Assessment of Ventricular Function in Coronary Artery Disease Using Nitroglycerin and Computerized Analysis of Left Ventriculograms

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ABSTRACT The ability to predict if abnormalities in regional wall motion are reversible would assist in selecting patients for aortocoronary bypass operation. This study shows that asynergic areas of the ventricle may be reversed by nitroglycerin. Thirty-four asynergic areas in 30 patients with coronary artery disease were studied before and after administration of nitroglycerin. Nineteen patients with previous infarction, diagnostic Q waves in their electrocardiogram, and akinetic areas in the left ventricle had no change in their akinetic areas after nitroglycerin administration. Nine of these patients did show increased motion in other hypokinetic areas of the myocardium. Five of 11 patients with no evidence of previous infarction showed a dramatic improvement in akinetic areas after nitroglycerin, while of the remaining 6, 5 showed mild improvement. This illustrates that recoverable asynergic areas may be recognized by nitroglycerin.

Abnormalities in regional wall motion are not uniformly improved following aortocoronary bypass operation [1, 2, 7]. This may be due in part to the inability to predict whether asynergic areas in the left ventricular wall are composed of irreversibly damaged tissue or of ischemic but viable muscle. Since areas of asynergy may have pronounced influence on left ventricular function, it is important to differentiate reversible from irreversible asynergy. Such information would help in patient selection for bypass operation.

Recent studies have shown that administration of nitroglycerin will improve or totally correct asynergic areas of left ventricular myocardium in some patients with coronary artery disease [5, 6, 8]. This study reports our experience with changes in left ventricular contractility produced by nitroglycerin and relates these changes to available clinical data and operative findings in those patients who have undergone operation. We found, too, that additional information is gained by using computerized analysis of left ventriculograms to quantitatively describe ventricular function.

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Methods

The patients studied were those routinely scheduled for selective coronary arteriograms with ventriculographic analysis carried out prior to the selective coronary examinations. All patients studied with nitroglycerin had obstructive coronary artery disease with abnormal ventriculograms. Patients with valvular heart disease or other cardiovascular defects were excluded from this study. The series includes 41 patients ranging in age from 44 to 68 years. Each patient was premedicated with amytal sodium (200 to 300 mg, depending on weight). Using the transfemoral approach, a 100 cm multiple-hole catheter was passed retrograde across the aortic valve and positioned in the mid left ventricular cavity. After heart rate and left ventricular pressures were measured, a left ventricular angiogram was performed at a 30-degree right anterior oblique angle using 45 ml of meglumine diatrizoate (Renografin 76%) injected at a rate of 15 ml per second for three seconds. Angiograms were recorded at 60 frames per second. The patient was left in this right anterior oblique position after the first injection, and, without moving the image intensifier, 0.6 mg of nitroglycerin was administered sublingually. Five minutes after complete absorption of the pill, a second left ventricular angiogram was taken in an identical manner.

DATA REDUCTION AND ANALYSIS

In addition to recording on cine film, the left ventricular angiograms were recorded on videotape or disc or both. Using a computer program previously described [3], the border of the dye-filled ventricle was automatically determined for each video field during systole. Since there are 60 video fields per second, approximately 20 contours of the left ventricular border are sequentially determined for each systole. After a sequence of contours was determined, ventricular dynamic function was quantitated in the following manner [4]. For each contour, a reference point is established by the program as the midpoint of the major axis of the ventricle (the line connecting the midpoint of the base to the apex). Radii are drawn from this reference point to the ventricular wall at 5-degree increments around the contour (Fig. 1). For a view of the left ventricle in a 30-degree right anterior oblique position, the radius at 0 degrees goes to the center of the aortic valve. Between 80 and 180 degrees is the inferior wall, at 180 degrees is the apex, and the anterior wall is the region between 180 and 330 degrees. The radial lengths and a mean of all 72 radii are calculated for each of the approximately 20 contours during systole.

Temporal change in the length of a given radius represents the segmental wall motion in that region. This motion is expressed quantitatively by the linear regression slope of lengths at a given angle against the corresponding time sequence of the average radius for each contour (Fig. 2). The magnitude of the regression slope at each angle gives the relative contractility for that wall segment. For example, if the slope is greater than 1, that segment moves more vigorously than the average for the ventricle. If the slope is negative, the segment has paradoxical motion. The correlation coefficient is calculated for each regression as a measure of the correctness of fit. A high correlation coefficient indicates

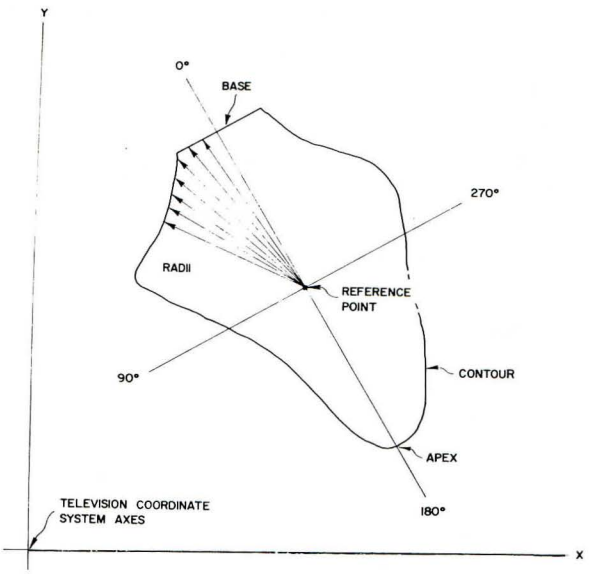
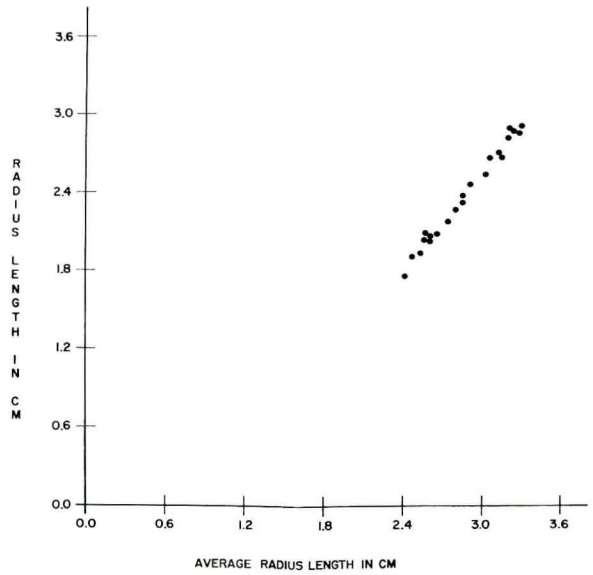


FIG. 1. Orientation of the radii used to quantitate left ventricular function. The base represents the aortic valve.

that the given muscle segment contracts synchronously when compared with the average ventricular motion and that the linear regression is a valid measure of its motion [4].

The correlation coefficients and regional contractility for a normal human ventricle are shown in Figure 3. The 72 values of the regression slope and correlation coefficient are stored in patient records as a quantitative measure of left ventricular dynamic function. This information can then be used to assess the results of operation or to evaluate the time course of disease by comparison with other studies.

FIG. 2. Regression relationship for a normal muscle segment at a given radius (vertical axis) *plotted against the average for the ventricle* (horizontal axis).



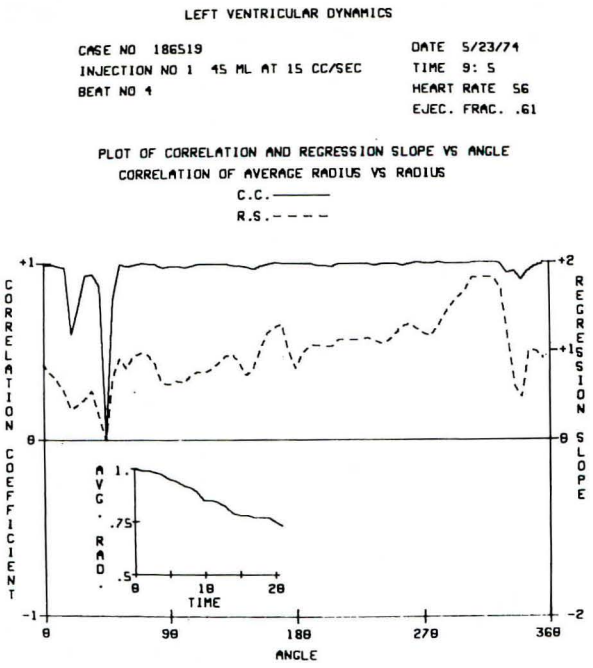


FIG. 3. Plot showing the values of the regression slope (dotted line) *and correlation coefficient* (solid line) *as a function of location in a normal ventricle.*

Results

The ventriculograms of 41 patients before and after nitroglycerin administration were analyzed as previously described. In 11 patients with normal or near-normal ventriculograms there was no measurable effect on dynamic function of the ventricle. Hemodynamic data, including ventricular diastolic pressures, will not be reported here. The second ventriculogram was obtained about six minutes after the first injection, and diastolic pressure may have been influenced by the first injection of contrast medium as well as by the nitroglycerin. Other studies, however, have shown that there was no significant difference in ventricular diastolic pressures or heart rate when 25 to 30 minutes was allowed to pass before the second injection of contrast material [8].

The data obtained from 1 patient who exhibited a marked improvement in ventricular contraction following administration of nitroglycerin are shown in Figures 4 and 5. This patient had progressive angina pectoris with no history or electrocardiographic evidence of a previous myocardial infarction. There was an area of 90% narrowing in the proximal left anterior descending coronary artery. The control ventriculogram showed an akinetic area in the anterior wall and apex. Following nitroglycerin administration the contractions were normal. Note that the regression slope before nitroglycerin was zero in the region of the anterior wall (270 degrees) and the correlation coefficient was markedly reduced (see Fig. 5). After nitroglycerin was given, both regression slope and correlation coefficient returned to a normal range.

In contrast, Figures 6 and 7 show data from a patient who had no response to nitroglycerin. This patient had had a previous myocardial infarction, and a recent

electrocardiogram showed Q waves over the precordium. The left anterior descending coronary artery was totally obstructed, as was the posterior division of the circumflex. Again, an akinetic anterior wall was noted in the control ventriculogram. Following administration of nitroglycerin there was slightly improved contraction along the inferior border with some worsening of the akinetic segment, probably due to increased vigor of contraction of the muscle surrounding this scar tissue. This is shown also by changes in the regression slope following nitroglycerin administration in the part of the border that is infarcted as well as along the inferior border.

The data from ventriculograms taken before and after nitroglycerin administration were compared with clinical data. Nineteen of the 30 patients had previously documented myocardial infarction and significant Q waves in their recent electrocardiogram with areas of akinesia in their control ventriculogram. None of these areas of akinesia responded to nitroglycerin, although 9 patients had increased motion in other areas of the myocardium. In 5 of these 9 patients the increased motion was adjacent to the akinetic areas, and in the remaining 4 the improvement was in an area associated with significant disease of other arteries.

Eleven of the patients had no Q waves in their recent electrocardiogram, and all had current angina pectoris. Five showed marked improvement in akinetic areas following nitroglycerin administration with return to normal or near-normal contractions. Of the remaining 6 patients, 1 had an akinetic area that

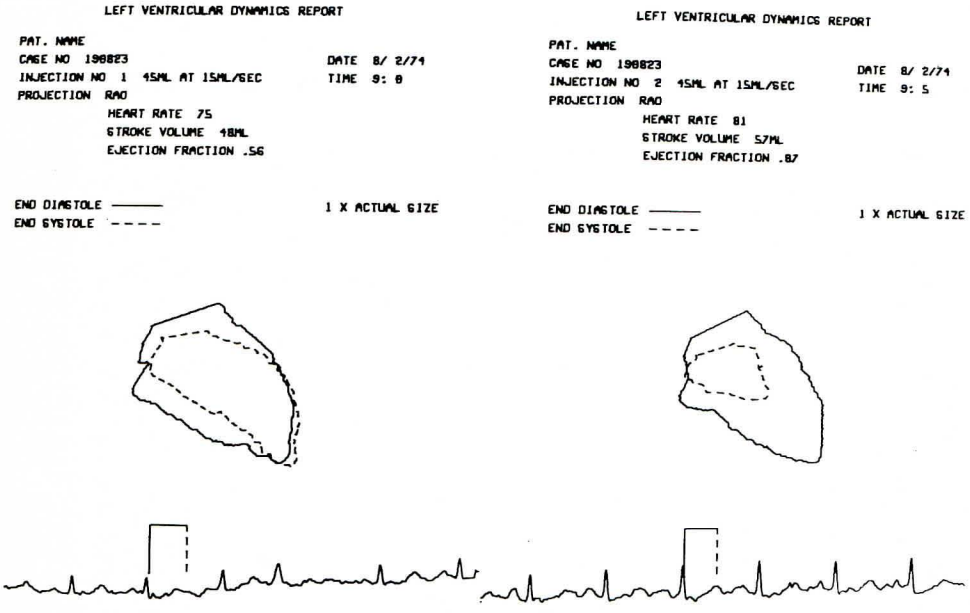


FIG. 4. Plot showing the computer-determined borders of the left ventricle at end-diastole (solid line) *and end-systole* (dotted line), *before* (left) *and after* (right) *administration of nitroglycerin. At the bottom of the panels are electrocardiograms that were recorded on tape and reproduced on the panel. The particular beat used for this analysis is marked at end-diastole* (solid line) *and end-systole* (dashed line).

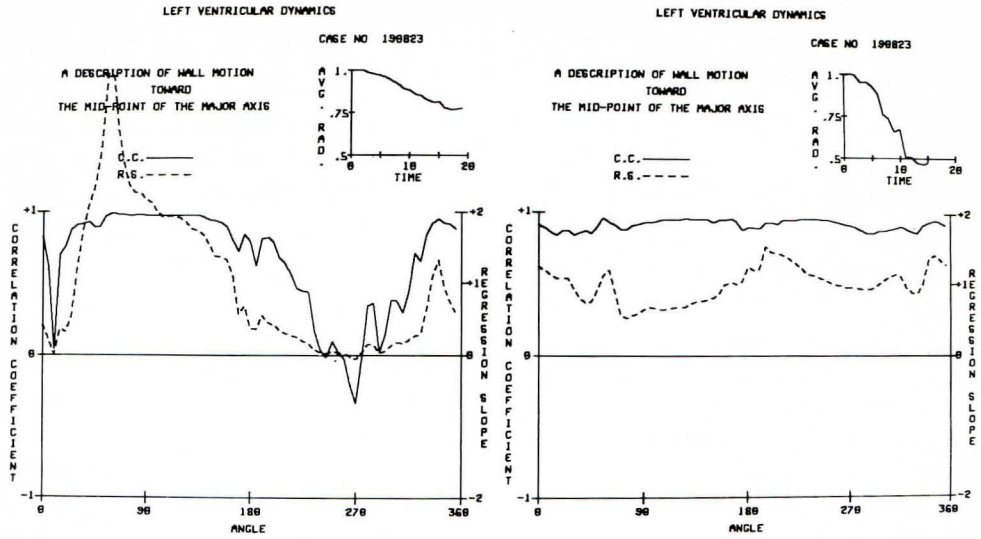


FIG. 5. Values of the regression slope (dotted line) *and correlation coefficient* (solid line) *as a function of location in the ventriculogram analysis shown in Figure 4. The left panel shows the plot before and the right panel the plot after administration of nitroglycerin.*

showed only mild improvement and 5 had areas of hypokinesia; 4 of these 5 had areas of only mild improvement.

Twelve of the patients have had aortocoronary bypass operations in which special attention was paid to the appearance of the myocardium. In 7 of these 12 patients a good response in ventricular contractility following administration of

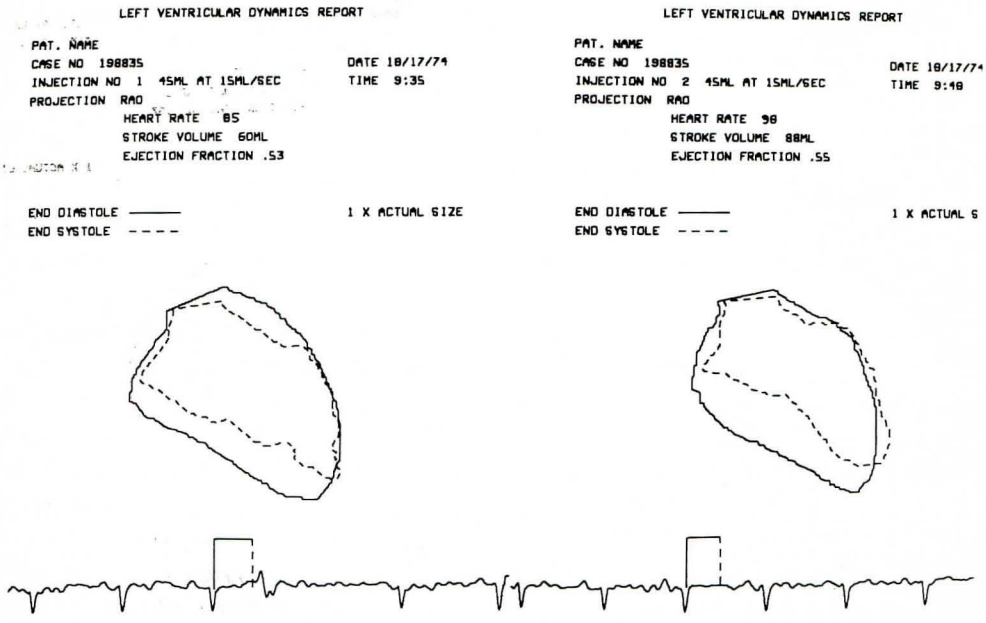


FIG. 6. Plot showing the effect of nitroglycerin on ventricular contraction. See Figure 4 for description of the plot.

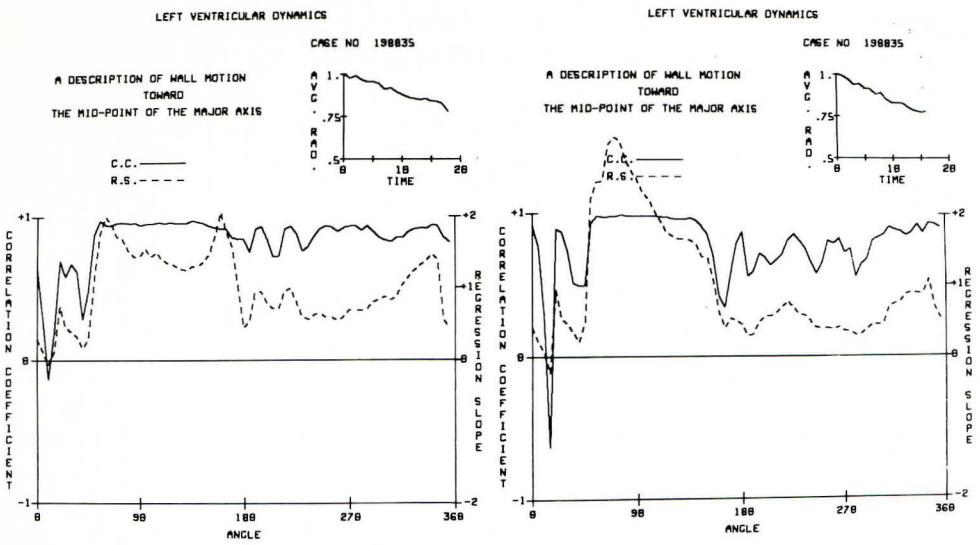


FIG. 7. Values of regression slope (dotted line) *and correlation coefficient* (solid line) *for the angiograms shown in Figure 6. The left panel is before and the right is after administration of nitroglycerin.*

nitroglycerin suggested that viable muscle was present in asynergic areas. The heart muscle appeared normal at surgical observation in all these patients. In the remaining 5 individuals there was no response to nitroglycerin, and the assumption was made that either scar tissue or irreversibly damaged muscle was present in the affected areas. Surgical observation showed scar tissue present as predicted in 4 of the 5 patients. The exception was a patient with severe three-vessel disease and generally reduced contractions in whom no abnormality of the myocardium was noted at operation.

Comment

This study confirms that the contraction pattern of asynergic wall segments as well as their adjacent areas may be modified by administration of nitroglycerin. This may be due to alteration in loading conditions of the ventricle, resulting in an improved myocardial oxygen demand/supply ratio. There are a number of mechanisms by which nitroglycerin could affect regional wall motion. These have been discussed by Sniderman and associates [8], who noted a significant decrease in end-diastolic volume following nitroglycerin therapy and postulated, according to LaPlace's law, a reduction in wall tension as a result of the decrease in ventricular volume. Our observations show that whereas the ventricular volume did occasionally decrease following nitroglycerin, this was not a consistent finding. The decrease in end-diastolic volume could not be correlated with improvement in asynergy following nitroglycerin administration.

Correlation coefficients and regression slope values obtained from computer analysis were averaged over each of four border segments; these were: the proximal (80 to 135 degrees) and distal (135 to 180 degrees) inferior wall and the distal (180 to 280 degrees) and proximal (280 to 330 degrees) anterior wall. These

values were then compared with available clinical data and visual inspection of the ventriculograms. It was found that if the average value of the correlation coefficient in an area of myocardium was less than 0.90, there was a high probability that scar tissue was present. This hypothesis was tested in areas of the myocardium in which very minor improvements in contraction appeared to be present visually. In those patients in whom all available data, including clinical, laboratory, and surgical findings, strongly supported the presence of scar tissue in this area, the correlation coefficient was found to be less than 0.90. If this hypothesis is true, then in these patients the areas of increased movement are apparent rather than real, possibly due to more vigorous contraction of ventricular muscle in adjacent areas, to displacement of the whole ventricle during systole, or to both factors.

Similarly, correlating the effect of nitroglycerin on ventricular asynergy with clinical data is impressive, although, as could be expected, discrepancies did occur. We conclude that combining all these factors — including the clinical history, angiographic data, regression slope, and correlation coefficient plus the status of the coronary arteries — into a multivariant analysis program that evaluates each segment of the ventricular wall should give better information concerning each segment of the left ventricle than could be obtained from inspecting the ventriculograms alone [9]. Although such studies are under way, the necessary correlations can be obtained only when careful follow-up data are available on these patients.

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Discussion

DR. LIDDLE: The technique of computer analysis of left ventricular wall motion, which has been so nicely described by Dr. Marshall, was designed in Dr.

Homer Warner's department in our city. Its purpose is to distinguish areas of viable, recoverable left ventricular myocardium from areas of ventricular scar. The importance of this information to the surgeon is self evident. By virtue of reducing afterload, nitroglycerin permits akinetic or dyskinetic viable myocardium to demonstrate contractility and changes in wall motion induced by nitroglycerin which can be recognized by visual study of left ventriculograms. However, the computer is capable of recognizing much more subtle changes in wall motion than one can discern visually. There is some evidence to suggest that computer analysis of left ventricular wall motion, even in the absence of nitroglycerin, may be able to identify recoverable segments of apparently akinetic left ventricular myocardium.

NOTICE FROM THE SOUTHERN THORACIC SURGICAL ASSOCIATION

The Twenty-second Annual Meeting of the Southern Thoracic Surgical Association will be held at the Fairmont-Roosevelt Hotel, New Orleans, La., on November 6–8, 1975. Reservations may be made by writing to the Reservations Manager, Fairmont-Roosevelt Hotel, New Orleans, La.

Application for membership in the Southern Thoracic Surgical Association, on forms provided by the Association, should be sent directly to J. Alex Haller, Jr., M.D. [Chairman of the Membership Committee], The Johns Hopkins Hospital, Baltimore, Md. 21205. The deadline for application to membership is September 1, 1975.

Papers that are accepted for the program will be considered for publication in *The Annals* and must be submitted to the Editor by October 15, 1975.

James W. Brooks, M.D.
Secretary-Treasurer