Left Ventricular Cavity-to-Myocardial Count Ratio: A New Parameter for Detecting Resting Left Ventricular Dysfunction Directly from Tomographic Thallium Perfusion Scintigraphy

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Patients with reduced left ventricular function or aneurysms have cavities that appear dark on SPECT thallium scintigrams. We hypothesized that a quantitative index, which relates thallium activity in the left ventricular cavity to that in the myocardium (C/M ratio), could provide information on left ventricular function. A group of 80 patients who had both exercise SPECT thallium imaging and cardiac catheterization were studied. The C/M ratio was obtained from the short-axis tomogram on both exercise and rest images. Counts in a 2 × 2 pixel region of interest in the left ventricular cavity were divided by the number of counts in the "hottest" area of the myocardium. Plotting the angiographically determined ejection fraction against the C/M exercise and rest ratios, we observed a linear correlation between ejection fraction and both C/M ratios, $r = 0.65$ for C/M exercise and $r = 0.67$ for C/M rest ratio ($p < 0.00001$). Using data from 12 normal cardiac catheterization patients, we established the lower limit of normal; 50% for ejection fraction and 0.40 for the C/M ratios. A C/M exercise ratio ≤0.40 identified 26 of 31 patients with an ejection fraction ≤50%. A C/M exercise ratio >0.40 identified 39 of 49 patients with an ejection fraction >50%. These calculations yielded a sensitivity of 83% and specificity of 78% for the C/M exercise ratio. A similar analysis for C/M rest ratio revealed sensitivity of 61% and specificity of 92%. The present study shows that an abnormal C/M ratio correctly distinguishes patients with abnormal from normal ejection fractions with an accuracy of 81%. The C/M ratio is easily obtained, requires minimal processing time and is highly reproducible. These attributes may enable this index to add supplementary information regarding left ventricular function in addition to perfusion from thallium imaging.

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Tomographic thallium perfusion scintigraphy is an established method for diagnosing coronary artery disease, but it is not commonly used as a means of assessing left ventricular function (*1*). Computer modeling experiments have indicated that the size, appearance and count density of the left ventricular cavity on thallium perfusion imaging are related to left ventricular ejection fraction (*2*). Clinical reports have noted that patients with left ventricular aneurysms or reduced left ventricular performance have thallium perfusion scintigrams in which the left ventricular cavity appears unusually dark or count-poor relative to myocardium (*3–6*). These observations suggest that a simple quantitative ratio of the thallium activity within the left ventricular cavity to that in the myocardium—the cavity-to-myocardial count ratio—might correlate directly with left ventricular ejection fraction (LVEF). This study was performed to determine if a direct relationship exists between the cavity to myocardial count ratio and LVEF, and whether this ratio could be used to obtain clinically useful information on left ventricular function directly from routine thallium scintigrams.

METHODS

We retrospectively analyzed a group of 80 patients who were undergoing evaluation of chest discomfort or of known or suspected coronary disease. All patients had both exercise SPECT thallium imaging and coronary angiography with left ventriculography. No patient had significant valvular heart disease. Each patient's scintigraphic and angiographic studies were performed within a 3-mo period. No patient had angioplasty, bypass surgery or hospitalization for myocardial infarction or unstable angina in the interval between catheterization and thallium scintigraphy.

Exercise SPECT Thallium Scintigraphy

Graded treadmill exercise was performed using a Bruce or modified Bruce protocol. One minute prior to the end of exercise, 3.0–3.5 mCi of ^{201}Tl-chloride was injected intravenously. Postexercise and delayed thallium tomograms were acquired on a rotating gamma camera (Elscint Apex 409) equipped with a low energy, medium resolution collimator (APC-3) centered on the 68–83 keV photopeak of thallium with a 10% window. A 180-degree circular orbit from 45 degrees RAO to 45 degrees LPO was used. Sixty frames were acquired on a 64 × 64 matrix and were corrected for nonuniformity and center of rotation. Transaxial slices were generated following filtered backprojection using a first-order raised Hanning filter in combination with a ramp filter (cutoff frequency of 0.73 cycles/cm). An operator-dependent computerized algorithm was then used to generate horizontal, vertical and short-axis tomograms (*7*).

Cavity-to-Myocardial Count Ratio

The short-axis tomogram from the mid-left ventricle was used for computation of the cavity-to-myocardial count ratio (C/M ratio). A 2 × 2 pixel region of interest (ROI) was placed in the visually determined center of the left ventricular cavity and the number of counts was obtained. The ROI was moved to the "hottest" area (identified by overrange blanking) in normal-appearing myocardium and the number of counts determined. The ratio of counts in the left ventricular cavity to that in the myocardium was calculated as the C/M ratio (Fig. 1). The C/M ratio was determined for both the exercise (C/M exercise) and 4-hr delayed (C/M rest) short-axis tomograms in each patient. Intraobserver and interobserver reproducibility for the exercise and rest C/M ratios were determined in a group of 30 randomly selected patients. The correlation for intra- and interobserver reproducibility was 0.98 for both exercise and rest C/M ratios ($p < 0.0001$).

Lung Thallium Uptake

Lung thallium uptake was quantified as the ratio of counts in a region of interest placed over the "hottest" area of lung compared to the "hottest" area of myocardium. This ratio was then termed the lung-to-heart (L/H) ratio. Based on a previous analysis of patients in our laboratory with <5% pre-test probability of coronary disease, a ratio of >0.45 (more than 2.5 standard deviations above the mean value) is considered abnormal.

Cardiac Catheterization

Selective coronary arteriography was performed using the Sones or Judkins technique. Significant coronary disease was defined as a stenosis ≥50% of the luminal diameter. Left ventriculography was performed in the right anterior oblique projection and ejection fraction was calculated by a single observer using the planimetry area-length method.

Study Group

There were 58 men and 22 women, with a mean age of 64 ± 15 yr (range 39 to 81 yr). Twelve patients in the study group had normal coronary angiography and left ventriculography. Sixty-eight patients had significant angiographic coronary artery disease. Sixteen of these patients had a previous history of myocardial infarction and significant Q-waves (duration ≥0.04 sec, amplitude of 1/3 of the R-wave) on resting ECG.

Analysis

The correlation between angiographic LVEF and the C/M exercise and C/M rest was determined using linear regression and Pearson's coefficient.

The 12 normal patients in the study group were used to establish the lower limits of normal for LVEF and for C/M ratios at exercise and rest. The lower limit of normal was taken as 2.5 standard deviations below the mean values for these parameters in the normal patients. The ability of an abnormally low C/M ratio to identify patients with reduced LVEF was then calculated using the chi-square statistic. The chi-square statistic was also used to compare the C/M ratio in patients with and without previous myocardial infarction.

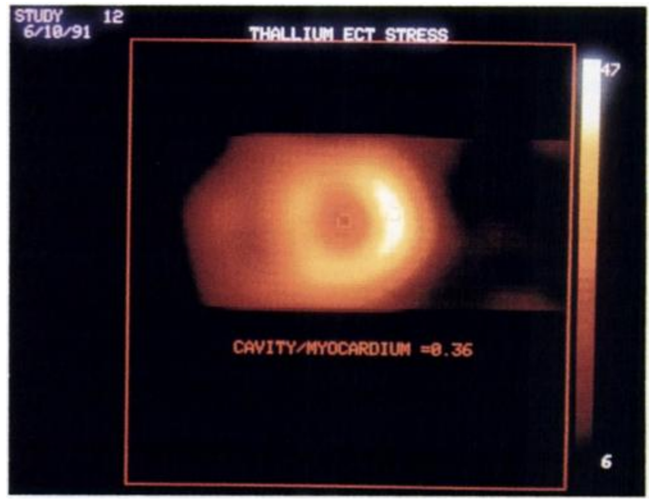

FIGURE 1. Mid short-axis left ventricular thallium tomogram. A 2 × 2 pixel ROI is placed in the visually determined center of the left ventricular cavity and moved to the "hottest" area of myocardium. Total counts are determined in each area and the C/M ratio is calculated.

The data from all study patients were used in the correlation and intergroup comparisons.

RESULTS

There was a positive linear correlation between LVEF measured angiographically and C/M exercise ratio (EF = 32 ± 0.54 C/M; r = 0.65, s. e. e. ± 0.075, $p < 0.00001$) and with C/M rest ratio (EF = 24 ± 0.60 C/M; r = 0.67, s. e. e. ± 0.81, $p < 0.00001$) (Figs. 2 and 3).

The 12 patients with normal catheterization findings had a mean LVEF of 74% ± 9%, a C/M exercise of 0.68 ± 0.11, and a C/M rest of 0.69 ± 0.11. The lower limit of normal for ejection fraction was thus 50%. The lower limit of normal for C/M exercise and C/M rest was 0.40.

The ability of an abnormal C/M ratio (≤0.40) to identify patients with left ventricular dysfunction (ejection fraction ≤50%) is presented in Tables 1 and 2. A C/M exercise ratio ≤0.40 correctly identified 26 out of 31 patients with an ejection fraction ≤50%. Four of the five patients not identified had ejection fractions ranging from 42% to 48%. A C/M exercise ratio >0.40 correctly identified 39 out of 49 patients with an ejection fraction >50%. Seven of the ten misclassified patients had wall motion abnormalities on left ventriculography but overall LVEF was above 50%. Thus, a C/M exercise ratio of ≤0.40 had a sensitivity of 83%, a specificity of 79% and an overall diagnostic accuracy of 81% for identifying patients with left ventricular dysfunction ($p < 0.00001$). A similar analysis for the C/M ratio at rest yielded a sensitivity of 61%, a specificity of 92% and a diagnostic accuracy of 80% ($p < 0.0001$).

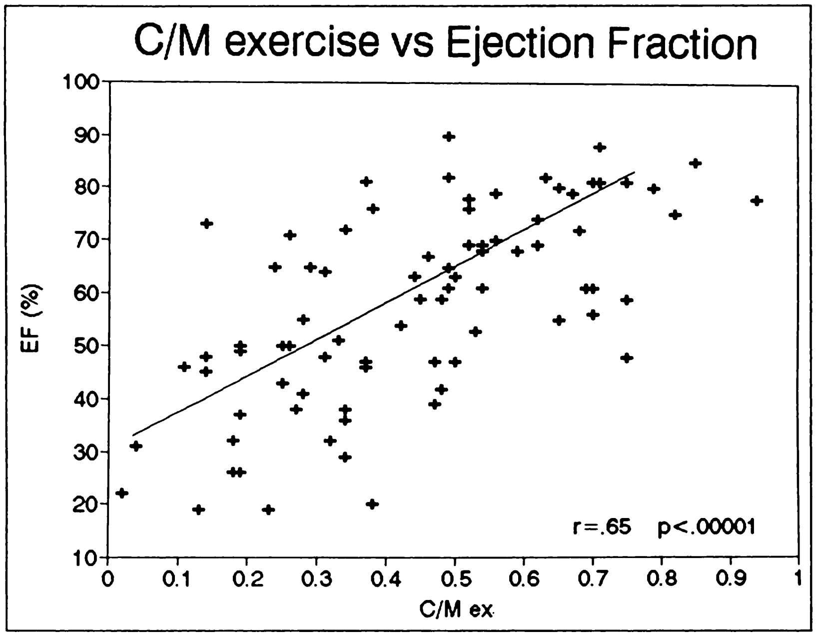

FIGURE 2. Graph of C/M exercise ratio versus LVEF.

A total of 16 patients had a previous myocardial infarction. By electrocardiographic criteria, 6 were anterior and 10 were inferior. The relationship between C/M ratio and previous myocardial infarction is depicted in Table 3. The frequency of myocardial infarction in patients with C/M exercise ≤0.40 is no different from the group with C/M exercise >0.40. Patients with infarction appear more frequently in the group with C/M rest ≤0.40 versus C/M rest >0.40. However, the number of patients with infarction with C/M exercise ≤0.40 (10) was similar to the number with infarction who had C/M rest ≤0.40 (9). A C/M ratio ≤0.40 occurred with equal likelihood in patients with anterior versus inferior infarction. Five of the patients with C/M exercise or C/M rest ≤0.40 had anterior infarction, the rest were inferior infarctions (Table 3).

The relationship between the C/M ratio and another scintigraphic marker of decreased left ventricular function, lung thallium uptake (quantified as the lung-to-heart ratio), is illustrated in Tables 4 and 5. An abnormal L/H ratio (≥0.45) correctly identified 24 out of 31 (77%) patients with an ejection fraction ≤50%, while a normal ratio correctly identified 32 out of 49 (65%) patients with an ejection fraction >50%. The sensitivity and overall diagnostic accuracy of lung thallium uptake is thus comparable to the C/M ratio for identifying left ventricular dysfunction. The concordance between C/M exercise and the L/

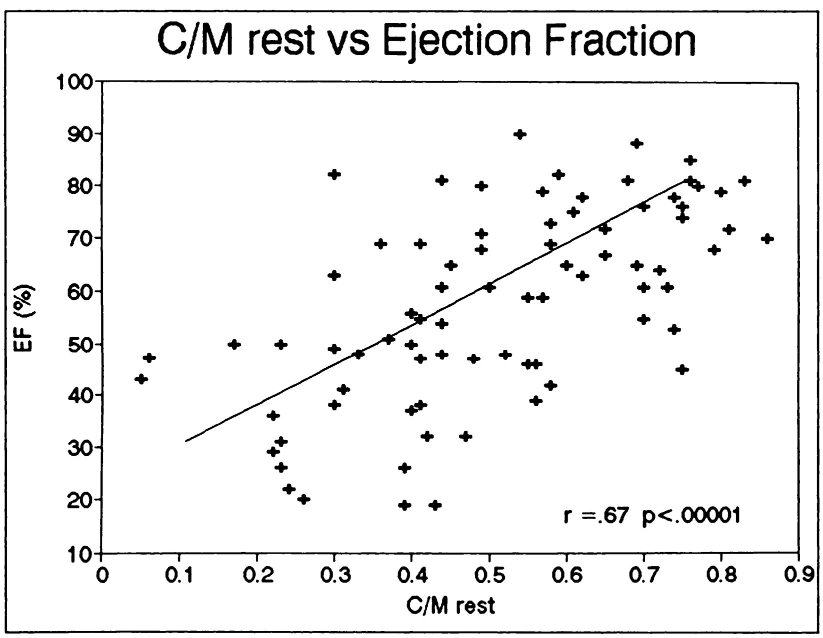

FIGURE 3. Graph of C/M rest ratio versus LVEF.

TABLE 1
Diagnostic Accuracy of C/M Exercise Ratio for Detecting Resting Left Ventricular Dysfunction

	LVEF		
	≤50%	>50%	
C/M exercise ≤0.40	26	10	$x^2 = 28.3$
C/M exercise >0.40	5	39	$p < 0.0001$

Sensitivity of C/M exercise for ejection fraction ≤50% = 83%. Specificity of C/M exercise for ejection fraction >50% = 79%. Overall diagnostic accuracy = 81%.

H ratio is depicted in Table 5. C/M exercise agreed with the L/H ratio in predicting left ventricular function in 57 of 80 (71%) patients. Of the 26 patients with both abnormal C/M and L/H ratios, 21 had reduced LVEF. Of the 31 patients with both normal C/M and L/H ratios, 29 had normal left ventricular function. In 23 patients, the C/M ratio and L/H ratio were discordant in predicting left ventricular function. Five of the eight patients with an abnormal C/M ratio and normal lung thallium uptake had reduced LVEF. Twelve of the 15 patients with a normal C/M ratio and abnormal L/H ratios had normal LVEFs.

DISCUSSION

This study demonstrates that the cavity to myocardial count ratio, which relates thallium activity in the left ventricular cavity to that in the myocardium, has a direct correlation with LVEF. A low C/M ratio, <0.40 in this laboratory, may be considered a potential scintigraphic marker of patients with reduced left ventricular function. These findings support previous observations (*3–6*) that the count density in the left ventricular cavity on thallium scintigrams is strongly influenced by multiple factors directly related to resting left ventricular performance.

Several sources contribute to thallium activity and count density within the left ventricular cavity during perfusion scintigraphy:

1. Spillover activity from the myocardium, as the wall thickens, dynamically overlaps the ventricular cavity and cavity size decreases during systole (*2,8*).
2. Activity from myocardial wall segments that directly overlie or surround the ventricular cavity en face (*9*). On reconstructed short-axis tomograms, this activity would appear to emanate from the ventricular cavity itself (*6*).
3. Activity within the cardiac blood pool, which is low relative to myocardial activity.
4. Activity within the ventricular cavity due to Compton scattering which is dependent on body habitus and soft-tissue attenuation (*10*).

TABLE 2
Diagnostic Accuracy of C/M Rest Ratio for Detecting Resting Left Ventricular Dysfunction

	LVEF		
	≤50%	>50%	
C/M rest ≤0.40	19	4	$x^2 = 23.6$
C/M rest >0.40	12	45	$p < 0.0001$

Sensitivity of C/M rest for ejection fraction ≤50% = 61%. Specificity of C/M rest for ejection fraction >50% = 91%. Overall diagnostic accuracy = 80%.

TABLE 3
C/M Ratio in Patients With and Without Myocardial Infarction (MI)

	MI	no MI	
C/M exercise ≤0.40	10	25	$x^2 = 0.52$
C/M exercise >0.40	06	27	p = NS
C/M rest ≤0.40	09	13	$x^2 = 4.12$
C/M rest >0.40	07	39	$p < 0.05$

The reduced thallium activity in the ventricular cavity and low C/M ratio seen in coronary disease patients with reduced left ventricular function is probably caused by several mechanisms. Impaired contractility results in reduced wall thickening and less spillover activity into the ventricular cavity (*11*). Focal perfusion defects in myocardial segments which surround or overlie the ventricular cavity will also reduce cavitary thallium activity (*9*). The left ventricle elongates and dilates in response to failing contractility (*12*). The enlarged left ventricle is filled with count-poor blood, decreasing the total activity in the center of the left ventricular cavity compared to myocardium.

The relative contribution of each of these mechanisms in causing a low C/M ratio in ventricular dysfunction probably varies among individual patients. In our series, only a minority of patients with a low C/M ratio and ventricular dysfunction had an electrocardiographic infarct and there was no difference in the number of patients with myocardial infarction in the low versus normal C/M groups. Previous attempts to assess left ventricular function by simply quantifying the size of resting thallium perfusion defects using planimetry, circumferential count profiles and polar maps have yielded only a loose correlation (*13,14*). These facts suggest that fixed perfusion de-

TABLE 4
L/H Ratio Versus Ejection Fraction

	LVEF		
	≤50%	>50%	
L/H ratio >0.45	24	17	$x^2 = 5.72$
L/H ratio ≤0.45	07	32	$p < 0.02$

Sensitivity of L/H ratio for ejection fraction ≤50% = 77%. Specificity of L/H ratio for ejection fraction >50% = 65%. Overall accuracy = 70%.

TABLE 5
C/M Exercise Ratio Versus L/H Ratio

	L/H >0.45	L/H ≤0.45	Total
C/M exercise ≤0.40	26	08	34
C/M exercise >0.40	15	31	46

Of 26 concordant and abnormal ratios, 21 were associated with a low ejection fraction. Of 31 concordant and normal ratios, 29 were associated with a normal ejection fraction. Of 23 mismatched results, the C/M exercise was correct in 5 of 8 results. Conversely, L/H ratio was correct in only 3 of the remaining 15.

fects in myocardium overlying the left ventricular cavity may not be the full explanation for the low cavitary counts and low C/M ratios we observed in our study population with reduced ejection fractions. The other mechanisms mentioned such as reduced systolic function and ventricular dilatation with an enlarged, count-poor, blood pool may play a significant role.

All the factors which tend to decrease cavitary count density as left ventricular dysfunction occurs would be accentuated by myocardial ischemia induced by exercise. This may explain our observation that the C/M exercise ratio is more sensitive than the C/M rest ratio for detecting patients with subnormal resting ejection fractions in our study group.

The correlation between C/M ratio and left ventricular function is not sufficiently close as to allow precise quantitation of the ejection fraction directly from the C/M ratio. This is not unexpected, since multiple factors can influence cavitary count density, as discussed above. Other causes for the variance in the correlation between ejection fraction and C/M ratio include the fact that scintigraphic and angiographic studies were separated by as much as 3 mo in some patients in this series. Although no cardiac event or invasive procedure occurred in any subject during this period, subclinical events may have occurred to alter left ventricular function or coronary perfusion in this interval. Varying body habitus and soft-tissue attenuation factors may influence the amount of Compton scatter in the thallium images and change the cavitary count density independent of left ventricular function.

Despite the appreciable variance in the relationship between the C/M ratio and ejection fraction, a C/M exercise ratio ≤0.40 correctly separated patients with normal versus abnormal ejection fractions with a diagnostic accuracy of 81%. The C/M ratio may thus represent an easily obtained measurement which integrates multiple factors that directly relate to ventricular performance and affect cavity count density in order to yield an approximation of overall ventricular function.

Increased lung thallium uptake is another scintigraphic parameter derived from perfusion imaging which has been used to identify patients with impaired left ventricular function (*15*). In this study, the C/M exercise ratio and the L/H ratio were concordant in predicting left ventricular function in 71% of patients and had similar sensitivities for detecting patients with abnormal ejection fractions. When the C/M ratio and lung thallium uptake were discordant, the C/M ratio was correct 74% of the time, particularly when LVEF was normal. The comparable sensitivities of the C/M ratio and lung thallium uptake and possible improved specificity of the C/M ratio suggest that these parameters could complement each other in screening for left ventricular dysfunction when reviewing thallium scintigrams.

The lower limit of normal for the C/M ratio may depend on the type of imaging equipment, acquisition parameters and reconstruction algorithms employed for thallium imaging. The techniques used in this study for tomographic thallium imaging and processing are similar to routine methodologies already widely employed (*7*). However, each nuclear cardiologic laboratory should establish its own normal limits for the C/M ratio by performing a scintigraphic/angiographic correlative study.

Since this series included only subjects with coronary artery disease and a group of subjects with normal catheterization findings, the applicability of these results to other forms of heart disease, such as cardiomyopathy or valvular disease, is not yet established.

CONCLUSION

This report introduces a new parameter, the C/M ratio, which is derived from routine tomographic thallium scintigraphy. The C/M ratio directly correlates with LVEF. An abnormally low C/M ratio can accurately identify coronary disease patients who have resting left ventricular dysfunction. Further work is needed to confirm these findings prospectively and to determine the ability of this ratio to assess left ventricular dysfunction in patients with other forms of heart disease.

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SELF-STUDY TEST

Pulmonary Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program 1*, published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of a heading followed by lettered options related to that heading. Select the one lettered option that is best for each item. Answers may be found on page 233.

For each scintigraphic pattern (items 1-5), select the most appropriate interpretation (answers A-E)

A. normal
B. low probability of pulmonary embolism
C. intermediate probability of pulmonary embolism
D. high probability of pulmonary embolism
E. additional information is necessary before interpretation

1. There are multiple, large, matching ventilation-perfusion abnormalities involving about 75% of the total lung volume. The chest radiograph shows no infiltrates, effusions, or atelectasis.

2. Perfusion is absent in the entire posterior basal segment of the left lower lobe. The chest radiograph and ventilation study are normal.

3. Perfusion defects involve all of the posterior basal segment and the superior segment of the right lower lobe. The chest radiograph shows only a very small infiltrate in the superior segment of the right lower lobe and the ventilation study is normal.

4. There are large perfusion defects in the superior segment and posterior basal segment of the right lower lobe. The ventilation study shows subtle washin abnormalities in these regions, but the washout phase is normal. A portable chest radiograph obtained 18 hours before the scintigrams shows a very small infiltrate in the superior segment of the right lower lobe.

5. There are matching ventilation and perfusion abnormalities in the anterior segment of the right upper lobe. The chest radiograph shows consolidation of the same segment

For each of the following situations (items 6-10), select the most appropriate estimate for the post-test probability of pulmonary embolism (answers A-E)

A. very high (>99%)
B. high (85%-98%)
C. moderate (16%-84%)
D. low (1%-15%)
E. very low (<1%)

6. An elderly woman experiences acute chest pain, shortness of breath, and tachypnea 3 days after undergoing surgery for a femoral neck fracture. Perfusion images show a large, wedge-shaped perfusion defect with a corresponding radiographic infiltrate.

7. A middle-aged man with mild chest pain has known coronary artery disease and classic clinical and radiographic findings of congestive heart failure. The ventilation-perfusion study is normal except for a washin ventilation defect and a perfusion defect corresponding to a large right pleural effusion.

8. Ventilation-perfusion scintigraphy is requested as part of a screening evaluation of a healthy kidney donor. The study is normal except for a single, medium-size perfusion defect.

9. A patient on hemodialysis for chronic renal failure has only minimal, vague respiratory complaints and a normal chest radiograph. A ventilation-perfusion study reveals two segmental perfusion defects and normal ventilation.

10. Four wedge-shaped, segmental, matching ventilation-perfusion defects are seen in a patient who has cancer and who has experienced the acute onset of pleuritic chest pain, dyspnea, and tachypnea 2 hours ago. The chest radiograph is normal.

For each patient profile (items 11-15), select the most closely associated functional description (answers A-E)

A. Increased alveolar compliance, increased airways resistance, regions of increased xenon clearance time.
B. Normal alveolar compliance, transiently increased airways resistance, decreased global xenon clearance time.

(continued on page 233)