Experimental and Clinical Validation of a Radionuclide Angiographic Method for Assessing Myocardial Dyskinesis

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Editors Note: This manuscript received the first Editorial Technologist Award given by the Education and Research Foundation, the Society of Nuclear Medicine. The monetary award was made possible by donations to the E&R Foundation.

This study examines the physiologic and clinical validity of a new radionuclide angiographic (RNA) technique for assessing regional left ventricular (LV) dysfunction. This technique uses time-activity curves from normal and abnormal regions of interest to identify sites of passive myocardial dyskinesis (i.e., early-systolic bulge and early-diastolic shortening or recoil). A quantitative RNA image of early-systolic bulge was created by subtracting the end-diastolic frame from the frame with maximum counts (defined by the abnormal region); an image of early diastolic recoil was created by substracting the frame with minimum counts (abnormal region) from the end-systolic frame. These RNA indices of regional dysfunction were first validated in 12 closed chest dogs subjected to acute coronary artery occulsion and varying loading conditions; the RNA data correlated highly with direct ultrasonic crystal recordings of myocardial early systolic bulge (mean r = 0.93) and early diastolic recoil (mean r = 0.86). Subsequently, RNA studies performed in 36 consecutive patients who had cardiac catheterization for presumed coronary artery disease were interpreted visually and by RNA bulge and recoil analysis. Contrast ventriculograms were interpreted visually and quantitatively by shortening of 100 chords. Of 86 wall segments that were normal by chord shortening, visual interpretation of contrast and RNA studies was correct in 79% and 78% of the studies, while RNA bulge/recoil analysis was correct in 93% (p = 0.028 for this difference in specificity). Of 22 quantitatively abnormal segments, visual interpretation of both contrast and RNA studies was correct in 82% of the studies, while RNA bulge/recoil analysis was correct in 68% (p = 0.09 for this difference in sensitivity). This method for RNA assessment of regional LV dyskinesis is physiologically valid, objective, applicable clinically, and ideal for serial quantitative evaluations.

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Clinical assessment of left ventricular (LV) segmental myocardial wall motion is usally made qualitatively by visual inspection of contrast and radionuclide angiographic (RNA) studies. In view of the important diagnostic (*1,2*) and prognostic (*3–5*) implications of wall motion analysis in patients evaluated for coronary artery disease, a large number of quantitative approaches, both invasive and noninvasive, have been used. In developing and applying such techniques, few investigators have presented direct experimental evidence verifying that their methods for measuring segmental wall motion bear a consistent and meaningful relationship to myocardial segment motion under varying conditions. Recent experimental (*6*) and clinical (*7*) studies of myocardial segment motion during ischemia have noted paradoxical early-systolic lengthening (outward motion) in association with early-diastolic shortening (inward motion). This study presents an objective, quantitative technique developed and validated in the animal laboratory using equilibrium RNA to assess asynchronous myocardial early systolic "bulge" and early diastolic "recoil"; the technique was tested in 36 patients who underwent cardiac catheterization and contrast ventriculography for presumed coronary artery disease.

MATERIALS AND METHODS

Animal Studies

Using sterile technique, 12 mongrel dogs weighing 20–30 kg underwent left thoracotomy under sodium pentobarbital anesthesia (25mg/kg i.v.). The left anterior descending (LAD) coronary artery was dissected free after its first diagonal branch, and a hydraulic cuff or a loop-type snare occluder was positioned around it. Pairs of ultrasonic crystals were inserted in both the normally perfused myocardium of the lateral wall and in a zone to be rendered ischemic in the center of the LAD perfused area. The crystal pairs at each site were implanted subendocardially parallel to the LV short axis for the measurment of segment length (*8,9*). Pacing electrodes were sutured to the left atrial appendage. The wires and

catheter were exteriorized to the back of the animal, and the animals were allowed to recover from the operation for 4–7 days.

Studies were performed while the dogs were sedated with morphine sulphate 30 mg IM and diazepam 10 mg IM and lying quietly on the right side. Using local anesthesia, catheter-tipped microtransducers were introduced through carotid artery cutdowns to the level of the aortic valve cusps and into the left ventricle. Dogs were atrially paced initially at a rate of 100 beats/min. In the control state, baseline hemodynamics and regional contraction were recorded, and RNA studies were performed (*10,11*). Care was taken to ensure that camera position relative to the thorax remained constant between data acquisitions; weighted support pads were used to stabilize the chest position. Complete and permanent LAD occlusion was then produced by pulling the snare. After 15 min of coronary occlusion, hemodynamic, sonomicrometric, and RNA recordings were repeated.

Loading conditions were then varied in two steps. First, 500 ml of blood was withdrawn through a femoral venous catheter to reduce preload acutely. Five minutes after the completion of blood withdrawal, all functional measurements were repeated. Second, 800 ml of blood (including the dog's own previously withdrawn blood as well as 300 ml stored, pH corrected donor blood) were transfused rapidly and recordings were repeated; in some cases, recordings were made after the first 500 ml of blood had been transfused. Six dogs underwent repeat study seven days after coronary occlusion, with repetition of the same protocol for varying loading conditions. Myocardial segment lengths were measured at end diastole (EDL), defined as the time of abrupt pressure change of (dP/dt) of the LV during diastole; and end systole (ESL), defined as the time when LV pressure fell below the diastolic notch of the aortic cusp pressure tracing. When a dyskinetic pattern of segment motion occured, the maximum length (MaxL) and the minimum length (MinL) were measured. Myocardial early-systole bulge and early-diastolic recoil were computed (*12*) when appropriate using the following equations:

$$\text{Bulge}\ (\%) = \frac{(\text{MaxL} - \text{EDL})}{\text{EDL} * 100}$$

$$\text{Recoil}\ (\%) = \frac{(\text{ESL} - \text{MinL})}{\text{EDL} * 100}$$

Strip chart records of myocardial segment length and LV pressure and hard copy records of RNA regional time-activity curves were traced manually, beginning at the time of the R-wave of the electrocardiogram, using a digitizing tablet interfaced to a computer. Measurment error in converting recorded analog data to digital data was at most 0.2%. Data smoothing was performed using the proportional three-points method and data linear interpolation. Approximately 800 points per sec were collected by hand tracing and were extrapolated to 1,000 points at 1 msec intervals. These digital data were normalized according to time, and pressure length loops and pressure count loops were created.

Patient Studies

Thirty-six consecutive patients aged 58 ± 10 years with presumed coronary artery disease undergoing elective cardiac catheterization with right anterior oblique (RAD) contrast ventriculography were studied. Twenty-five patients were male and 11 were female. RNA studies were performed at rest a mean of 2 ± 6 days from the day of catheterization. Sixteen patients had a history of myocardial infarction. Eighteen patients had significant Q-waves (40 msec duration) on the electrocardiogram. Coronary arteriograms were evaluated in conference by two experienced observers; 5 patients had three-vessel coronary artery disease (at least 70% luminal diameter narrowing), 10 had two-vessel disease, 11 had one-vessel disease, and 10 had no significant coronary disease.

Radionuclide Angiographic Techniques

For both animal and patient studies, multigated equilibrium RNA was performed after modified in vivo red blood cell labeling (*13*). R-wave synchronized images were acquired using a mobile scintillation camera equipped with a high resolution parallel-hole collimator and interfaced to computer. The cardiac cycle was divided into 24 consecutive image segments in a 64 × 64 byte mode matrix with ~ 200,000 counts acquired per frame. Animal images were acquired in the anterior or ventral projection with slight caudal angulation (*10,11*). Patient studies were recorded in the left anterior oblique (LAO) (best septal separation) 20° RAO and left lateral projections and were visually analyzed in routine conference by two observers blinded to the results of cardiac catheterization. Anterior, apical, and inferior LV wall segment motion was interpreted as normal, hypokinetic, or akinetic/dyskinetic. Septal and posterolateral wall segment interpretation (LAO projection) was not utilized for this study since these segments were not assessed by quantitative contrast ventriculography.

Radionuclide Image Processing

The image processing technique for assessing asynchronous LV myocardial wall motion consists of three analytical steps: 1) preprocessing; 2) assignment of normal and abnormal regions; and 3) quantitation of overall LV bulge and recoil. Steps 1 and 2 are described in detail in the Appendix. To identify and quantitate the functional differences between the abnormal and normal zones, the regional time-activity curves were examined (Fig. 1). Abnormal regions typically demonstrated increasing counts early in systole (early-systolic bulge) until a maximum value was reached, and then decreasing counts through the remainder of systole and well into early diastole (early-diastolic recoil) until a minimum value was reached. The following parametric images of bulge and recoil for the entire left ventricle were created from preprocessed RNA studies:

1. The bulge image formed by subtracting the end-diastolic frame (defined by maximum counts in the normal zone) from the frame at which the abnormal zone demonstrated maximum counts (Fig. 1).
2. The recoil image created by subtracting the frame at which the abnormal zone attained its minimum count value from the end-systolic frame (Fig. 1) (defined by minimum counts in the normal zone).

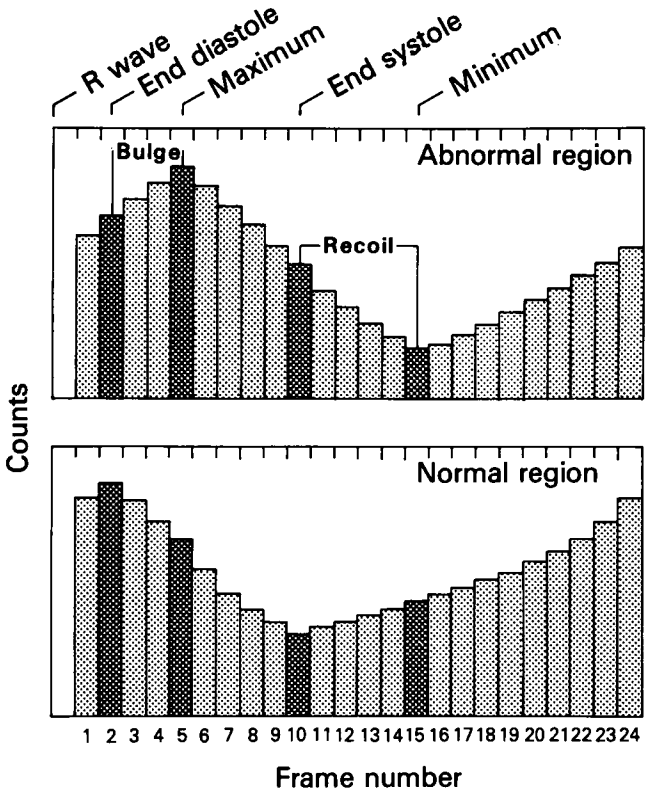

FIG. 1. Idealized 24-frame radionuclide count histograms for an abnormal region (top) and a normal region (bottom) of a LV. In the normal region, following the R-wave of the electrocardiogram, counts may increase slightly from Frame 1 to Frame 2 as a result of electromechanical delay; the frame with maximum counts in this region is taken as end diastole. Counts then decrease progressively in the normal region during the ejection period until minimum counts are reached. The frame with minimum counts is defined as end systole. Counts then gradually increase during the diastolic filling period. In the abnormal region, counts often increase for several frames early in systole (early-systolic "bulge") until a maximum, and then decrease for several frames past end systole (early-diastolic "recoil") until a minimum. In this and subsequent examples, count bars for the end-diastolic and end-systolic frames and for the frames at which the abnormal region reaches maximum and minimum counts are darkly shaded.

Quantitation of these parametric images was performed then by determining the total number of image counts reflecting myocardial early-systolic bulge or early-diastolic recoil within the LV region of interest. Calculation of the following overall indices of LV myocardial bulge and recoil were performed:

$$\text{Bulge (\%)} = \frac{\text{Bulge Image Counts}}{\text{EDC} * 100}$$

and

$$\text{Recoil (\%)} = \frac{\text{Recoil Image Counts}}{\text{EDC} * 100}$$

where EDC is the end-diastolic count rate measured from the background-corrected global LV time-activity curves.

Contrast Ventriculography

Left heart catheterization was performed using the Judkins or Sones technique. Coronary arteriograms were performed in multiple projections. Contrast ventriculography was performed in the 30° RAO projection. Anterior, apical, and inferior wall segment motion was graded in conference by two blinded observers as normal, hypokinetic, or akinetic/dyskinetic.

Quantitative analysis of segmental wall motion from contrast ventriculograms was performed using the University of Washington method (*14,15*). Using cardiac cycles that were not preceded by a premature contraction and that demonstrated adequate chamber opacification, end-diastolic and end-systolic LV contours were hand traced onto transparent plastic overlays. The traced LV contours were digitized using a digital subtraction angiography computer. Segmental wall motion at 100 equally spaced chords perpendicular to a center line drawn midway between the end-diastolic and end-systolic contours was measured. Motion at each chord was normalized for heart size by dividing by the end-diastolic perimeter length. The normalized motion of each chord was expressed as units of standard deviation (s.d.) from the mean motion for that chord as determined by Sheehan et al. (*14*) in 64 normal patients. Analysis of regional wall motion was performed between chords 10 and 80 to exclude wall motion related to the cardiac valves (*15*). Chord motion was considered to be abnormal if it was −2 s.d. or less, or a least 2 s.d. below the normal mean (*15*). For comparison with visual wall motion assessment, chords defining the anterior, apical, and inferior walls were examined as a unit for abnormalities meeting this quantitative criterion.

Statistical Analysis

The relation between myocardial early-systolic bulge and early-diastolic recoil measured using ultrasonic crystals and using RNA in animal studies was examined with linear regression analysis. Differences in the ability of visual interpretation of contrast ventriculograms, visual interpretation of RNA studies, and anlysis of RNA bulge and recoil images to predict abnormalities in quantitative ventriculographic chord shortening in patient studies were tested for significance by Chi square analysis. Chi square analysis was also used to compare sensitivity and specificity for each technique when used to assess abnormal motion of particular wall segments.

RESULTS

Representative digitized ultrasonic crystal recordings and RNA recordings are shown in figure 2 for four dogs studied in the control state and following LAD coronary occlusion. Data were collected beginning at the time of the R-wave of the electrocardiogram, and were normalized relative to the end-diastolic myocardial segment length or to regional LV counts in the abnormal zone, which were set to 100%. In the control state, after a brief period of electromechanical delay, the myocardial segments destined to become ischemic demonstrated systolic shortening; after attaining minimum length, there was progressive diastolic lengthening. Following coronary occlusion, the segments showed passive early-systolic lengthening (bulge) until a maximum length, followed by slowly decreasing length during the ejection period; these segments

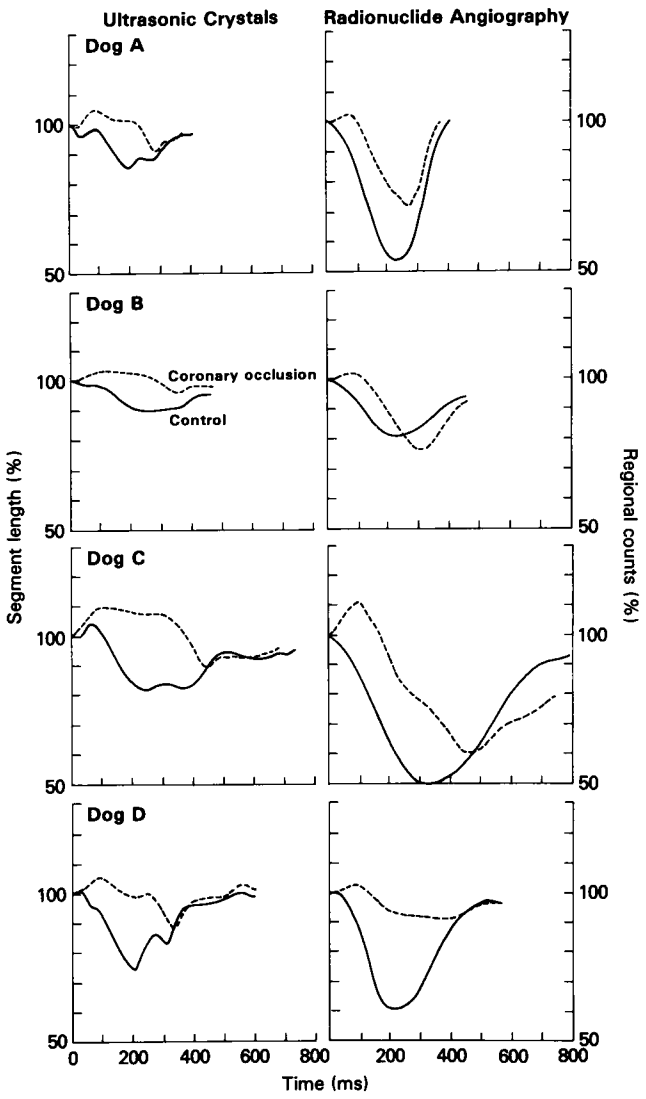

FIG. 2. Digitized ultrasonic crystal recordings of myocardial segment length (left) and RNA recordings of regional counts (right) for four representative dogs in the control state (solid lines) and following LAD coronary occlusion (dashed lines). Data were normalized relative to time (starting from the R-wave) and to the end-diastolic length or count value. Descriptions of the curves are given in the text.

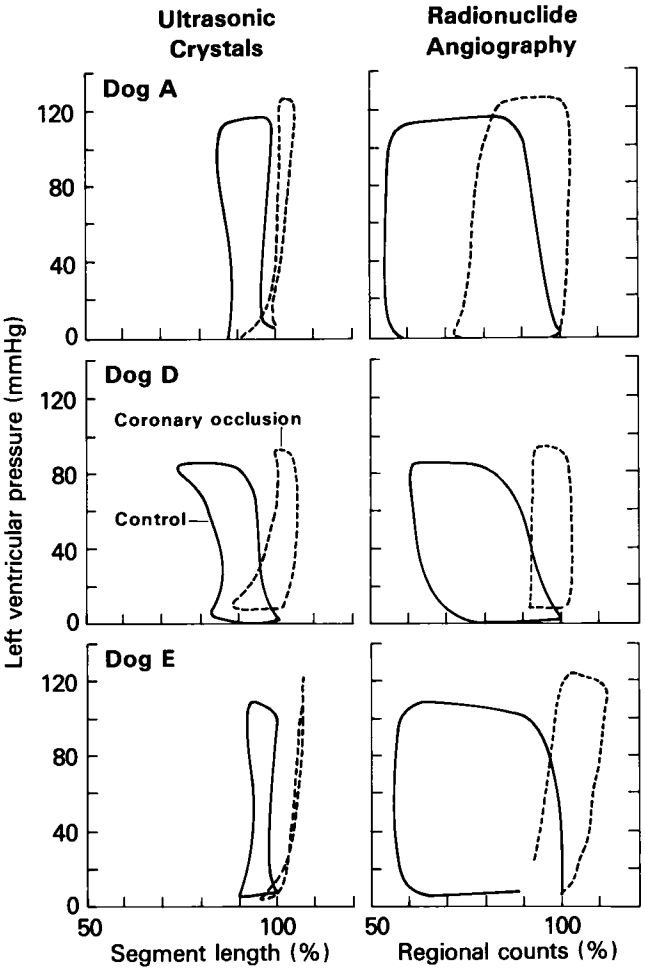

FIG. 3. Digitized LV pressure-segment length loops (ultrasonic crystals, left) and LV pressure-regional count loops (RNA studies, right) for three dogs in the control state (solid lines) and after coronary occlusion (dashed lines). Segment length and regional count data were normalized relative to time and to the end-diastolic measurement. Descriptions of the curves are given in the text.

showed an abrupt passive decrease in length (recoil) during the early-diastolic relaxation period. The pattern of regional LV count change in RNA studies performed in the control state also showed decreasing counts throughout systole and increasing counts throughout diastole. After coronary occlusion, there was typically an increase in counts (bulge) early in systole, followed by a decrease in counts through the remainder of systole that continued into early diastole (recoil).

In figure 3, digitized LV pressure-segment length loops (ultrasonic crystals) and LV pressure-regional count loops (RNA studies) are compared for three dogs in the control state and following coronary occlusion. During control, the pressure-length loops were formed in a counterclockwise direction and showed early-systolic (isovolumic systole) increase in LV pressure without change in length, followed by shortening with little pressure change (ejection phase of systole), decrease in LV pressure without change in length (isovolumic diastole), and lengthening with little pressure change (diastolic filling phase). Pressure-count loops in the control state showed a generally similar pattern, with greater percent changes relative to end-diastolic counts. After coronary occlusion, pressure-length loops revealed an exponential upstroke during systole, with passive early systolic bulge until the attainment of maximum LV pressure, and an exponential downstroke during diastole, with passive early diastolic recoil until the attainment of minimum LV pressure. Pressure-count loops after coronary occlusion suggest a similar pattern of passive, pressure-dependent bulge and recoil, although percent changes in counts continue to exceed percent changes in length.

Figure 4 plots RNA in comparison to ultrasonic crystal data for early systolic bulge and early diastolic recoil. Significant linear correlations were obtained in all 12 dogs studied in the control state, after coronary occlusion, and under varying loading conditions. The mean correlation coefficients were

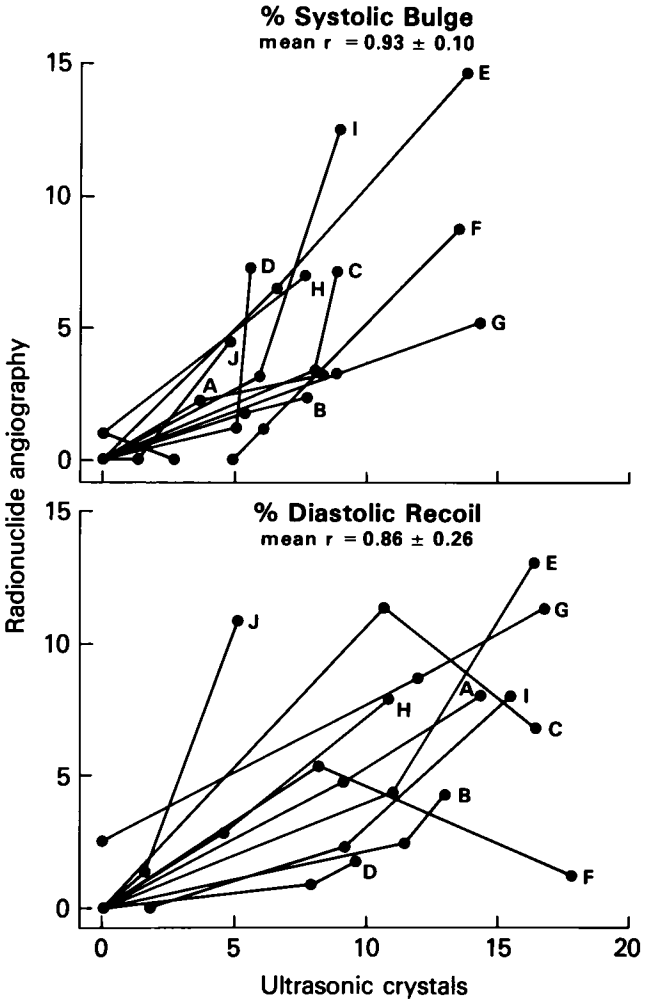

FIG. 4. Relations between measurements of myocardial early-systolic bulge and early-diastolic recoil made using the RNA technique and ultrasonic crystals. Linear correlations were obtained in all 12 dogs studied in the control state, after coronary occlusion, and under varying loading conditions; six dogs were studied at two sessions, seven days apart.

r = 0.93 ± 0.10 and r = 0.86 ± 0.26 for bulge and recoil, respectively.

Comparative RNA and contrast ventriculographic data are illustrated in figures 5–8 for four representative patients. Each figure presents: (a) RNA abnormal and normal region time-activity data (bar graphs plot relative counts for each frame of the RNA study); (b) RNA bulge and recoil images obtained in one or more projections; (c) superimposed end-diastolic and end-systolic LV contours from contrast studies indicating the 100 chords analyzed by computer; and (d) a graph indicating shortening at each chord expressed in units of s.d. relative to the normal mean. The RNA study of the patient illustrated in figure 5 showed an abnormal region with early-systolic bulge and early-diastolic recoil that was localized primarily to the apical region in the bulge and recoil images for the left lateral and RAO projections. By chord shortening analysis of the contrast ventriculogram, an apical zone of dyskinesis was confirmed (chords 35–65 showed "hypokinesis" or shortening at least 2 s.d. less than the normal mean).

The patient in figure 6 had an RNA region manifesting slight early-systolic bulge and significant early-diastolic recoil localized to the inferior wall in the bulge and recoil images in two projections. Chord shortening analysis confirmed an inferior zone of dyskinesis. Figure 7 presents a patient who had early systolic bulge and early diastolic recoil by RNA in an inferior region, best shown in the 60° LAO projection. Chord shortening also demonstrated that the inferior wall was hypokinetic, and that the apical wall, which was felt to be hypokinetic by visual interpretation, did not fulfill quantitative criteria for abnormality. Figure 8 is an illustration of a patient who had no systolic bulge but marked early diastolic recoil recorded in all three projections and localized to the anterior-apical walls and the septum. Contrast study analysis also showed severe anterior-apical dysfunction; the septum could not be evaluated from the right anterior oblique contrast ventriculogram.

Table 1 presents the results of comparisons performed between segmental chord shortening in contrast studies, which was taken as the "gold standard," visual interpretation of both contrast and RNA studies, and analysis of RNA bulge and recoil images. Of 86 wall segments that were quantitatively within normal limits, visual interpretation of contrast and RNA studies was correct in 79% and 78%, while analysis of bulge and recoil images was correct in 93%; this difference in

TABLE 1. Contrast Versus RNA Studies for Regional Asynergy

	Contrast Chord Shortening	
	−0 s.d.* −1 s.d.	−2 s.d. −3 s.d. −4 s.d.
Item	**Normal**	**Abnormal**
Segments (n)	86	22
Contrast Visual		
Normal	68	4
Hypokinetic	13	1
Akinetic/Dyskinetic	5	17
RNA Visual		
Normal	11	4
Hypokinetic	11	1
Akinetic/Dyskinetic	8	17
RNA Bulge/Recoil†		
None	80	7
Bulge or recoil	2	5
Bulge and recoil	4	10

*Numbers of standard deviations (s.d.) by which the measured chord shortening differs from the normal mean; a −2 s.d. difference was considered to be abnormal.

†Correct identification of normal contrast chord shortening (i.e., specificity) was 93% for RNA bulge/recoil analysis, 78% for RNA visual interpretation, and 79% for contrast visual interpretation (p = 0.028); correct identification of abnormal chord shortening (i.e., sensitivity) was 68% for RNA bulge/recoil analysis, and 82% for both RNA and contrast visual interpretation (p = 0.09).

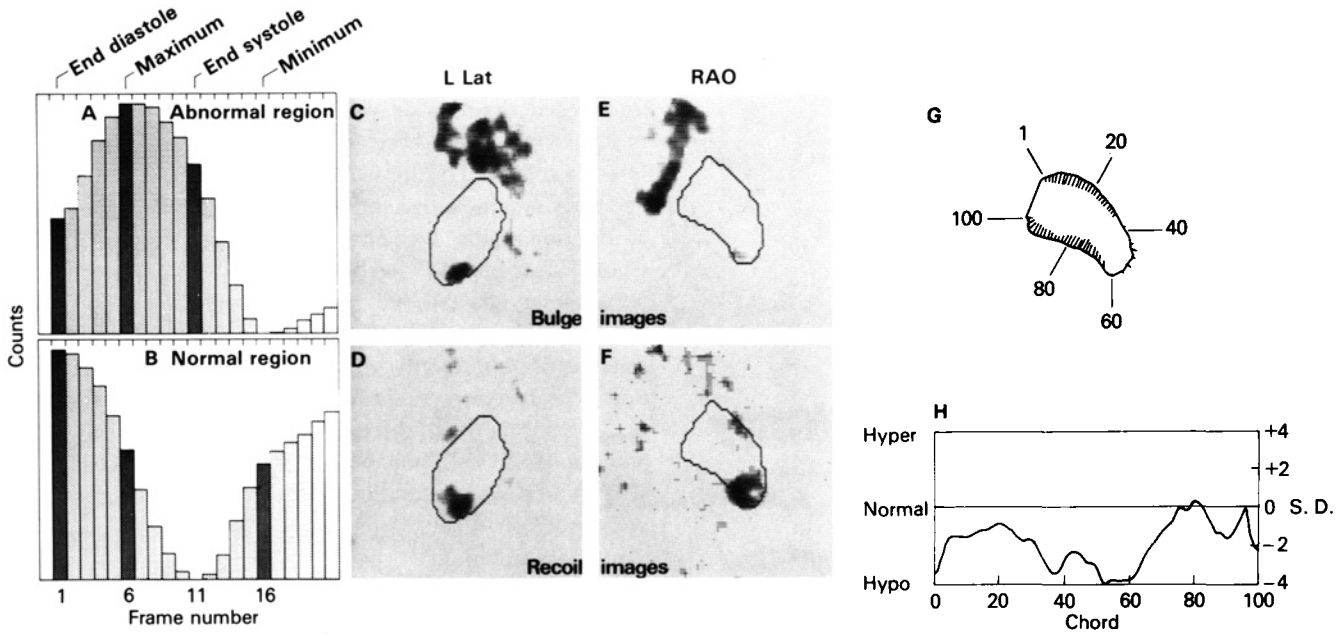

FIG. 5. Comparative RNA and contrast ventriculographic data for one patient. A and B present RNA count histograms for an abnormal and a normal region, demonstrating features similar to the idealized graphs in Figure 1. Early-systolic bulge and early-diastolic recoil were observed in the abnormal region. Darkly shaded bars indicate the end-diastolic, Frame 1, the end-systolic, Frame 11, and the frames at which the abnormal region reached maximum counts, Frame 6, and minimum counts, Frame 16. C is the bulge image, and D is the recoil image obtained in the L Lat projection; E is the bulge image, and F is the recoil image obtained in the RAO projection. The apical wall demonstrated both bulge and recoil in both projections, and a small anterior zone showed recoil but no bulge in the RAO projection. G shows the end-diastolic and end-systolic LV contours from contrast ventriculography with 100 perpendicular chords drawn by the computer; H presents shortening at each chord in s.d. units relative to the normal mean. Hyper indicates relative hyperkinesis; hypo indicates relative hypokinesis. In this example, chords 35–65 (apical wall) showed significant hypokinesis, defined as at least −2 s.d. less than the normal mean.

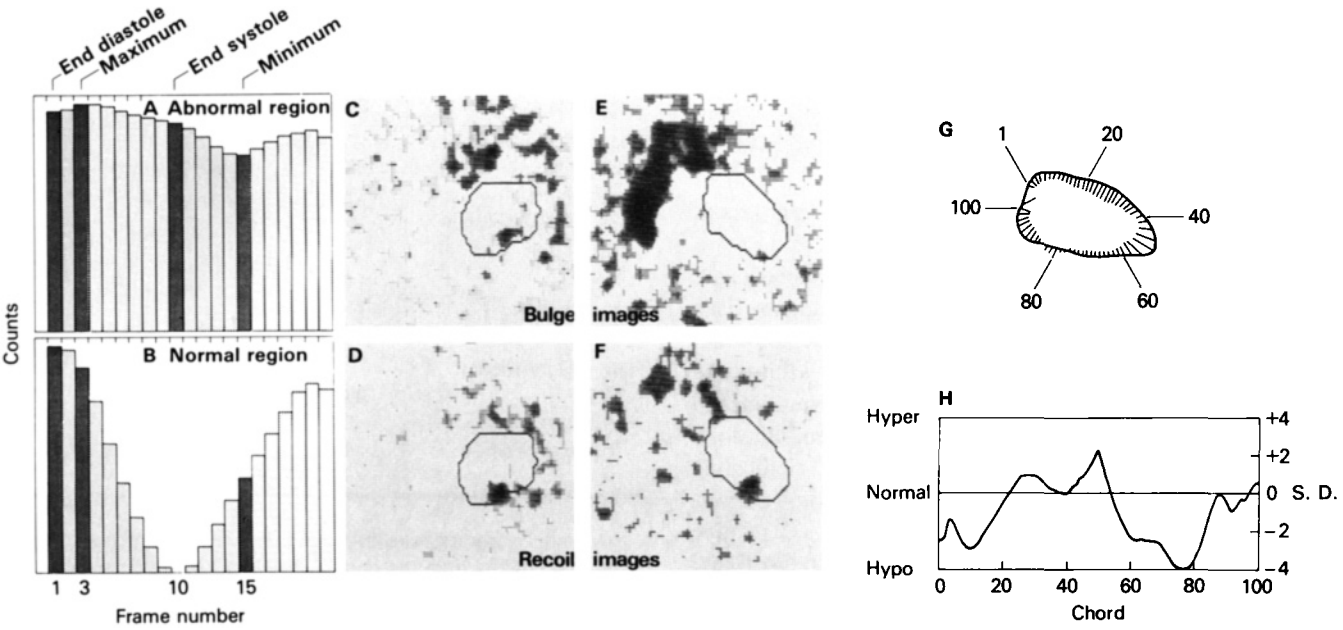

FIG. 6. RNA count histograms (A and B) for this patient reveal an abnormal region with slight early-systolic bulge (Frames 1–3) and significant early-diastolic recoil (Frames 10–15). In the L Lat projection (C and D) and in the RAO projection (E and F), bulge and recoil images demonstrate dyskinesis in the inferior wall. Chord shortening analysis of the contrast ventriculogram (G and H) confirms inferior wall asynergy, with significant hypokinesis (Hypo) between chords 60 and 80 (chord numbers > 80 were excluded from analysis).

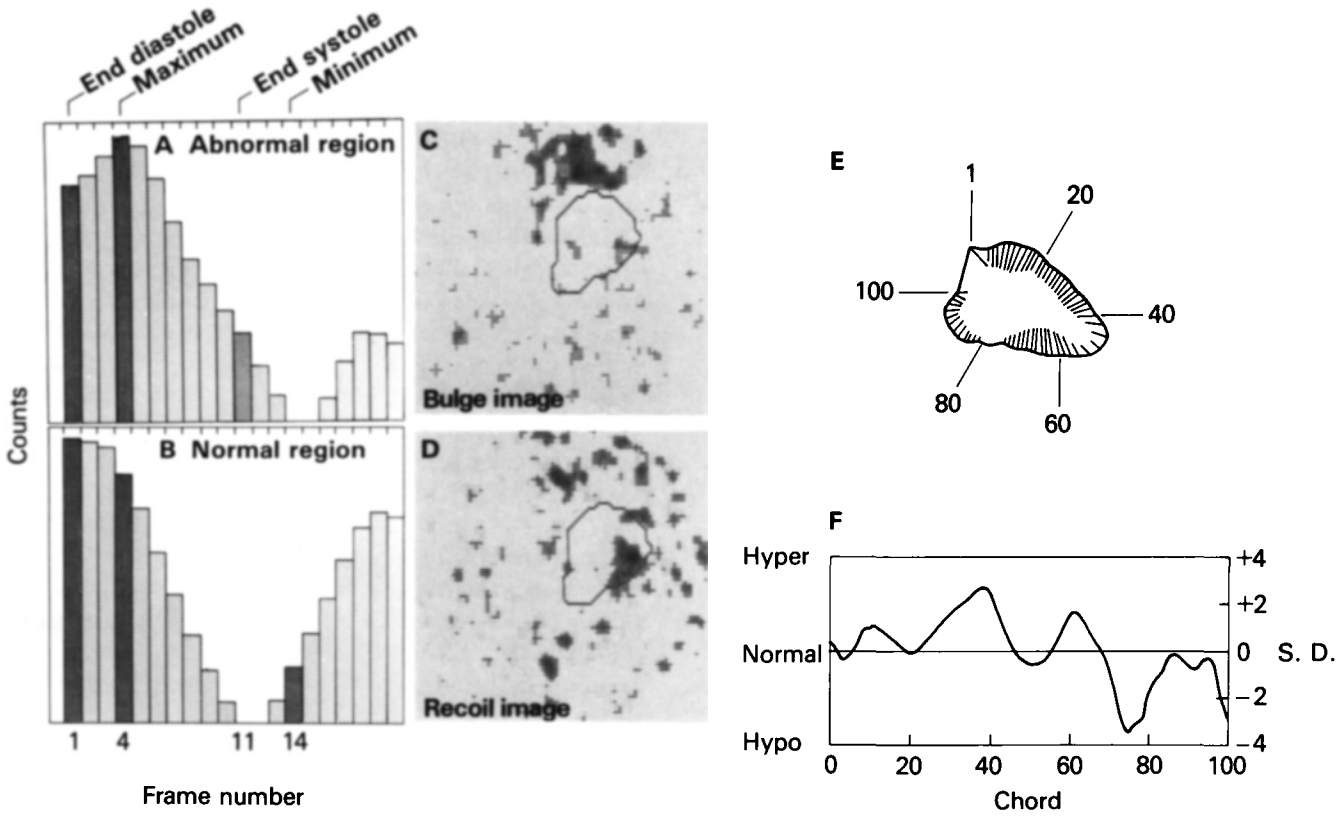

FIG. 7. RNA count histograms (A and B) for this patient manifest early-systolic bulge (Frames 1–4) and early diastolic recoil (Frames 11–14). In the 60° LAO projection (C and D), bulge and recoil images reveal dyskinesis in the inferobasal wall. Quantitative analysis of the contrast ventriculogram (E and F) also shows inferobasal wall asynergy, with significant hypokinesis (Hypo) between chords 72 and 80 (chord numbers > 80 were excluded).

specificity was significant ($p = 0.028$). Of 22 abnormal segments, visual interpretation of contrast and RNA studies were both correct in 82%, while analysis of bulge and recoil images was correct in 68%; this difference in sensitivity was not significant ($p = 0.092$).

In Table 2, specificity and sensitivity are compared for individual wall segments. For the inferior wall, there was no significant difference in specificity or sensitivity between visual interpretation of contrast studies, visual interpretation of RNA studies, and analysis of RNA bulge and recoil images. For the apical wall, specificity was highest (100%) for RNA bulge and recoil analysis ($p = 0.01$), and sensitivity did not differ. For the anterior wall, there was no difference in specificity or sensitivity

DISCUSSION

The clinical need to assess LV myocardial function in coronary artery disease has led to a proliferation of invasive and noninvasive methods. Equilibrium RNA studies are noninvasive, performed widely, may be repeated serially, and provide quantitative count data that reflect global and regional LV volume changes in a largely nongeometric manner. Previously described RNA method for quantitating regional LV function have not been correlated with direct physiologic measurements and have not had widespread clinical application. In this study, a physiologically derived and clinically applicable technique for assessing regional myocardial dyskinesis has been validated. In chronically instrumented dogs subjected

TABLE 2. Contrast Versus RNA Studies: Wall by Wall Analysis*

Item	Specificity	Sensitivity
Inferior Wall		
Contrast visual	21/26 (81%)	8/10 (80%)
RNA visual	20/26 (77%)	7/10 (70%)
RNA bulge/recoil	24/26 (92%)	6/10 (60%)
Standard deviation	p = NS	p = NS
Apical Wall		
Contrast visual	21/27 (78%)	7/9 (78%)
RNA visual	19/27 (70%)	8/9 (89%)
RNA bulge/recoil	27/27 (100%)	7/9 (78%)
Standard deviation	p = 0.01	p = NS
Anterior Wall		
Contrast visual	26/33 (79%)	3/3 (100%)
RNA visual	28/33 (85%)	3/3 (100%)
RNA bulge/recoil	29/33 (88%)	2/3 (67%)
Standard deviation	p = NS	p = NS

*Specificity and sensitivity were determined assuming contrast chord shortening to be the "gold standard" for assessing normal and abnormal regional wall motion.

to acute LAD coronary artery occlusion and evaluated serially under varying conditions, early-systolic bulge and early-diastolic recoil assessed using this RNA technique correlated linearly with measurements of myocardial segment motion made directly using ultrasonic crystals. In consecutively studied patients who had RNA examinations and cardiac catheterization with quantitative contrast ventriculography for presumed coronary artery disease, analysis of RNA bulge and recoil images compared favorably with visual interpretation of both RNA and contrast studies.

Over the past 15 yr, RNA studies have been widely applied in the clinical assessment of LV function. Measurement of LV ejection fraction at rest and during interventions has been shown to provide diagnostic (*16,17*) and prognostic (*18,19*) information in patients evaluated for coronary artery disease. However, the ejection fraction alone is inadequate to define a wide range of early or localized impairment in myocardial function. In addition, analysis of the effects of interventions on the ejection fraction may lead to misinterpretation. For example, although a decrease in the ejection fraction or its failure to increase in response to dynamic exercise has been considered to be a sign of myocardial ischemia, many patients without coronary artery disease have such a response (*20,21*). Moreover, during regional myocardial ischemia, regional contraction abnormalities may not discernibly reduce the EF if function in the nonischemic zone increases in a compensatory fashion. As a result, assessment of the functional consequences of myocardial ischemia requires quantitation of regional myocardial performance.

Estimation of regional myocardial function by RNA, as by contrast angiography, has most commonly been performed by qualitative visual inspection of moving LV walls imaged tangentially. Attempts have been made to quantitate regional wall motion in the RNA image by: (a) using geometric techniques, similar to those used experimentally to analyze contrast ventriculograms (*22,23*), and nongeometric approaches such as calculating count rate changes in defined LV regions (*24,25*); or (b) analyzing phase-angle histograms derived from count data (*26,27*). None of these methods has been sufficiently accurate or useful to be applied generally, and most clinicians still rely upon their visual impression of LV wall motion in making decision regarding: 1) the functional significance of coronary artery lesions; 2) the distinction of myocardial infarction or scar from myocardium that is normal or reversibly

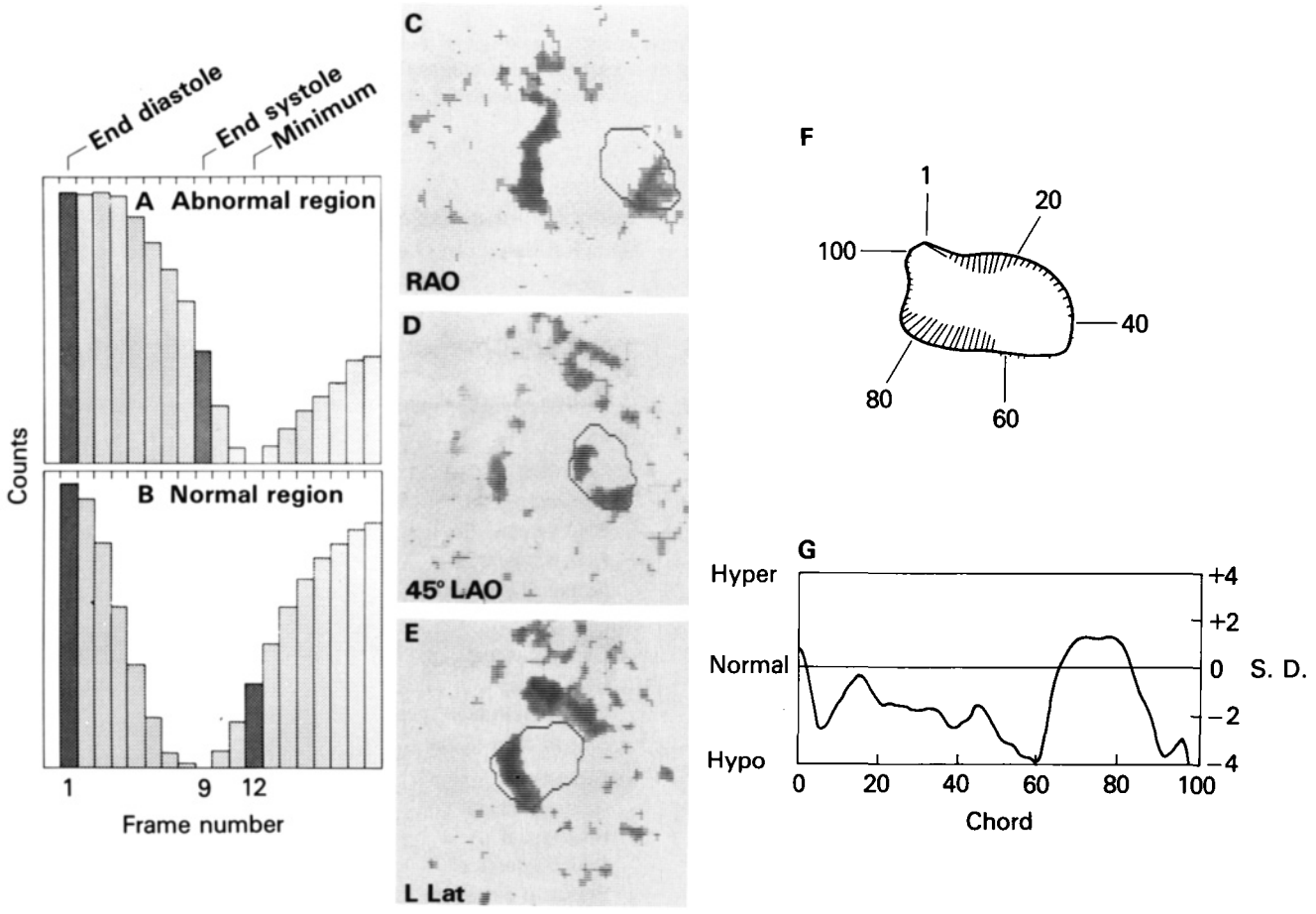

FIG. 8. RNA count histograms (A and B) for this patient demonstrate marked early-diastolic recoil (Frames 9–12), but no early-systolic bulge. Recoil images created for the RAO, 45° LAO, and L Lat projections depict anterior-apical and septal wall asynergy (C, D, and E). Contrast study analysis (F and G) confirms severe anterior-apical dysfunction, with significant hypokinesis (Hypo) between chords 36 and 63; the septum could not be evaluated quantitatively from the single-plane contrast ventriculogram.

ischemic (*28*); 3) the presence of a discrete LV aneurysm (*29*); and 4) the contribution of segmental as opposed to diffuse LV myocardial dysfunction to congestive heart failure.

There is surprisingly little published data regarding the relationship between functional measurements made using clinically applicable RNA techniques and direct physiologic measurements. Previous studies have validated RNA global LV time-activity curves by comparison with LV time-volume curves derived from aortic flow (*30*). Studies have also compared RNA global ejection fraction and ejection rate values with those derived using ultrasonic crystals that measured LV chamber dimensions (*31*). Measurements of global and regional LV ejection fraction following acute coronary artery occlusion have been correlated with the extent of acute LV ischemia measured using radioactive microspheres (*10*) or with ultimate infarct size assessed histologically (*11*). Although the extent of ischemia was linearly related both to the change in global ejection fraction and regional ejection fraction following acute coronary occlusion, analysis of regional ejection fraction did not add substantially to the information yielded by analysis of global ejection fraction alone (*10*). Moreover, because of spatial superimposition of coronary artery myocardial distributions in RNA images, regional ejection fraction analysis fails to permit useful anatomic localization of the site of coronary occlusion (*10*). No study has been reported that compares qualitative or quantitative measurement of regional wall motion by any available technique with directly measured regional myocardial segment motion under conditions of myocardial ischemia and infarction.

The present RNA method for assessing myocardial dyskinesis is based on findings in dogs subjected to graded coronary artery occlusion (*6,12*). Smalling et al. (*6*) showed that acute myocardial ischemia in dogs produced early-systolic akinesis and early-diastolic shortening; they interpreted these findings as reflecting delayed, active contraction of ischemic myocardium. Akaishi et al. (*32*) have demonstrated that even during moderate coronary inflow restriction (40 mmHg diastolic coronary perfusion pressure) in the dog, the ischemic myocardial segment passively lengthens (bulges) as LV pressure rises during the isovolumic phase of systole. Pressure-length curves also suggest that the ischemic segment passively shortens (recoil) as LV pressure rapidly fails during the isovolumic phase of diastole (*12*). In the present study, early-diastole recoil was observed from the time of end-ejection, assessed by measuring aortic root pressure, to the time of onset of the ventricular filling phase of diastole. The pressure-length loops in figure 3 confirm that the abrupt decrease in length during isovolumic diastole proceeds until minimum LV pressure is reached. The magnitude of recoil varies directly ($r = 0.95$) with the magnitude of bulge (*12*).

Many clinical investigators have noted that zones of LV asynergy in contrast ventriculograms frequently demonstrate delayed inward motion (*33–35*). Whether this delayed motion reflects active contraction or passive recoil has been uncertain. A relationship to delayed electrical activation of ischemic myocardium has not been excluded. Pressure-length loops derived in man by Sasyama et al. (*7*) using contrast ventriculography and a micromanometer-tipped LV catheter appear to support the concept that motion of ischemic or infarcted myocardium is passively related to LV pressure.

Whatever the mechanism of asynchronous, dyskinetic LV wall motion, its ocurrence has provided nuclear cardiologists with a rationale for analyzing phase-angle histograms derived for individual picture elements of the RNA image after Fourier transformation of the time-activity data (*26,27*). Recently, Green at al. (*36*) presented a method for defining the ischemic zone in equilibrium RNA images of the acutely ischemic canine left ventricle. These investigators recognized paradoxical count decrease in the abnormal region during early diastole, but not paradoxical count increase during early systole (*36*). They did not measure regional myocardial segment length changes, and so they could not correlate their findings with direct physiologic measurements. We have developed a similar method for defining and characterizing the abnormal and normal zones of the RNA image. Time-activity curves derived for the abnormal and normal regions using this technique have features qualitatively similar to time-length curves recorded for the ischemic and and nonischemic myocardial segments using ultrasonic crystals (Fig. 2).

This RNA approach to quantitating regional myocardial dyskinesis involves the generation of subtraction images that represent the overall volume of systolic bulge and diastolic recoil. The bulge image is constructed by subtracting the end-diastolic frame from the frame at which the asynchronous, abnormal zone reached maximum counts; the recoil image is created by subtracting the frame at which the abnormal zone reached minimum counts from the end-systolic frame; the end-diastolic and end-systolic frame numbers are defined by the normal zone. These images express both the amplitude of dyskinetic bulge and recoil in the asynchronous zone as well as the overall extent of volume.

This RNA method was validated clinically by comparison with chord shortening analysis of contrast ventriculograms in a consecutive series of patients who had both studies. A limitation of this and all such studies is the fact that there is no generally accepted, standard quantitative technique for LV wall motion by contrast ventriculography. An objective method developed in a large population of normal patients and utilized in subsequent investigations (*14,15*) was adopted for this study. When chord shortening was used as the criterion against which other methods were tested, RNA bulge and recoil analysis compared favorably with visual interpretation of either RNA or contrast studies. Specificity for wall motion abnormalities in the apical LV wall was significantly higher for RNA bulge and recoil analysis than for either means of qualitative assessment.

It is concluded that RNA bulge and recoil analysis of regional LV myocardial wall motion rests on a sound experimental and clinical foundation. Because equilibrium RNA studies are noninvasive, widely available, and readily performed in a serial fashion, this physiologically based technique should have wide clinical applicability as a quantitative means to assess regional myocardial dyskinesis. It may be of particular utility in patients evaluated over time for unstable angina pectoris, acute myocardial infarction, and LV aneurysm to enhance estimation of the functional consequences and, perhaps, the prognostic implication. Because of its objectivity and physio-

logic validity, this RNA technqiue should also be useful in assessing the LV myocardial response to diagnostic interventions, such as nitroglycerin administration (*28*), atrial pacing (*37*), dynamic exercise (*16,17*), and to therapies such as coronary bypass surgery and angioplasty in patients with coronary artery disease.

APPENDIX

Preprocessing

In each animal or patient study, the RNA images were preprocessed using a 3 × 3 spatial filter and a seven-point weighted temporal filter and then analyzed to obtain two related types of functional images that represent: (a) the relative time-to-minimum counts for all picture elements (pixels) within the LV region of interest; and (b) the number of pixels within the LV that share common timing for attainment of minimum counts. First, a "minimum" image was created by setting each pixel to the minimum count value it achieved in any frame of the cardiac cycle. The minimum image was then subtracted from each image in the RNA study sequentially, resulting in a functional dynamic series that represented stroke volume changes per pixel in every frame of the cardiac cycle.

Assignment and Quantitation of Normal and Abnormal Regions

The technique for assignment of normal and abnormal regions is similar to that described by Green et al. (*36*). An LV end-diastolic region of interest was manually drawn and superimposed on the functional dynamic image series, which was displayed in a cinematic format. This image sequence representing stroke volume changes was then visually evaluated and the first LV region that had counts set to zero (i.e., a black zone in the LV region of interest) in the functional dynamic image series was considered to be a "normal" zone; this region was typically in phase with the entire RV and was assumed to reach minimum counts at true end systole. The region of the LV that continued to have measurable counts (i.e., a white zone in the image) was considered to be "abnormal." The LV end-diastolic region of interest was then superimposed on this individual frame from the functional dynamic image, and normal and abnormal regions of interest were manually assigned that were clearly within the LV region. Background-corrected time-activity curves were then created by using the assigned normal and abnormal zones as fixed regions of interest, with the average background counts per pixel determined from a region created manually over the lung adjacent to the heart. Regional time-activity curves were evaluated for baseline differences in the timing of maximum and minimum counts in the two zones (Fig. 1).

ACKNOWLEDGMENTS

The authors wish to thank Kathy Tuppeny for secretarial assistance.

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