Evaluation of Left Ventricular Function (Ejection Fraction and Segmental Wall Motion) by Single Pass Radioisotope Angiography

JAMES A. JENGO, M.D., ISMAEL MENA, M.D., ARNOLD BLAUFUSS, M.D., AND J. M. CRILEY, M.D.

SUMMARY Changes in ejection fraction (EF) and segmental wall motion (SWM) have been shown to be sensitive indicators of left ventricular (LV) function. This information is only obtainable by contrast angiography or gated blood pool scans. Gated studies assume a fixed geometry for the LV for EF determinations, are lengthy and limited primarily to the LAO projection. We correlated contrast and Tc-99m pertechnetate angiograms by single pass radioisotope angiography (immediately preceding the contrast study) in 12 patients. EF was calculated from the LV time/activity curve and values ranged from .21 to .72. Angiographic correlation yielded r = 0.97. Regional LV wall motion was evaluated by dividing a summated cardiac cycle into 16 frames and dynamically and sequentially displaying these frames. Regional wall motion evaluation of four LV quadrants correlated well with angiography (r = 0.97). For quantitation these images were divided into four anterior and four inferior segments and the areas of respective segments were compared and expressed as a shortening fraction. SWM compared favorably with angiographic determinations (r ranged from 0.70 to 0.99). Thus, single pass radioisotopic determinations of EF and SWM in the RAO projection correlate well with the angiographic values and provide essential quantitative information on LV function otherwise unobtainable at the bedside.

THE ABILITY TO monitor hemodynamics in a critically ill patient, at the bedside, has increased our understanding of the pathophysiology of heart disease and the effects of therapeutic interventions on myocardial performance. Indices of left ventricular function which are usually measured include pulmonary artery wedge pressure, arterial pressure and cardiac output.1 However, none of these parameters are dependent entirely upon the absolute level of left ventricular function. They are affected by changes in ventricular compliance and/or fluctuations of the central volume. Therefore, measurements of these parameters of left ventricular function are often confusing and may even be misleading.

Ejection fraction has been reported to be a sensitive indicator of left ventricular function2 but it can also be misleading since it varies with changes in both afterload and preload, independent of changes in left ventricular function.3 Segmental wall motion has been shown to be one of the most sensitive indicators of left ventricular function4 but until recently has only been obtainable during cardiac catheterization.

Gated cardiac blood pool scans have been shown to be useful in determining ejection fraction and qualitatively evaluating regional wall motion.5-10 These studies are limited by assuming a fixed geometry for the left ventricular ejection fraction calculation, and by requiring lengthy acquisition times and a stable cardiac rhythm. They also are limited primarily to the left anterior oblique projection. The technique of single pass radioisotope angiography provides rapid bedside determination of ejection fraction and quantitation of segmental wall motion in the critically ill patient.

Methods and Materials

Twelve patients, age 27 to 67 (mean 51) years, were studied. Three patients had valvular heart disease, and nine patients had symptomatic coronary artery disease. All patients required cardiac catheterization for diagnosis and evaluation of coronary artery disease and/or evaluation of myocardial function.

The studies were performed in the cardiac catheterization laboratory. Using standard techniques a Swan-Ganz catheter was positioned in the right pulmonary artery and another catheter in the body of the left ventricle. The patient was placed in the 30° right anterior oblique projection. Twenty-five milliliter of Technetium-99m (2 ml of sodium pertechnetate) was placed in an extension tube connected to the distal lumen of the Swan-Ganz catheter. Ten milliliters of 5% dextrose solution was then rapidly injected through the extension tubing to achieve a bolus injection of the Tc-99m pertechnetate.

Imaging was accomplished using an Ohio Nuclear por-
table scintillation camera (series 120) equipped with a low energy high resolution parallel hole collimator. Data were recorded onto one-half inch magnetic tape at a speed of 50 inches per second, resulting in a data density of approximately 30,000 counts per second. The data were acquired for 30 seconds and then the scintillation camera was removed and a contrast left ventriculogram performed without changing the position of the patient. The contrast ventriculogram was performed at a filming speed of 60 frames per second no more than 3-5 minutes after completion of the radioisotope angiogram.

**FIGURE 2.** Radioactivity (y axis) vs. time (40 msec units) graph from the true left ventricular region of interest. Five full cardiac cycles can be seen where the peaks represent end-diastolic radioactivity and the valleys represent end systole.

**FIGURE 3.** Left ventricular volume curve with radioactivity (y axis) plotted for the 16 frames making up the composite cardiac cycle. The first frame of highest activity corresponds to end diastole, proceeding through systole to end systole which is represented as the frame with the lowest activity.

**Data Analysis**

The raw data were then transferred from magnetic tape to a digital computer (Informatek SIMIS-3) and stored on the disc in list (event-to-event) mode. The list mode acquisition was then summed and the resulting composite image displayed on the computer's television monitor in an interpolated 512 × 512 matrix. A region of interest was then defined encompassing the approximate area of the left ventricle using a keyboard controlled light pen. From this region of interest a preliminary time-activity curve was generated. The unit of time was 40 msec. Since changes in count rate represent changes in ventricular volume the peaks, or points of highest activity, represent the time of the largest blood volumes, that is, end diastole. The frames corresponding to the peaks from four successive cardiac cycles are then added together to yield a composite end-diastolic image which is displayed on the television monitor. Sequential isocount contours are automatically and sequentially generated and displayed superimposed on the end-diastolic image (fig. 1). An indentation or "pinch" results from this technique and corresponds to an interface or area of low activity between two areas of high activity. This indentation correlates well with the anatomic location of the aortic valve. A new "true" region of interest is then manually drawn through the level of the aortic valve to surround the area of the left ventricle. The plane of the mitral valve is approximated by extending the region of interest straight down from the right border of the aorta to the inferobasilar border of the left ventricle. The true left ventricular time-activity curve (40 msec time unit) is then plotted and displayed (fig. 2). The ejection fraction is then computed using the technique of sinusoidal analysis. Using this method no correction for background activity need be made since by injecting the radioisotope into the right pulmonary artery with the patient in the RAO projection, no activity appears in the right heart or left lung and therefore there is no background radioactivity surrounding or overlying the left ventricle.
In order to evaluate left ventricular wall motion each of four successive cardiac cycles is divided into 16 frames and the corresponding frames of each cycle are added together to yield one summated or composite cardiac cycle. The radioactivity from the left ventricular region of interest from each of the 16 frames is sequentially plotted, yielding a time-activity curve for one cardiac cycle, that is, a left ventricular volume curve (fig. 3). The highest activity corresponds to the end-diastolic volume and the lowest activity to the end-systolic volume. The highest and lowest points are then
selected by the computer as representing end-diastole and end-systole. The true end-diastolic image thus obtained is displayed on the television monitor in a 512 × 512 matrix. A color scale (242 levels) and isocounts are used to define the level of the aortic valve and the approximate contour of the ventricle. A region of interest is then drawn through the aortic valve plane to encompass the region of the left ventricle. A chimney-like projection is drawn over the aortic valve plane such that the two “break points” correspond to an isocount width of the aortic valve. Next, the end-systolic image is processed in the same manner taking care to redefine the level of the aortic valve during end-systole (figure 4a). Since the heart moves in the thorax with each contraction, it is important to define carefully the level of the aortic valve during diastole and during systole, that is, not to assume that the level of the aortic valve remains the same during the entire cardiac cycle.

The edge of the ventricle is then found for the area enclosed within these regions of interest. The technique consists of finding the second derivative of the matrix in two dimensions and displaying these points with all others set to 0.

Regional wall motion can then be qualitatively assessed in two ways. First, the end-diastolic and end-systolic outlines can be superimposed on the television monitor yielding the familiar image of wall motion (fig. 4b). Regional wall motion is assessed by dividing the RAO silhouette into four regions: anterobasal, anteroapical, inferoapical and posterobasal. Wall motion in these segments is compared with that of the angiographic image and rated as normal, hypokinet1c, akinetic or dyskinetic. Independent observations from three observers were used in evaluating 48 segments from the 12 patients.

For dynamic evaluation of regional wall motion, the 16 frames or images of the summated cardiac cycle are then rapidly and sequentially displayed producing a cine display (fig. 5). The true edge of each of these 16 sequential frames can be highlighted and the observer thus obtain a cine image of the “beating edge” of the ventricle.

Quantitation of left ventricular segmental wall motion is then accomplished. The long axis of the ventricle for end diastole and end systole is computed by connecting the midpoint of the aortic width (the “break points” of the chimney-like projection) to the apex of the ventricle. The long axis is then quadrisected, yielding eight segments (four anterior and four inferior) (fig. 6). This process is carried out separately for the end-diastolic and end-systolic images. The area of each of the eight segments is then determined for end diastole and end systole and the difference in areas is expressed as percent contraction. The same technique is used for analysis of the contrast-angiographically determined images.

In order to assess the reproducibility of the technique, six sequential first pass radioisotope angiograms were performed at two minute intervals in each of five patients using the radioisotope Krypton-81m. The technique was similar to the preceding with the exception that a catheter was first placed in the left atrium via the transatrial septal route and the Krypton injected into the left atrium.

Krypton-81m is an ultrashort-lived radioisotope, the product of the decay of Rubidium-81. Krypton-81m has a half-life of 13 seconds thereby making repeat isotope angiograms possible within two minutes after the initial injection. The administration was carried out in the following manner: A specially designed generator was made consisting of 40 mCi of Rubidium-81 adsorbed onto an ion exchange column in series with a second isotope-free ion exchange column. These two columns were housed within a lead container with 4 Fr entrance and exit tubes attached to stopcocks. The system was purged free of air with a 5% solution of dextrose in water and connected in series to the left atrial catheter. At the time of injection approximately 2 ml of the 5% dextrose solution was flushed through the generator into the left atrial catheter and then the resulting activity in the catheter flushed into the patient’s left atrium with a bolus of 5% dextrose solution. The acquisition and processing of the data were handled the same as for the Technetium-99m studies.

The student’s t-test for paired data, the two-sample rank test and standard regression analysis for calculating correlation coefficients were used for statistical analysis.

### Results

#### Ejection Fraction

The results of ejection fraction determinations in the 12 patients are listed in table 1. These results are compared to ejection fractions determined from the RAO cineventriculogram in figure 7. Ejection fractions varied from 21% to 72% and the correlation between the two techniques was good ($r = 0.97$). The slope of the regression line was 0.81 compared to the ideal value of 1.00.

### Table 1. Ejection Fraction Determination

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Regional Wall Motion

Results of qualitative assessment of regional wall motion are listed in table 2. The rank correlation with contrast angiography for the two techniques is excellent. Examples of the correlation of the two techniques can be seen in figures 8 and 9.

Segmental Wall Motion

The results of quantitative wall motion analysis are listed in table 3. The comparison of segmental wall motion for segments 2 through 7 revealed good correlation (r ranging from 0.70 to 0.99) and is plotted in figure 10. Poor correlation was found for segments 1 and 8, which can be explained by the artificial "hand-drawn" superior border for those segments made when the region of interest is drawn through the aortic valve plane. The fact that the left atrium occupies a variable portion of segment number 8 also affected the correlation.

There is good general correlation throughout the entire range of segmental wall motion: from −1% to +62% contractility with areas of dyskinesis being represented as well as areas of hyperkinesis.

Reproducibility

Determinations in five patients in each of whom six sequential studies were performed showed good reproducibility with a mean standard deviation of 2.0%. These data are listed in table 4.

Discussion

Hemodynamic monitoring at the bedside has increased our understanding of the pathophysiology of heart disease and allowed us to make objective measurements of cardiac function before and after therapeutic interventions. However, the conventional measures of left ventricular function do not purely reflect pump function but are affected by other factors such as central volume status and left ventricular compliance.

Ejection fraction is a sensitive indicator of left ventricular function but can only be determined accurately by contrast ventriculography or, more recently, gated cardiac blood pool scans. However, even ejection fraction may not faithfully reflect changes in ventricular function during ongoing ischemia (affected by both afterload and preload) nor may ejection fraction reflect the decreased ventricular function in a scarred ventricle when there is compensatory hypercontractility of the remaining viable myocardium.

Therefore, it is necessary to measure segmental wall motion in addition to ejection fraction and the hemodynamic parameters of left ventricular function. Changes in segmental wall motion have been shown to be sensitive indicators of ischemia and, conversely, show the return of contractility upon reversal of ischemia. Thus, besides augmenting the previous measures of left ventricular function, segmental wall motion has been found to be a better indicator of postinfarction remodeling.

**Figure 7.** Comparison of ejection fractions determined by contrast angiography and single pass radioisotope angiography. Regression equation: \( y = 0.81x + 0.06 \).

**Figure 8.** Comparison of regional wall motion by isotope angiography and contrast angiography. Uniform wall motion is seen throughout the entire cardiac silhouette by both techniques.

**Figure 9.** Comparison of regional wall motion by isotope angiography and contrast angiography. Both techniques revealed diffuse hypokinesis in this patient with severe triple vessel coronary artery disease.
TABLE 3. Segmental Wall Motion Determinations (% Contraction)

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Abbreviations: Isot = isotope angiogram; Cntst = contrast angiogram.

FIGURE 10. Comparison of segmental wall motion (percent segmental contractility) for isotope angiography on the y axis and contrast angiography.

wall motion, in itself, is a powerful indicator of regional myocardial function.

There have been no previous reports on the quantitation of segmental wall motion (percent contractility) using single pass radioisotope angiography. This technique has shown excellent qualitative and quantitative correlation and reproducibility in the evaluation of segmental wall motion.

With the advances being made in the treatment of acute myocardial infarction with therapeutic modalities that are potentially deleterious, the need for fast, accurate and reproducible evaluations of left ventricular function at the bedside is obvious.

Single pass radioisotope angiography is easily performed, rapid (requiring only 30 seconds of data acquisition), does not alter left ventricular function and can be performed in any projection. If a radioisotope with a short biological half-life is used (for example 99m-Technetium-DTPA) studies can be repeated after 2-3 hours.

This technique correlates well with contrast angiographic determinations of ejection fraction and segmental wall motion and allows for serial determinations of left ventricular function, and therefore is especially applicable to evaluating

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Mean ± sd
.48 ± 0.01 .37 ± 0.02 .57 ± 0.01 .24 ± 0.03 .72 ± 0.03

Mean standard deviation: 2.0%.
Mean coefficient of variation: 5.6%.
critically ill patients and can be incorporated into the management of these patients in an intensive care unit setting.

Acknowledgment

We gratefully acknowledge the technical expertise given by Dr. Thomas Nelson and Mr. Sheldon Chelsy and the secretarial assistance of Mrs. Ann Lubahn and Ms. Joy Morgridge.

References


Early Redistribution of Thallium-201 after Temporary Ischemia

JEFFREY S. SCHWARTZ, M.D., RICHARD PONTO, B.S., PETER CARLYLE, B.S., LEE FORSTROM, M.D., AND JAY N. COHN, M.D.

SUMMARY To define the time course of redistribution of thallium-201 (201TI), ischemia was induced in seven pigs by temporary occlusion of the circumflex coronary artery. After 1½ min of occlusion 201TI and labeled microspheres were injected into the left atrium. Flow was re-established 4 min after occlusion. Prior to reflow, the relative activities of 201TI and microspheres in the ischemic area were similar, but as early as 5 min after reflow the relative 201TI activity was considerably higher than the relative microsphere activity (average 6% of normal). Myocardial arteriovenous differences for 201TI were followed sequentially after 201TI injection in normal dogs and in dogs with temporary coronary occlusions. The results suggested both loss of 201TI from normal myocardium beginning 10 min after 201TI injection and increased extraction of 201TI from the blood pool immediately after release of a transient occlusion. Redistribution of 201TI therefore begins very soon after relief of myocardial ischemia and even a short delay in initiating myocardial imaging may decrease the sensitivity of the technique for detecting transient ischemia.

BECAUSE OF ITS FAVORABLE PHYSICAL AND BIOLOGIC PROPERTIES 201TI appears to be the best myocardial perfusion imaging agent presently available for intravenous use. Resting 201TI images have been used for the detection of myocardial infarction, and stress images have been used for the detection of myocardial ischemia. The initial distribution of 201TI has been shown to reflect regional myocardial perfusion. There has been recent clinical evidence, however, that a perfusion defect on a stress image fills in over several hours.

Redistribution has also been demonstrated clinically in patients with variant angina. Thallium-201 injected during angina resulted in large defects in images performed within 10–20 min of injection. Two or three hours later, after relief of angina, the defects had filled in. Redistribution has been studied in the experimental animal by occluding coronary arteries of dogs for 20 min during which 201TI and labeled microspheres were injected into the left atrium. After 100 min of reperfusion, the relative 201TI activity in the previously ischemic area was significantly higher than the microsphere activity indicating that redistribution of the 201TI had occurred.

The present study was undertaken to better define the time course and mechanism of 201TI redistribution. The pig was used as an experimental animal in the initial portion of this study because it has a less extensive and less variable collateral circulation than the dog.
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