Fourier Amplitude Ratio: A New Way to Assess Valvular Regurgitation

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The stroke-volume ratio determined from the equilibrium gated blood-pool study has been utilized to assess valvular regurgitation, but it is difficult to get reproducible results using generally available equipment. We have developed a new approach utilizing the Fourier amplitude ratio of the left and right ventricles, which is easily implemented and reproducible. Initial clinical experience shows that 17 patients with valvular regurgitation were clearly distinguished from 30 patients without valve disease.

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Patients with valvular insufficiency are often characterized by the regurgitant fraction (*1*). A reliable, noninvasive technique that would evaluate changes in regurgitant fraction in response to interventions would be desirable. Several groups (*2–7*) have used the ventricular stroke-count ratio from equilibrium gated blood-pool scans in assessing regurgitation, and Sorensen et al. (*8*) have calculated the regurgitant fraction from radionuclide angiography. Some of these studies were obtained using a slant-hole collimator, and others with a parallel-hole collimator. Gandsman et al. (*9*) compared the two techniques and found that the parallel-hole collimator gave results less reliable than those obtained with the slant-hole. Slant-hole collimators, however, are not generally available. Another problem with stroke-count ratios is the image overlap of the right atrium and ventricle (*10*), which makes it difficult to define accurately the right-ventricular region of interest.

From first-harmonic Fourier analysis of gated blood-pool scans, one can generate two functional images (*11,12*). These respectively provide pixel-by-pixel information on timing of contraction (the phase image) and the magnitude of count-density change during the cardiac cycle (the amplitude image). The phase image has been used to document asynchronous contraction patterns and areas of dyskinesis (*12,13*), and characteristic patterns in patients with left bundle branch block have been described (*14*). Little use, however, has been made of the amplitude image. Its principal role has been as an aid in defining the borders of the ventricles—especially in separating the right atrium from the right ventricle and defining the pulmonary-valve plane (*15*).

The present study was designed to evaluate whether the ratio of amplitude values of the left and right ventricles would distinguish patients with valvular insufficiency from normals. Because regional wall-motion abnormalities are reflected in the amplitude image (*12*), we included a group of coronary disease patients in the analysis.

METHODS

Patient population. This consisted of 47 patients undergoing gated cardiac blood-pool scanning for clinical indications. *Group 1* consisted of 14 subjects with normal left-ventricular function and no evidence of valvular disease by history or physical exam. Seven of these patients had atypical chest-pain syndrome, three of whom had normal results from cardiac catheterization and angiography. The other seven patients in Group 1 were starting on chemotherapy with doxorubicin, and baseline evaluations of left-ventricular function were being obtained. The mean left-ventricular ejection fraction in Group 1 was 60% (range 52 to 79).

Group 2 comprised 16 patients with clinically apparent coronary artery disease. All had abnormal re-

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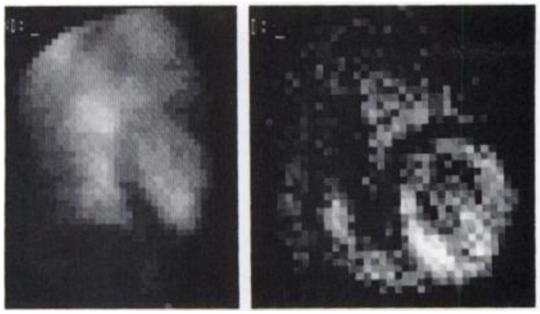

FIG. 1. Left panel shows a 40° left anterior oblique view of cardiac blood pool. Separation of chambers is difficult, as is precise determination of location of ventricular boundaries. Right panel shows the amplitude image generated from this study. Clear separation between atria and ventricles is evident.

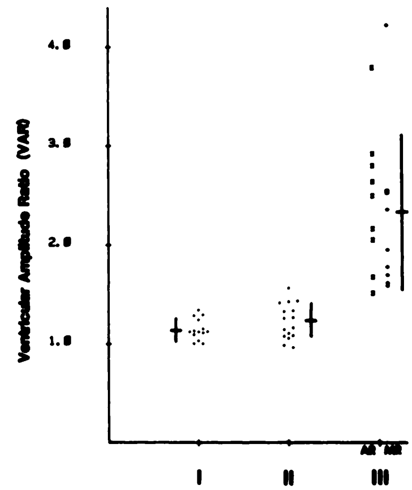

FIG. 3. Ventricular amplitude ratios (VAR) for our 47 patients, with mean and standard deviation for each group. Patients with valvular regurgitation (Group 3) include nine with aortic regurgitation (X), seven with mitral (◊), and one with combined valvular regurgitation (δ). Mean VAR in Group 3 is significantly higher than those in Groups 1 and 2.

gional wall motion by gated blood-pool scan (7 with hypokinesis, 6 with akinesis, and 3 with dyskinesis). The mean ejection fraction was 43% (range 32 to 69).

Group 3 included 17 patients with significant valvular regurgitation, characterized as "moderate" or "severe" at the time of cardiac catheterization. The catheterization preceded gated cardiac blood-pool scanning in all cases and the time intervals between catheterization and scanning ranged from two weeks to three years. There were nine patients with aortic regurgitation, seven with mitral, and one with combined aortic and mitral. Five of the patients were also enrolled in a research program to evaluate left-ventricular function in aortic regurgitation during exercise, but only the resting (pre-exercise) data were evaluated for the present study. Left-ventricular ejection fraction in Group 3 patients was 54% (range 18 to 94).

Data collection. Multigated equilibrium blood-pool scans were obtained after in vivo red-cell labeling with 20 mCi pertechnetate (Tc-99m), using an Anger camera equipped with a parallel-hole collimator. In 42 cases the 40° left anterior oblique study consisted of 24 frames spanning the entire cardiac cycle. In five cases the data were collected as part of an exercise study, and two separate 2-min resting data collections were obtained consisting of 18 frames spanning the cardiac cycle. Data were stored in a 64 × 64 matrix.

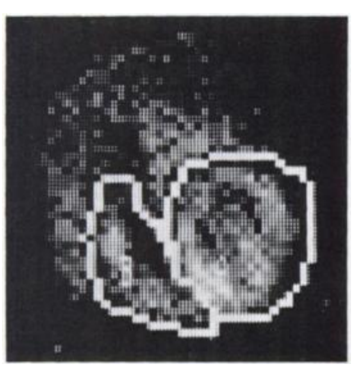

FIG. 2. Irregular regions of interest have been drawn around ventricular regions identified in Fig. 1B. Because the boundary areas have low values, inclusion of a few extra pixels in a ventricular ROI does not strongly affect amplitude value.

Data analysis. The analysis used a first-harmonic Fourier analysis program. The program establishes two 64 × 64 functional images containing the phase and amplitude data. From each pixel of the gated blood-pool study, a time-activity curve (TAC) is obtained and the first Fourier harmonic of this TAC provides an amplitude value and a phase-shift value; these are stored in the appropriate pixel location in the functional images.

Figure 1 shows the blood-pool and amplitude images obtained from a normal subject. In the amplitude image, the four cardiac chambers are clearly delineated as the four areas that have a significant amplitude. To generate a ventricular amplitude ratio (VAR), an irregular region of interest was drawn around each ventricle in the amplitude image (see Fig. 2). In cases where there were very low stroke counts (and low amplitude values), the regions of interest were drawn to approximate the configuration of the ventricles as noted on the blood-pool image. The regions of interest provided a total amplitude value for each ventricle. The ratio of these values, left ventricle to right, is the VAR.

Statistical analysis. Data were expressed as the mean ± standard deviation. Differences between groups were evaluated by analysis of variance. Reproducibility and subject variability were assessed using linear regression techniques.

RESULTS

The VARs for the 47 patients are plotted in Fig. 3. The mean VAR in Group 1 was 1.14 ± 0.11 (s.d.). This was not significantly different in Group 2 (1.22 ± 0.18). The mean VAR in Group 3 (2.31 ± 0.77) was signifi-

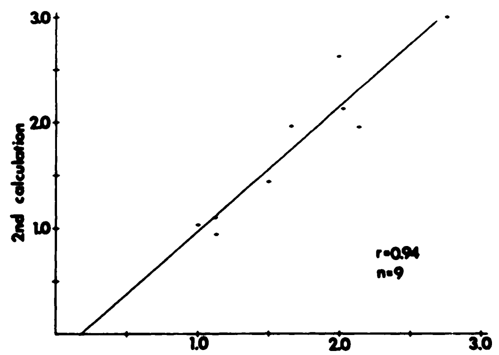

FIG. 4. Intra-observer variability results on basis of repeat calculations in nine subjects by the same observer.

cantly higher than in the other two groups ($p < 0.001$).

Intra-observer variability was evaluated by recalculating the VAR in the nine patients with aortic regurgitation (Fig. 4) and the results were found to be highly reproducible ($r = 0.94$, $p < 0.01$). Similarly, the VAR values were determined separately by two observers in 27 patients (9 from each group) and high inter-observer agreement was found ($r = 0.94$, $p < 0.01$). Subject variability was assessed in the five patients from Group 3 who had two sequential 2-min scans (Table 1). The VARs from sequential studies correlated closely ($r = 0.95$, $p < 0.05$).

DISCUSSION

Patients with valvular insufficiency may tolerate their disease for many years before requiring surgical correction (*16*). The usual method for characterizing the degree of regurgitation and impairment of left-ventricular function is cardiac catheterization, at which time the regurgitant fraction can be determined, based on the comparison of cardiac outputs measured by the Fick and angiographic techniques (*1*). However, cardiac catheterization does not lend itself to serial evaluation, so that the regurgitant fraction is often assessed at only one point in the natural history of the disease.

Radionuclide angiography, on the other hand, is a noninvasive technique that is ideally suited for serial studies. For this reason, several investigators have evaluated its utility in assessing valvular regurgitation (*2–9*). Most of these groups have characterized patients by the ratio of stroke counts, left ventricle to right. A number of different approaches have been employed: parallel-hole collimator with fixed (*2,4,5*) or variable (*7,8*) regions of interest around each ventricle; the slant-hole collimator (*3,9*), or the converging collimator (*6*). The mean stroke-volume ratio in normal subjects reported by these methods ranged from 1.07 to 1.34.

These approaches have limitations. In some cases, special equipment is required (e.g., slant-hole or converging collimators) which is not routinely available in all hospitals. The reason some groups have chosen to use the slant-hole collimator in this regard is that it appears to give more reliable data in normal subjects (*9*). This may be due to the difficulty of separating the right atrium from right ventricle, whose images may overlap considerably (*9,10*). In an effort to overcome this drawback, various groups have used functional images to assist in defining the ventricular regions of interest for blood-pool analysis (*5,9*). Despite this, Lam et al., using a parallel-hole collimator and regions of interest that were defined using functional images, have reported stroke-volume ratios greater than 2.0 in normal people (*5*).

TABLE 1. VAR REPRODUCIBILITY IN SEPARATE DATA COLLECTIONS

Patient	VAR 1st Study	VAR 2nd Study
1	2.02	1.99
2	2.16	2.24
3	2.12	2.62
4	2.46	2.84
5	3.75	3.80

First-harmonic Fourier analysis of gated blood-pool scans has recently generated considerable interest (*11–15*). The spatial distribution of phase (the phase image) has been utilized to assess patterns of ventricular emptying in a variety of disorders of contraction or conduction. The spatial distribution of amplitude (the amplitude image) generated from the same mathematical algorithm has been used less frequently. Adam et al. (*11*) have used the amplitude image to quantitate left-ventricular wall-motion abnormalities. Mena et al. (*15*) have pointed out that the atria, ventricles, and valve planes are clearly delineated on the amplitude image, which may facilitate analysis of blood-pool scans.

The amplitude image provides clear separation between atria and ventricles because pixels overlying a single cardiac chamber have large count-rate variations during the cardiac cycle, whereas pixels with significant overlap of atrium and ventricle have little net change in counting rate. Because of this apparent separation of chambers, we investigated whether *direct* analysis of the amplitude image could be used to assess valvular regurgitation. Since the amplitude value of a pixel is proportional to the stroke counts of the pixel, we reasoned that the total amplitude value of each ventricle would reflect its own stroke volume.

Although the right atrium and right ventricle can be clearly separated on the amplitude image, the projected overlap of the chambers is still present. The advantage of the VAR method lies not in avoiding chamber overlap, but in making the results less sensitive to the boundaries of the region of interest. It is because of atrioventricular overlap that this is necessary. This overlap, however, does cause the right-ventricular amplitude term to underestimate the right-ventricular stroke counts. This is why the normal VAR averages 1.14 rather than 1.00.

As shown in Fig. 3, the VAR in the 17 patients in Group 3 (valvular regurgitation) was significantly higher than in Group 1 (normals). This is similar to previously reported results of stroke-volume ratios (*2*,*3*). The high degree of intra-observer agreement (Fig. 4) probably reflects the relative insensitivity of the VAR method to the inclusion of additional (low-amplitude) pixels in the region of interest.

A potential limitation of this technique may exist in patients with ventricular dyskinesis. The dyskinetic region of a ventricle has amplitude values that do not reflect ejected blood (*11*). The basic assumption of our method—that total amplitude is proportional to stroke counts—is therefore not fulfilled. Akinesis should not pose a problem, since akinetic pixels have very low amplitude values (*11*). The Group 2 patients (coronary artery disease with abnormal wall motion) were included to determine how the VAR technique is affected by asynergy. Although Group 2 was a heterogeneous group (hypokinesis, akinesis, and dyskinesis), there was no significant difference in the VAR (Fig. 3). The VAR in the three Group 2 patients with dyskinesis averaged 1.34. Since dyskinesis is usually evident from either the movie display of the blood-pool study or from details of the phase image (*13*), situations with this potential drawback should be easily recognized.

In conclusion, the VAR derived from the amplitude image appears to provide a reliable means for identifying patients with valvular regurgitation. The advantages over stroke-volume ratio determination derive from the reproducibility and the relative insensitivity to small changes in the selection of regions of interest. This approach obviates the need for specialized collimators.

REFERENCES

1. Grossman W, Dexter L: Profiles in valvular heart disease. In *Cardiac catheterization and angiography.* Grossman W, Ed. Philadelphia, Lea & Febiger, pp 313-321, 1980
2. Rigo P, Alderson PO, Robertson RM, et al: Measurement of aortic and mitral regurgitation by gated cardiac blood pool scans. *Circulation* 60:306-312, 1979
3. Bough EW, Gandsman EJ, North DL, et al: Gated radionuclide angiographic evaluation of valve regurgitation. *Am J Cardiol* 46:423-428, 1980
4. Arquhart J, Patterson RE, Packer M, et al: Quantification of valve regurgitation by radionuclide angiography before and after valve replacement surgery. *Am J Cardiol* 47:287-291, 1981
5. Lam W, Pavel D, Byrom E, et al: Radionuclide regurgitant index: Value and limitations. *Am J Cardiol* 47:292-298, 1981
6. Thompson R, Ross I, Elmes R: Quantification of valvular regurgitation by cardiac gated blood pool imaging. *Br Heart J* 46:629-635, 1981
7. Manyari DE, Nolewajka AJ, Kostak WJ: Quantitative assessment of aortic valvular insufficiency by radionuclide angiography. *Chest* 81:170-176, 1982
8. Sorensen SG, O'Rourke RA, Chaudhuri TH: Noninvasive quantitation of valvular regurgitation by gated equilibrium radionuclide angiography. *Circulation* 62: 1089-1098, 1980
9. Gandsman EJ, North DL, Shulman RS, et al: Measurement of the ventricular stroke volume ratio by gated radionuclide angiography. *Radiology* 138:161-165, 1981
10. Maddahi J, Berman DS, Matsuoka DT: A new technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy. *Circulation* 60:581-589, 1979
11. Adam WE, Tarkowska A, Bitter F, et al: Equilibrium (gated) radionuclide ventriculography. *Cardiovasc Radiol* 2:161-173, 1979
12. Links JM, Douglass KH, Wagner HN: Patterns of ventricular emptying by Fourier analysis of gated blood pool studies. *J Nucl Med* 21:978-982, 1980
13. Botvinick E, Dunn R, Frais M, et al: The phase image: Its relationship to patterns of contraction and conduction. *Circulation* 65:551-560, 1982
14. Swiryn S, Pavel D, Byrom E, et al: Sequential regional phase mapping of radionuclide gated biventriculograms in patients with left bundle branch block. *Am Heart J* 102: 1000-1010, 1981
15. Mena I, Chelsy S, Carmody J, et al: Usefulness of phase analysis in cardiovascular nuclear medicine. *Clin Nucl Med* 5:S2, 1980 (abst)
16. Braunwald E: Valvular heart disease. In *Heart disease.* Braunwald E, Ed. Philadelphia, W.B. Saunders Company, pp 1113, 1141, 1980