Left Ventricular Regional Wall Motion Assessment by Radionuclide Ventriculography: A Comparison of Cine Display with Fourier Imaging

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Radionuclide ventriculography and contrast ventriculography were performed in two comparable projections on 50 patients with suspected coronary artery disease. The efficacy of conventional cine display and Fourier image analysis of the radionuclide ventriculogram was compared using contrast ventriculography as the gold standard. Of seven different combinations of Fourier images, the combination of left anterior oblique amplitude and phase and left posterior oblique amplitude and phase provided the highest sensitivity (87%), specificity (83%), accuracy (86%), and kappa coefficient (0.64). To increase statistical power, segment data were collapsed to global data in which a heart was considered normal if all segments were normal and abnormal if one or more segments were abnormal. Fourier images had higher sensitivity (Fourier 87%, cine 47%); lower specificity (Fourier 83%, cine 92%), higher accuracy (Fourier 86%, cine 58%), and higher kappa coefficient (Fourier 0.64, cine 0.25), and these differences were statistically significant ($p < 0.01$).

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Equilibrium-gated radionuclide ventriculography (*1*) is a standard noninvasive method for the evaluation of regional wall motion abnormalities (RWMA). The evaluation is usually performed subjectively by visual interpretation of an endless cinematic display of images of the cardiac cycle acquired by multiple gated acquisition. However, cine display suffers from several disadvantages: it ties the observer to a computer and to the inconvenience of a cumbersome archiving process and there is no hard copy. Various quantitative functional imaging techniques have been derived from the radionuclide ventriculogram to improve the assessment of RWMA and provide the advantage of hard copy. Of these techniques, the Fourier first harmonic amplitude and phase analysis (*2*) has several advantages over others: it does not require background subtraction; it uses data from the entire cardiac cycle and is therefore not dependent on frame selection; and it is unaffected by cardiac morphology, since it delineates functional borders (*3*). Despite these advantages, Fourier analysis has not been widely adopted for the detection of RWMA (*4*), and one authority has recently stated that "Fourier analysis of gated blood-pool data will never replace the subjective evaluation of the cinematically displayed data by an experienced observer" (*5*). Of the several possible reasons for this situation, the most important are the use of only one projection and the use of only the phase image by most authors. This study compares the efficacy of Fourier amplitude and phase images in two projections with cine display in two projections for the assessment of RWMA, using contrast ventriculography as the gold standard.

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METHODS

Patients

Fifty patients (49 men, 1 woman) had radionuclide ventriculography within 48 hr of biplane contrast ventriculography after coronary arteriography for suspected coronary artery disease. Three patients had entirely normal coronary arteries, 5 had single-vessel disease, 9 had two-vessel disease, and 33 had triple-vessel disease. Ten patients had conduction abnormalities: right bundle branch block, 5; first-degree atrioventricular block, 4; left bundle branch block, 1; the remaining 40 patients had no conduction abnormality. By contrast ventriculography, 38 patients had one or more regional wall abnormalities and 12 patients had none; 176 segments were abnormal and 324 were normal.

Radionuclide Ventriculography

After injection of 20–30 mCi of ^{99m}Tc-labeled human serum albumin, ECG-gated images of the supine patient at rest were obtained with a Picker Dynacamera 4/11 and a low-energy, all-purpose collimator. The camera was interfaced with an ADAC system IV-A computer with software version 2C. Each patient was imaged in a modified left anterior oblique (LAO) view, with the angulation adjusted for optimal ventricular separation. After acquisition of the LAO image, the patient was rotated 90° onto his right side: this orientation allowed data acquisition in the left posterior oblique (LPO) projection without moving the camera. For each view, 16 frames in a 64 × 64 matrix were acquired over the cardiac cycle, with a ±10% beat rejection window. Data were acquired until one pixel reached the maximum count of 255, resulting in approximately 500,000 counts per view in about 10 min. Two experienced operators obtained a left ventricular ejection fraction (LVEF), and the mean value was recorded. Each frame was smoothed spatially with a 3 × 3 matrix of equal weights.

Data Processing

After the spatial smoothing described above, the frames were smoothed temporally with a three-element filter of unequal weights (0.175, 0.150, 0.125) and the background was subtracted. The resulting images were then evaluated in a cine display in a 16-level gray scale.

Amplitude and phase images were created from first harmonic Fourier analysis of the spatially-smoothed images on a pixel-by-pixel basis (*6*). The value of each pixel in the amplitude image is proportional to the amplitude of the first harmonic of its corresponding pixel in the cine display, and the value of each pixel in the phase image is proportional to the relative phase or time delay of the maximum amplitude. Images were displayed with the 16-level rainbow color scale recommended by Pavel (*7*), in which each color level represents 6.25% of the maximum change in blood volume in the amplitude image and a 22.5° increment over the cyclic range from 0° to 360° in the R-R interval in the phase image. Four images were generated for each patient: LAO amplitude, LAO phase, LPO amplitude, and LPO phase.

Data Analysis

Two experienced cardiologists (SK, TW) independently graded RWMAs of the contrast ventriculogram without knowledge of the patient's clinical findings or the hemodynamic and angiographic results. The left ventricle wall was divided into 10 segments using the following standard nomenclature: LAO projection: basal septal (BS), apical septal (AS), inferolateral (IL), posterolateral (PL), superolateral (SL); RAO projection: anterobasal (AB), anterolateral (AL), apical (A), diaphragmatic (D), and posterobasal (PB). The standard five-point grading system (*8*) was used: 3 = normal, 2 = mild hypokinesis, 1 = moderate-to-severe hypokinesis, 0 = akinesis, and −1 = dyskinesis. Each observer evaluated RWMA in the 10 segments for all 50 patient studies twice, in random order, to obtain a measure of intraobserver variation. The average of these two scores was then determined for each observer; a mean score of more than 2 (2.1–3) was recorded as normal, and a mean score of 2 or less was recorded as abnormal. Segments in which the mean score for one observer was normal and for the other observer was abnormal were reexamined by both observers simultaneously for a final score by consensus. These values were then considered the gold standard with which two display methods of radionuclide ventriculography were compared.

Two observers, an experienced cardiologist (SK) and an experienced nuclear radiologist (CW), assessed both display methods. These observers were unaware of the patients' clinical findings or cardiac catheterization results but were aware of the LVEF. Knowledge of the LVEF in Fourier imaging is necessary in the assessment of RWMA because all pixels are scaled to the maximum amplitude and presented on a relative basis. When the LVEF is less than 35%, the region with the maximum amplitude is almost always hypokinetic and the other segments are even more hypokinetic, akinetic or dyskinetic; therefore, knowledge of the LVEF is essential in interpreting the amplitude and phase images. The same five-point grading system was also used for analysis of the Fourier images by a modification of the criteria of Alcan et al. (*9*), listed in Table 1.

Sensitivity, specificity, accuracy, and kappa coefficients (*10*) were used to compare the agreement of the two display methods with contrast ventriculography. The kappa coefficient determines the overall level of agreement, while correcting for the proportion of the agreement expected by chance. Kappa values range from −1 to +1, with −1 corresponding to perfect disagreement and +1 corresponding to perfect agreement. Negative values indicate poor agreement; the range 0.00–0.20 indicates slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00 almost-perfect to perfect agreement (*11*). Tests for significant differences between pairs of test methods were performed with McNemar's Test, using a chi-square approximation with correction (*12*).

RESULTS

Intraobserver Agreement

Intraobserver agreement was excellent for all imaging modalities with each observer agreeing with himself within

TABLE 1
Criteria for Fourier Amplitude and Phase Analysis

	Grade	Amplitude image*	Phase image†
3	Normal	Top eight levels (50%–100%)	0–1 level (<45°)
2	Mild hypokinesis	Next four levels (25%–50%)	2–3 levels (45°–90°)
1	Moderate-to-severe hypokinesis	Last four levels (0%–25%)	4–5 levels (90°–135°)
0	Akinesis	No amplitude (black pixels)	No phase (black pixels)
−1	Dyskinesis	Any level with markedly abnormal phase	More than five levels (>135°)

* Scale 1–16 levels; 0%–100% of maximum amplitude; 1 level = 6.25%.
† Scale 1–16 levels; 0°–360°; 1 level = 22.5°.

a 1.0 grading level in 90%–100% of the segments. Intraobserver agreement was also estimated by means of the kappa coefficient. For this calculation, the mean for each segment of each observer's two grades before consensus was assigned to one of two categories: normal (2.1–3) or abnormal (2 or less). The kappa coefficients determined from these two categories (Table 2) show that the two observers were in substantial-to-almost perfect agreement with themselves for all modalities.

Interobserver Agreement

The percent agreement between observers before consensus was determined for each segment and display method. Agreement within a 0.5 grading level ranged from 81% to 86% among segments and methods; within a 1.0 grading level, the percent agreement ranged from 94% to 96%. The mean of each observer's two grades for each segment before consensus was assigned to a normal or abnormal category for the determination of Kappa coefficients. The kappa coefficients showed substantial agreement (0.66) for contrast ventriculography, almost perfect agreement (0.92) for cine display, and moderate agreement (0.50) for Fourier images.

Determination of Optimum Combination of Fourier Images

To determine the optimum combinations of Fourier images, evaluations were carried out for each of the following images or combination of images: LAO phase, LAO amplitude, LAO phase and amplitude, LPO phase, LPO amplitude, LPO phase and amplitude, and LAO and LPO phase and amplitude. Images were randomly sorted between viewings and each combination was viewed twice before analysis. Agreement with contrast ventriculography between observers within a 0.5 grading level ranged from 54% to 84% (mean, 65%), and within a 1.0 grading level ranged from 70% to 100% (mean, 86%).

After coding segments as normal or abnormal and resolving disagreement between observers by consensus, each heart was categorized globally as normal when all segments were normal, and as abnormal when one or more segments were abnormal. Sensitivity, specificity, accuracy, and kappa coefficients were then calculated for each of the seven combinations of images (Table 3). For both projections, it was found that phase images when viewed alone had lower sensitivities and higher specificities than amplitude images viewed alone. However, when both phase and amplitude images in both projections were examined together, sensitivity, specificity, and accuracy ranged from 83% to 87%. Kappa coefficients from 0.28 to 0.38 for the first six combinations indicated fair agreement, while the kappa coefficient of 0.64 for the combination of all four images indicates substantial agreement.

TABLE 2
Kappa Coefficients for Intraobserver Agreement

	Observer 1	Observer 2
Contrast ventriculography	0.65	0.88
Cine display	0.80	0.88
Fourier images	0.79	0.84

TABLE 3
Evaluation of Fourier Images

	Sensitivity	Specificity	Accuracy	Kappa coefficient
LAO phase	50	83	62	0.28
LAO amplitude	81	56	72	0.38
LAO phase and amplitude	72	56	66	0.28
LPO phase	57	85	64	0.31
LPO amplitude	68	69	68	0.30
LPO phase and amplitude	73	69	72	0.36
LAO and LPO phase and amplitude	87	83	86	0.64

In the LAO projection, comparison by McNemar's test of the phase image alone with the amplitude and phase images together indicated that out of 50 patients 14 diagnoses disagreed with the reference standard (eight favoring the conclusion that the LAO amplitude and phase images together are better than the LAO phase image alone and six favoring the conclusion that the LAO phase image alone is better than the LAO amplitude and phase images together), with a resultant χ_c^2 value of 0.07 ($p > 0.25$). In the LPO projection, comparison of the phase image alone with the amplitude and phase images together showed that 12 diagnoses disagreed with the reference standard (eight in favor of the LPO amplitude and phase images together and four favoring the LPO phase image alone), with a corresponding χ_c^2 of 0.75 ($p > 0.20$). Although these results are not statistically significant, due to a lack of power for small sample sizes, they do indicate that in our sample the use of amplitude and phase images together provided more accurate diagnoses, when compared with only the phase image alone.

Regional Wall Motion Analysis

After determining that the optimum combination of Fourier images was both phase and amplitude images in both LAO and LPO projections, the two radionuclide ventriculography test methods were then compared for the diagnosis of wall motion abnormalities in each of five segments in both LAO and LPO projections. The percent agreement within the 0.5 level and within the 1.0 level with contrast ventriculography is listed in Table 4. The results of the statistical analysis for the 10 segments are listed in Table 5. On a segmental basis, the results were not statistically significant at the 95% confidence level. This nonsignificance was due to a lack of power because of the small number of cases in which pairs of methods disagreed. Although the agreement measured by the kappa coefficient ranged from slight to substantial, depending on the segment, the total number of disagreements was much

TABLE 4
Percent Agreement with Contrast Ventriculography After Consensus

	LAO					LPO					
	BS	AS	IL	PL	SL	AB	AL	A	D	PB	Mean
Cine display											
0.5 level	56	62	54	74	86	88	64	58	58	60	66
1.0 level	82	80	72	94	98	94	80	82	86	80	85
Fourier images											
0.5 level	64	58	60	78	78	78	60	60	58	56	65
1.0 level	86	86	80	96	94	100	84	76	88	84	88

smaller in the comparison of each individual segment with the global wall motion; however, they were consistently in favor of the Fourier method.

Global Wall Motion Analysis

For each case, the presence of one or more RWMA indicated that the left ventricle could be considered abnormal; therefore, only when all segments were normal was the heart considered normal. Sensitivity, specificity, accuracy, the kappa coefficient, and McNemar's test statistics are presented in Table 6 for the left ventricle considered as a whole. Out of 50 patients, cine display and Fourier images disagreed in their diagnoses in 16 cases (15 favoring the conclusion that the Fourier method is better and 1 favoring the conclusion that cine display is better), with a resultant χ_c^2 value of 10.56 ($p < 0.01$). This significance at a 99% level of confidence indicates that Fourier imaging is superior to cine display. The kappa coefficients were 0.25 for cine display and 0.64 for Fourier images. As a kappa coefficient greater than 0.61 is considered to reflect substantial agreement, these results show that the Fourier method is in substantial agreement with the reference standard, whereas cine display is only in fair agreement with contrast ventriculography.

TABLE 6
Global Wall Motion Analysis

	Cine display	Fourier images
Sensitivity (%)	47	87
Specificity (%)	92	83
Accuracy (%)	58	86
Kappa coefficient	0.25	0.64
McNemar's statistic	10.56 (p < 0.01)	

DISCUSSION

The generally accepted gold standard for assessment of RWMA by radionuclide ventriculography is contrast ventriculography. However, there are several factors that may cause differences between RWMA determinations by the two methods:

1. Interobserver variability exists in both procedures.
2. There is inferior resolution of radionuclide ventriculography compared to contrast ventriculography.
3. Displays of the radionuclide ventriculogram encompass the entire blood pool, so that in some projections activity in the right ventricle and great vessels obscures left ventricular activity.
4. The heart is usually imaged in somewhat different projections in the two methods.
5. Different loading conditions of the heart in the two methods may affect regional wall motion as well as global function; and during contraction the heart

TABLE 5
Evaluation of Test Methods by Segment Analysis

	BS	AS	IL	PL	SL	AB	AL	A	D	PB	Mean
Sensitivity (%)											
Cine display	24	55	48	62	43	40	54	64	38	27	46
Fourier images	81	60	48	69	43	20	63	59	57	59	56
Specificity (%)											
Cine display	79	90	76	84	91	93	89	86	79	96	86
Fourier images	69	83	86	89	84	84	96	89	76	71	83
Accuracy (%)											
Cine display	56	76	64	78	84	88	72	76	62	66	72
Fourier images	74	74	70	84	78	78	80	76	68	66	75
Kappa Coefficient											
Cine display	0.03	0.47	0.24	0.44	0.34	0.33	0.43	0.50	0.18	0.26	0.32
Fourier images	0.48	0.44	0.35	0.58	0.23	0.04	0.59	0.50	0.33	0.31	0.39
McNemar's χ_c^2 Statistic*											
Cine display vs. Fourier images	3.76	0.00	0.80	0.31	0.44	1.78	1.50	0.17	0.36	0.06	

* None of the χ_c^2 values in this table are significant ($p > 0.05$).

may undergo rotational and translational motion so that changes in a given location may not correspond exactly to the same anatomical segment.

In spite of these factors, the correlation between the two methods for the assessment of RWMA has been high (*13*, *14*). The most detailed study of the accuracy of RWMA by cine display using contrast ventriculography as the gold standard is that of Okada et al. (*14*). They found that regional wall motion scores agreed within a 0.5 grade in 64% of segments and within a 1.0 grade in 84% of segments. Our results of 66% and 85%, respectively, are in excellent agreement with theirs. We conclude that despite the differences between the two methods, contrast ventriculography is the only practical gold standard against which cine display and Fourier images can be compared.

There are only a few reports in which Fourier images have been compared to contrast ventriculography as the gold standard. Walton et al. (*15*) compared RWMA detected by LAO phase images with RWMA assessed by an LAO projection of the contrast ventriculogram. They found an overall good correlation for location and severity of RWMA but did not determine sensitivity, specificity, accuracy, or Kappa coefficients. Pavel et al. (*16*) compared RWMA detected by qualitative assessment of the LAO projection of the contrast ventriculogram with quantitative assessment of the LAO phase images. However, they measured only the inferolateral and posterolateral segments of the left ventricular wall. In this analysis, they were able to distinguish normal from abnormal segments with a sensitivity of 83%, specificity of 94%, and accuracy of 89%. Our results for amplitude and phase image analysis for all segments are less impressive on a segmental basis (Table 4) but are comparable with these figures on a global basis.

It has long been standard practice to evaluate the cine display of the radionuclide ventriculogram in at least two projections. The reason for this practice is that RWMA of the inferior wall cannot be evaluated adequately with the conventional best septal LAO projection, because the apical segment overlaps the inferior wall. Several groups have shown that the sensitivity of detection of inferior wall RWMA can be significantly increased by adding the steep LAO (*17*) or left lateral (*18*) projection to the standard best septal LAO projection. Although this problem was recognized by Adam in his original publication (*2*) on Fourier image analysis, he did not incorporate a lateral projection in subsequent studies. In a recent publication (*19*), Adam analyzed LAO amplitude and phase images in 24 patients with previously documented myocardial infarctions. In six patients in which both amplitude and phase images were normal, the scar tissue was located in the inferior wall. Inferior wall abnormalities could be identified by visual inspection of the cine display of a left lateral projection in three of the five patients in which the projection was employed, but Fourier analysis was not used because "this additional left lateral projection does not lend itself to meaningful quantitative amplitude and phase analysis because of overprojection of adjacent cardiac structure." Presumably for this reason, the single LAO projection alone has been employed in almost all of the studies of Fourier analysis of the radionuclide ventriculogram.

Akins et al. (*6*) have recently shown that, contrary to Adams, the lateral projection is amenable to Fourier amplitude and phase analysis. The left atrium is clearly distinguished from the left ventricle by the plane of the mitral valve in both amplitude and phase images of the heart in the LPO projection. As a result, the anterobasal and posterobasal segments of the left ventricle are seen clearly in Fourier amplitude and phase images, while in cine display, these segments are partially obscured by noncyclic radioactivity in the left atrium, pulmonary arteries, aorta, vena cavae, and pulmonary veins. It is true that some radioactivity in the right ventricle is detected in the field of view of the left ventricle, but in the LPO projection, the right ventricle is on the opposite side of the left ventricle from the camera face. Thus, the smaller volume of the right ventricle as compared to the left, the inverse square law, and the attenuation through the left ventricle together reduce the contribution of the right ventricular blood-pool activity seen by the detector in the LPO projection to a small fraction of the activity from the left ventricle. Therefore, although the right ventricular blood-pool activity is theoretically capable of obscuring left ventricular RWMA in the LPO projection, this study demonstrates that the accuracy of detection of inferior wall RWMA by use of the LPO projection is as good with Fourier imaging as it is with cine display. Maximum accuracy for detection of RWMA by cine display analysis of the radionuclide ventriculogram is obtained by observation of the heart in at least two projections. This study conclusively demonstrates that maximum accuracy for detection of RWMA by Fourier analysis also requires two projections.

Another reason that Fourier analysis has not achieved widespread use is the failure to use the amplitude image in concert with the phase image. Fourier analysis results in the simultaneous generation of two functional images (amplitude and phase) by the same algorithm. Phase abnormalities may represent either conduction abnormalities or contraction abnormalities (*20*). It is therefore essential to interpret the phase image in conjunction with the amplitude image, because a ventricular region with delayed activation (phase delay) represents a contraction abnormality (regional wall motion abnormality) only if it is coupled with decreased amplitude at the same location. Although the importance of using the amplitude image in conjunction with the phase image has been emphasized by several authors (*3*, *9*, *20*, *21*), others have ignored the amplitude image in their analyses (*22–24*). This study demonstrates that the amplitude image must be viewed together with the phase image to achieve maximum accuracy in the diagnosis of RWMA by Fourier imaging.

In summary, the use of both amplitude and phase images in both LAO and LPO projections provides maximum accuracy of diagnosis of RWMA. This is because inferior wall lesions can be missed in an LAO projection alone, septal or lateral wall lesions can be missed in an LPO projection alone, and conduction abnormalities may be mistaken for contraction abnormalities when a phase image alone is used. In clinical practice, creation of the four Fourier images with existing software requires only about 10 additional minutes of technologist time. Because the accuracy of Fourier analysis is equal to cine display on a segmental basis and is significantly better on a global basis, and because of the rapidity with which the diagnosis can be made and the convenience with which the images can be viewed, archived, and retrieved, we have employed Fourier image analysis rather than cine display for the routine clinical interpretation of the radionuclide ventriculogram for the past 4 yr.

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EDITORIAL

Radionuclide Ventriculography: Should Fourier Analysis Replace the Cine Display?

Nuclear cardiology was, for all practical purposes, born 20 years ago with the description of the radionuclide ventriculogram, a "noninvasive scintophotographic method for measuring left ventricular function in man" (*1,2*). The first studies consisted of only end-diastolic and end-systolic images, but nevertheless permitted evaluation of left ventricular ejection fraction and regional wall motion using manually drawn outlines of the left ventricle and area-length methods. Subsequent application of computer technology has led to the development of multi-image gated studies, easy storage and retrieval of digitized images, semi- or fully-automated methods for detecting left ventricular edges, and count-based methods for measuring left ventricular ejection fraction and other functional parameters, such as left ventricular ejection and filling rates. Increased quantitation provided by the application of computers has been universally recognized as an impor-

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