasty) (Fig. 2B). The mean ejection fraction at rest after angioplasty remained at 0.62 ± 0.08; however, the exercise ejection fraction increased slightly to 0.64 ± 0.12 (p = NS).

The average change in ejection fraction from rest to exercise was −0.3 ± 8.4% before angioplasty and 2.0 ± 8.8% after angioplasty. The changes before and after angioplasty were not statistically significant.

To demonstrate the individual changes in ejection fraction after intervention, the rest and exercise ejection fractions before and after angioplasty for each patient are plotted in pairs in Figure 3A and B, respectively. There was no significant change in rest or exercise ejection fraction in this group before and after angioplasty.

Pulmonary blood volume ratio. This ratio was abnormally high in 26 patients (81%) before angioplasty, a proportion of patients that was not significantly higher ($p = 0.15$) than the proportion of patients (66%) with an abnormal ejection fraction response before angioplasty. Hemodynamic and gated blood pool variables were compared (Table 1) in patients with a high or a normal pulmonary blood volume ratio before angioplasty; the only trend evident was that the high pulmonary blood volume group demonstrated more frequent exercise-induced deterioration in wall motion before angioplasty.

After angioplasty, only 12 (38%) of 32 patients had an abnormally elevated pulmonary blood volume ratio (p <

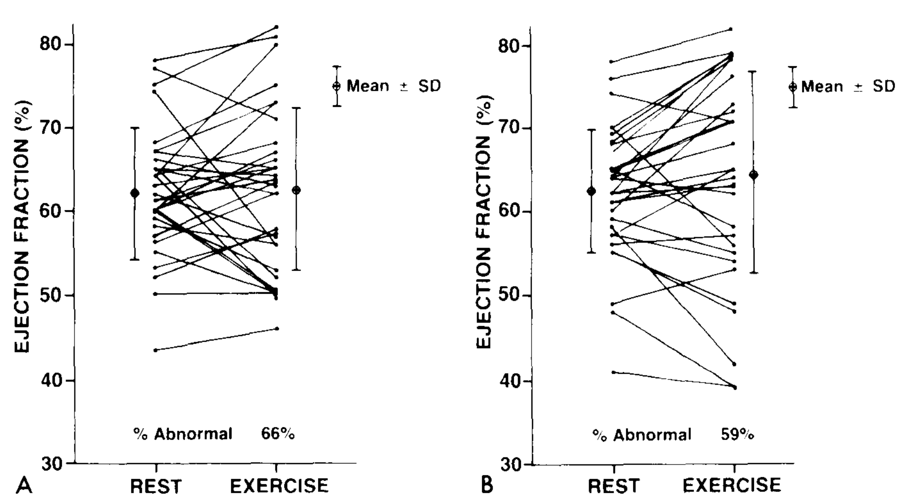

Figure 2. Comparison of ejection fraction response at rest and during exercise. **A**, Before angioplasty (PTCA) and **B**, after angioplasty.

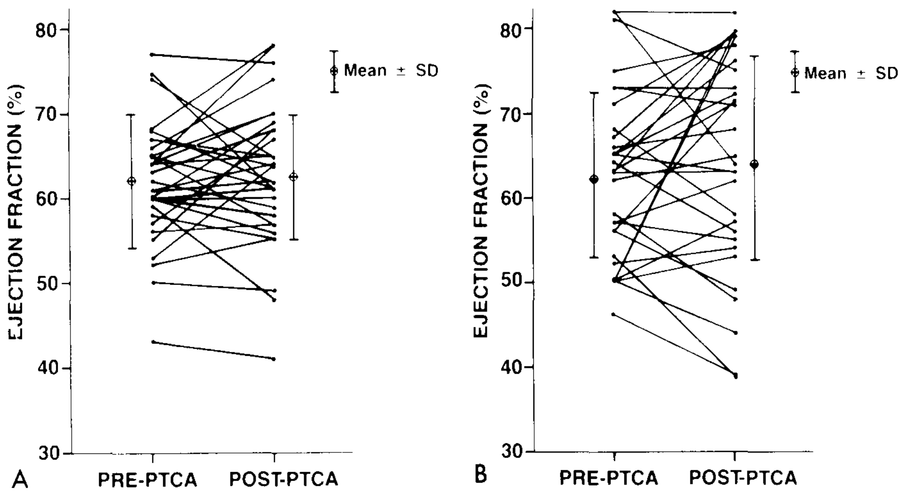

Figure 3. Comparison of rest (**A**) and exercise (**B**) ejection fraction response before and after angioplasty (PTCA).

0.05 compared with before angioplasty). The mean value for this ratio also decreased significantly from 1.15 ± 0.10 before angioplasty to 1.02 ± 0.16 after angioplasty ($p < 0.01$) (Fig. 4).

To examine the potential relation between pulmonary blood volume ratio and clinical indicators of ischemia, we compared the incidence of exercise-induced angina and ST segment changes with the pulmonary blood volume response (Table 2). Patients with a high pulmonary blood volume were more likely to have angina on exercise, but this trend also did not reach significance. There were no significant differences in the type of chest pain, residual stenosis or gradient, ejection fraction or the presence of hypertension between patients with and without a normalized pulmonary blood volume ratio after angioplasty. There was a trend toward a higher incidence of wall motion abnormalities in patients whose ratio failed to normalize but, because of the small sample size, this also did not reach statistical significance.

Exercise-induced wall motion changes. Abnormal wall motion changes induced by exercise were observed in 13 patients (41%) before angioplasty. The addition of this criterion to ejection fraction response to define abnormality did not significantly improve the sensitivity of detecting the impact of the coronary stenosis on ventricular function. This is partly because of the relatively strict criterion of ejection fraction response used, such that most patients with abnormal wall motion also had an abnormal ejection fraction response. In fact, only one patient demonstrated exercise-induced wall motion changes in the presence of a normal ejection fraction response.

After angioplasty, the incidence of abnormal wall motion was reduced to 5 (16%) of 32 patients; this did represent a significant change with a probability (p) value of 0.03. In addition there appeared to be an association between pulmonary blood volume ratio changes and reduction in wall motion abnormalities, as outlined earlier.

Table 1. Clinical and Hemodynamic Comparisons of Patients With High Versus Normal Pulmonary Blood Volume Ratios

	Pulmonary Blood Volume Ratio		
	High	Normal	p Value
No. of patients	26	6	
Age (yr)	53 ± 10	49 ± 6	NS
Medication			
Nitrates	13	3	NS
Beta-blockers	10	4	NS
Calcium channel blockers	10	2	NS
Coronary translesional gradient (mm Hg)	51 ± 14	49 ± 9	NS
Angiographic stenosis (%)	82 ± 9	87 ± 6	NS
Duration of exercise (min)	8.1 ± 2.6	8.7 ± 3.1	NS
Percent of patients showing deterioration of segmental wall motion on exercise (%)	65	33*	0.15

NS = not significant.

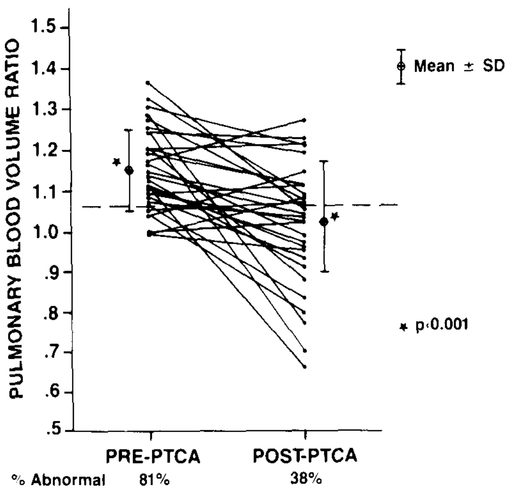

Figure 4. Changes in pulmonary blood volume ratio before and after coronary angioplasty (PTCA).

Discussion

The results of our study indicate that, before angioplasty the pulmonary blood volume ratio is abnormal at least as frequently in isolated left anterior descending coronary artery disease, as is the ejection fraction response to exercise. The pulmonary blood volume ratio is also more sensitive than ejection fraction as an indicator of improvement in ventricular functional reserve after revascularization by angioplasty.

Abnormal ventricular function before angioplasty. The high prevalence of an abnormal pulmonary blood volume ratio in this group of patients with isolated left anterior descending coronary artery disease (81%) is consistent with previously published data in similar population groups (2).

Table 2. Comparison of Associated Indicators of Ischemia With Pulmonary Blood Volume Before and After Coronary Angioplasty

	Pulmonary Blood Volume Ratio	
	High	Normal
Before angioplasty		
No. of patients	26	6
Angina on exercise	14 (54%)	1 (17%)
ST changes on exercise	12 (46%)	3 (50%)
Congestive heart failure	0	0
After angioplasty		
No. of patients	12	20
Angina on exercise	3 (25%)	0
ST changes on exercise	3 (25%)	2 (10%)

This abnormality occurs at least as frequently as systolic dysfunction as represented by ejection fraction response in the same patients. This finding supports the concept that impairment in left ventricular filling, an energy-dependent process, occurs early during ischemia, and is a sensitive index of the impact of coronary artery disease on left ventricular function. In addition we have utilized a very strict definition of abnormal ejection fraction response, that is, failure to increase by 5% with exercise. If a more liberal criterion such as a lack of increase in ejection fraction with exercise had been used, fewer patients would have shown an abnormal ejection fraction response, and pulmonary blood volume ratio may have turned out to be significantly more sensitive than ejection fraction as a marker for the impact of coronary artery disease on left ventricular function.

Similar conclusions have also been reached by other laboratories by examining left ventricular diastolic filling patterns on time-resolved gated radionuclide ventriculograms at rest (8,9). The abnormalities at rest are thought to result from diastolic regional asynchrony (10). We did not examine other radionuclide ventricular filling variables such as peak filling rate and time to peak filling because the temporal resolution of our data was not rigorous enough to calculate these variables. In addition, small variations in heart rate can make these data difficult to interpret. However, ischemia in coronary disease is present much more frequently during exercise than at rest, and left ventricular filling pressure in turn has been shown to elevate dramatically during supine exercise (11). Thus pulmonary blood volume ratio has the advantage of reflecting abnormal increases in left ventricular filling pressure during exercise and is simple to use and interpret (3).

Changes in ventricular function after angioplasty. Conversely, the reduction in pulmonary blood volume ratio after angioplasty seen in our group of patients is probably related to the alleviation of exercise-induced ischemia after successful angioplasty. On the other hand, diastolic filling variables at rest have also been observed to improve after angioplasty by Bonow et al. (10,12), suggesting that the diastolic filling abnormalities are indeed reversible on revascularization. Interestingly, a significant proportion of our patients continued to have an abnormal pulmonary blood volume ratio after angioplasty. This residual abnormality could be related to a mild degree of residual ischemia as a result of incomplete revascularization in some patients. A recent report (13) has also indicated that there thallium scans may demonstrate continued improvement up to 3 months after angioplasty, suggesting the possibility of continued improvement in perfusion in the vascular territory subjected to angioplasty. A second possibility is that previous repeated ischemic episodes may have led to relatively slow but prolonged impairment of ventricular function, which may be unable to recover immediately after revascularization.

Our data after angioplasty indicated no change in rest ejection fraction and only a statistically in significant trend toward an increase in exercise ejection fraction. This is in agreement with the findings of Bonow et al. (10,12), who demonstrated no change in systolic function as assessed by ejection fraction at rest in patients before and after angioplasty, but found a significant change on exercise. However, some other investigators (14,15) have reported significant improvement in both rest and exercise ejection fraction after angioplasty. These differences are best explained on the basis of differences in patient groups. Our data may have failed to demonstrate a significant change in ejection fraction for at least two possible reasons. First, all of our patients had only single vessel disease, and the mean ejection fraction at rest was still in the normal range at baseline, making it difficult to demonstrate additional physiologic improvement. Second, a number of patients were studied with the continuation of antianginal medications, which may blunt the potential changes in ejection fraction after intervention.

Dissociation of systolic and diastolic function in single vessel disease. The observed dissociation between systolic and diastolic variables of left ventricular dysfunction may in fact be most marked in this subset of patients with single vessel disease. Because the abnormality in single vessel disease is most frequently regional, global measures of ventricular systolic function such as ejection fraction may be too insensitive to detect changes in regional perfusion. Pulmonary blood volume ratio is linearly related to an increase in left ventricular filling pressures during exercise, and the left atrial pressure is elevated during exercise in patients with ischemia as a compensatory mechanism to augment diastolic filling (11). Thus, the pulmonary blood volume ratio is a simple and readily applied variable of ventricular filling that appears to be a sensitive indicator of changes in ventricular function after an intervention.

Conclusions. In patients with single vessel coronary artery disease, the pulmonary blood volume ratio, an index of the left ventricular filling pressure response during exercise, is abnormal at least as frequently as is ejection fraction, an indicator of global ventricular function. The ejection fraction failed to change significantly after successfully isolated left anterior descending coronary artery revascularization, whereas the pulmonary blood volume ratio improved significantly. This discordance between systolic and diastolic dysfunction variables in single vessel coronary artery disease suggests that the pulmonary blood volume ratio may be more sensitive than the ejection fraction as an indicator of changes in ventricular function.

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