Importance of temporal heterogeneity in assessing the contraction abnormalities associated with acute myocardial ischemia

A. E. WEYMAN, M.D., T. D. FRANKLIN, JR., PH.D., R. D. HOGAN, PH.D.,
L. D. GILLAM, M.D., P. S. WISKE, M.D., J. NEWELL, B.S., E. F. GIBBONS, M.D.,
AND RODNEY A. FOALE, M.D.

ABSTRACT A number of recent two-dimensional echocardiographic studies have attempted to relate quantitative changes in short-axis left ventricular radial wall motion to underlying myocardial ischemia/infarction. The significance of temporal variation in the contraction sequence within these ischemic regions in the overall evaluation of segmental left ventricular dysfunction, however, remains undefined. To assess this, we examined the motion of 192 individual radii that intersected known ischemic segments at 16.7 msec intervals from end-diastole to end-systole. The studies were performed in 13 dogs 1 hr after acute coronary ligation (six of the left anterior descending and seven of the circumflex coronary artery). Zonal of infarction were confirmed by triphenyltetrazolium chloride staining at the termination of the experiment and by a corresponding decrease of more than 75% in myocardial perfusion at the 1 hr sampling period. Dyskinesis (defined for each radius as negative or outward excursion relative to the end-diastolic reference on two consecutive fields) was noted along 168 of 192 radii (88%) at some point in the contraction sequence. The maximal outward or dyskinetic motion occurred most commonly in the fourth decile of the normalized contraction sequence. In 147 of the 168 dyskinetic radii (88%) the maximal outward motion occurred during the first half of systole while in only two radii in one animal was the maximal outward motion noted at end-systole. The total number of radii showing dyskinetic motion at any given point in the contraction sequence likewise varied with time. Although again the greatest number of radii showed abnormal motion during the fourth decile of the normalized contraction sequence, only 66 of 168 or 39% remained dyskinetic to end-systole. No relationship was observed between the point of maximal dyskinesis (time-weighted average of all dyskinetic radii for a given animal) and (1) the total number of radii showing dyskinesia, (2) the total number of radii within the infarct zone, or (3) the infarct area expressed as a percent of the slice area. The major factor determining persistence of dyskinesis to end-systole for any radius was the maximal outward motion of the endocardial segment at the point of maximal dyskinesis. Therefore, simple measurement of endocardial excursion from end-diastole to end-systole may fail to detect important wall motion abnormalities and, in some cases, may miss dyskinetic segments completely.

in the systolic contraction period rather than at end-systole, we decided to examine the temporal pattern of dyskinetic motion and its effect on the echocardiographic analysis of abnormal wall motion in an ischemic preparation. The purpose of this study, therefore, was to determine (1) whether there is significant temporal variability in the dyskinetic motion that characterizes ischemic myocardial dysfunction, and (2) whether temporal variability, if present, has an important effect on the echocardiographic analysis of abnormal wall motion.

Methods

To determine the temporal sequence of contraction within ischemic regions, serial short-axis cross-sectional echocardiographic studies of the left ventricle were performed in 13 closed-chest mongrel dogs before and at 1 hr after acute coronary ligation.

Animal preparation. To permit consistent echocardiographic visualization of the entire left ventricle in both the short- and long-term experimental settings, a closed-chest animal preparation specifically designed for echocardiographic studies was prepared 4 to 5 days before the actual experiment by a previously described technique. During the surgical preparation of the animals they were anesthetized with sodium pentobarbital (30 mg/kg iv) and ventilated with room air with the use of a Harvard respirator (model 940). A left thoracotomy was performed in each dog and a portion of one or two ribs (fifth and/or sixth) was removed from the left sternal margin laterally 5 to 6 cm to expose the anterior surface of the heart. The pericardium was then incised and a pericardial cradle was created by suturing the free edges of the pericardium to the inner surface of the chest wall. In this series of experiments, a silk snare (size 1) was then placed around either the left anterior descending coronary artery (LAD) distal to the first septal branch (six dogs) or the circumflex coronary artery distal to the first marginal branch (seven dogs). The silk snare was threaded inside a Teflon catheter, which was anchored to the thorax and tunneled under the skin to a pouch in the nape of the neck. A multihold silicone rubber catheter was also inserted into the left atrium via the atrial appendage for perfusion determinations and secured by a purse-string suture. This catheter was filled with heparinized Ringer’s solution and also tunneled under the skin to the previously mentioned pouch.

Epicardial markers made from acrylic-coated metal spheres (3 mm diameter) were then sutured in place at 2 cm intervals along the anterior, lateral, and posterior walls of the left ventricle to permit precise alignment of the imaging planes during subsequent echocardiographic studies. The thorax was then closed and the pneumothorax evacuated. After a 4 or 5 day recovery period, a preliminary echocardiographic study was performed to assess the adequacy of the preparation. If there was satisfactory visualization of the left ventricle from apex to base, the animals were premedicated with morphine sulfate (3 mg/kg im) and reanesthetized with either sodium pentobarbital (30 mg/kg) in the LAD series, or α-chlorolose (60 mg/kg) in the circumflex series. The α-chlorolose was dissolved in 5% dextrose in water at 42° C and continuously stirred with a magnetic stirrer throughout the entire experimental period. Usually about 120 ml (1200 mg) were required for initial anesthesia and this was supplemented with 45 ml (450 mg) every hour, as necessary. A 20-gauge, 2 inch angiocatheter was secured in the brachial vein for administration of the anesthetic. Both femoral arteries were cannulated to the level of the aorta for reference blood samples and a Millar micromanometer-tipped catheter (model PC471) was placed in the left ventricle via the carotid artery. A lead II electrocardiogram, the left ventricular pressure, and the first derivative of the left ventricular pressure were recorded throughout the experiment on a Beckman multichannel strip-chart recorder (model R611) and displayed on a multichannel oscilloscope (EO-18).

Collection of echocardiographic data. Before coronary ligation, control short-axis cross-sectional echocardiographic scans were obtained at multiple levels of the ventricle. These studies were performed with an ATL Mark III mechanical sector scanning system with either a 3.0 or 5 MHz transducer and recorded on 1/2 inch videotape with the use of a Panasonic NV 8200 VHS videorecorder. The location of the examining plane at each level was fixed by triangulation with the three strings of epicardial markers described earlier. In addition to permitting precise alignment of each plane, the epicardial markers also provided a fixed external reference that could be used to correct for the rotation of individual planes and for realignment of sequential planes. The number of planes visualized in each experiment was determined by the size of the ventricle, the distance between the epicardial markers, and the adequacy of recording at each level. Once the control echocardiographic study was completed, radiolabeled microspheres were injected to confirm the presence of normal coronary flow before coronary occlusion. After the microsphere injection, the previously ensnared coronary artery was ligated. One hour after the ligation, the echocardiographic studies were repeated and coronary perfusion was again assessed with a second radioactive marker.

Analysis of echocardiographic data. Results of all echocardiographic studies were initially reviewed to select areas of optimal endocardial visualization. Selected cycles were then transferred to a videodisk (Sony SVM 1010) for field-by-field analysis. Figure 1 illustrates the normal short-axis appearance of the canine ventricle and the type of image available for analysis.

To assess the temporal pattern of contraction, the position of the endocardial interface during each video field from end-diastole to end-systole was digitized with a track-ball digitizer and an FS computer image display and analysis system. End-diastole was defined as the field with the largest cavity area following the R wave of the electrocardiogram and preceding the initial inward motion of the noninfarcted wall, while end-systole was taken as the field with the smallest cavity area. For purposes of this study, the endocardial outlines from only the plane intersecting the second of the series of equally spaced epicardial markers, which correspond roughly to a short-axis plane through the base of the papillary muscles, was digitized. Once digitized, the centroid for each frame was calculated as the endocardial center of area and from these individual centroids, an average center for all frames (a nominal point in space) was calculated. This average center was then used as the fixed reference point to which all radial motion was related. To compare contraction at similar points around the ventricular short axis for all fields in all animals, the endocardial outline for each field was translated in space and rotated around the centroid until the zero reference of the radial coordinate system was aligned such that it bisected the papillary muscles. The boundaries were then smoothed with a convex-hull algorithm that eliminates points that are not concave toward the centroid and therefore cannot contribute to contraction. Radial distance from the center was then normalized and motion expressed as percent excursion along each of 36 individual radii separated by 10 degree intervals. Figure 2 illustrates, in simplified diagrammatic format, the relationship of the radial coordinate system to the endocardial outlines of the ventricle as well as the method for depicting endocardial motion along each radius over time.
Histologic definition of infarct area. At the end of the experiment (6 hr after ligation) the animals were killed, their hearts were excised in toto, and the coronary ligatures were removed. The left coronary artery of each was then perfused with 300 ml of triphenyltetrazolium chloride (TTC) solution (2,3,5-triphenyltetrazolium chloride, 5 g/250 ml normal saline) with the use of a Grey cannula and perfusion pressure of approximately 85 mm Hg. The right coronary artery was subsequently perfused in a similar fashion with 200 ml TTC. The heart was then frozen to facilitate sectioning. Once frozen, the heart was sectioned parallel to the ventricular short axis along planes defined by each set of epicardial markers. The two surfaces of each cut section were then photographed and the area of infarction was defined relative to the region of TTC uptake.

Perfusion determination with microspheres. To establish that regional myocardial perfusion was not altered in the preparation of the animals, as well as to document that the coronary ligation resulted in a decrease in regional perfusion at the 1 hr sampling period, regional left ventricular blood flow was measured during the control period, at 1 hr after ligation and before termination of the experiment. Perfusion was determined with 7 to 11 μm microspheres (New England Nuclear). For each flow measurement, the vial containing the microspheres was mechanically agitated for at least 3 min to disperse the spheres. The microsphere-containing solution was then injected rapidly into the left atrium via the preplaced catheter and the catheter was flushed with 5 ml of saline. Beginning 1 min before injection and continuing for 3 min thereafter, blood for determination of reference flow was withdrawn simultaneously from the two femoral artery catheters at 2.0 ml/min. Radiolabels were randomly selected from six different markers (146Ce, 131Sn, 85Sr, 51Cr, 46Sc, 131I, 95Nb). At the end of the experiment, after the ventricular slices were photographed for histologic mapping, each slice was sectioned into approximately 2 g pieces. Each piece was then further subdivided into an endocardial and epicardial half. By standard techniques, the myocardial and reference blood samples were then counted and myocardial blood flow for each segment was calculated (in ml/100 g/min).

Identification of echocardiographic radii falling within infarct zones. Having defined the zone of histologic infarction from the region of TTC uptake for each slice, the endocardial outline from the photographed anatomic section was digitized and the center of area for the slice was calculated. With the use of this center of area as a central reference, the margins of the area of infarction were first defined as indicated in figure 3. A clear plastic overlay with radii separated by 10 degrees was then superimposed on the anatomic section and rotated until the 0 degree reference of this radial coordinate system bisected the papillary muscles. This alignment was similar to that used to orient the echocardiographic coordinates, and echocardiographic rays falling within the region of histologically defined infarction were thus determined. Once these radii were identified they were analyzed individually for (1) the presence of dyskinesis at any point in the contraction sequence, (2) the point in the contraction sequence at which maximal dyskinesis along each radius occurred, and (3) the total number of radii within the infarct zone showing dyskinetic motion at each sampling period.

Only radii showing evidence of dyskinesis were chosen for analysis because dyskinesis is a clearly defined phenomenon and is generally accepted to be abnormal. Hypokinesis is a less clear descriptor because of the wide range of normal values and therefore has a tendency to be a relative value.2 True absence of motion, or akinesis in the intact beating heart, was virtually never observed in this or subsequent studies. Dyskinesis was defined as a negative or outward movement along any radius that was present during two consecutive sampling points not including the initial increment in the contraction sequence. This definition was used to exclude any small residual shape change occurring in the initial step in the contraction sequence as well as the random outward movements occasionally noted throughout the ventricle in both normal and abnormal areas.

Interobserver and intraobserver error estimates. Expected errors in fractional excursions (FE) measured from two-dimensional echocardiograms with average–centroid translation correction were estimated. To obtain these estimates, three cycles from each of six animals were digitized by two different echocardiographers (raters) at each of two independent times. A total of 720 frames were digitized and FEs between frames were measured along 72 radii. These data were input to the BMDP Statistical Software22 running on a VAX 11/780 computer and all subsequent analyses were performed with the use of BMDP programs (BMDP8V).
Expressing FE as percentage excursion (PE), the components of variance of PE estimated for this model by P8V were as follows: animals 177, cycles 10.6, reps (raters and times) 14.3. The animals component of variance only describes normal expected interanimal variation in PE (in this case, SQRT (177) = ±13.3%) and therefore was discarded. The reps component represents intraobserver error insofar as it can be separated from normal cycle-to-cycle variation in PE, which in turn is estimated by the cycles factor. Therefore, the resulting best estimate of error expected in a single PE measurement in SQRT (10.6 + 14.3) = ±5%. This ±5% error in PE is due about equally to normal intercycle variation and interobserver variation and therefore could be reduced by averaging several cycles, e.g., for four cycles approximate SQRT (10.6/4 + 14.3) = ±4.1%. For a large number of averaged cycles this error reduces at a minimum to the interobserver error alone, or SQRT (14.3) = ±3.8%.

**Statistical analysis.** In assessing the significance of difference in parametric data, an unpaired t test was used. The correlation coefficients and linear regression equations for pairs of data were calculated by the method of least squares. A p value less than .05 was considered significant.

**Results**

A total of 192 individual radii were identified that intersected zones of histologically defined infarction. Of these 192 radii, 168 (88%) showed evidence of dyskinetic motion at some point in the systolic contraction sequence. The point within the normalized contraction sequence at which the maximal degree of dyskinetic motion occurred along each of the 168 dyskinetic radii is illustrated in figure 4. As this graph indicates, the maximum abnormality in motion occurred most commonly in the fourth decile of the normalized contraction sequence (57/168, 34%). Furthermore, along 88% of these radii (147/168) the maximal outward or dyskinetic motion occurred in the first half of the normalized contraction period, while in 70% (118/168) it occurred in the second quartile. Importantly, the maximal outward or dyskinetic motion was

![FIGURE 2. The relationship of the radial coordinate system to the endocardial intercepts of the ventricular cavity. Left. The radii are plotted at 30 degree intervals for simplicity and the endocardial intercepts are depicted only at end-diastole and end-systole. In actual practice, radial excursion was measured at 10 degree increments and all the fields from end-diastole to end-systole were digitized. Right. The type of three-dimensional plot that can be generated from this data. In this plot, the change in normal distance of the endocardial intercept of each radius from the ventricular centroid is plotted over time for three cycles. In this idealized example, ventricular contraction and relaxation are assumed to be symmetric and area is represented as a sine wave. At end-diastole the endocardial intercept along each radius is at its greatest distance from the ventricular centroid while at end-systole, the endocardial intercept is closest to the centroid and therefore the ray length is shortest. The distance from the peak of each wave to the nadir represents an individual systolic contraction. In this example, rays were again plotted at 30 degree intervals for simplicity.](http://circ.ahajournals.org/content/circulation/70/1/105)

![FIGURE 3. Method for defining radii that intersect the area of anatomic infarction. Initially, the centroid for the endocardial area of the anatomic slice is calculated and the rays that intersect the two margins of the infarct or the infarct tangent are defined. The echocardiographic coordinate system is then superimposed on the infarct plot and is oriented to achieve comparable alignment. All echocardiographic rays falling within the infarct tangent are then identified and their contraction patterns are analyzed independently.](http://circ.ahajournals.org/content/circulation/70/1/105)
shown to occur after the first half of the systolic contraction period by only 12% of all radii, while only two radii in a single animal showed maximal outward motion at end-systole. In five of the 13 animals all radii within the infarct zone showed evidence of dyskinesis while in the remaining eight animals individual radii did not. In each of these eight cases, however, the dyskinetic radii were contiguous.

The total number of radii within the ischemic zones showing evidence of dyskinesis during each decile of the normalized contraction sequence is illustrated in figure 5. Significantly, there was no point in the contraction sequence at which all 168 dyskinetic radii were moving abnormally. Again, the greatest number of radii showed abnormal motion during the fourth decile of the normalized contraction sequence, with only 66 of 168 (or 39%) remaining dyskinetic to end-systole.

Figure 6 graphically depicts the effects of this temporal pattern of dyskinesia on any analysis of segmental wall motion. This three-dimensional plot depicts, for a single animal, the absolute excursion of the endocardium from end-diastole to end-systole in 10 degree increments from 0 to 360 degrees. The radii falling within the zone of infarction are indicated by the heavier dark line. In this graphic display, there is an obvious dyskinetic bulging in the early portion of the contraction sequence in the ischemic area. By end-systole, however, the position of the endocardial interface is closer to the center of the ventricular cavity than at end-diastole, indicating a positive inward motion and that the amplitude of contraction of individual radii overlaps that of radii derived from normal zones. Thus, in this example, simple analysis of end-diastole and end-systole would have resulted in the profound dyskinetic motion present earlier in the contraction sequence being overlooked.

Effects of infarct size and location on the temporal pattern of contraction. The percent histologic infarction (measured as planimetered infarct area/total slice area) was larger for the animals with anterior wall infarction (LAD group) (mean 38%, range 27% to 50%) than for the group with posterior wall infarcts (circumflex group) (mean 25%, range 11% to 37%; p = .05). The

FIGURE 4. Histogram depicting the number of radii showing maximal dyskinetic or outward motion at each decile of the normalized systolic contraction sequence.

FIGURE 5. Histogram showing the total number of radii showing dyskinetic motion at any point in the normalized contraction sequence.

FIGURE 6. Actual three-dimensional plot of radial wall motion from end-diastole to end-systole for each of 36 radii around the circumference of the ventricle. The segment plotted here corresponds to the end-diastolic to end-systolic period illustrated in figure 2, right. The ray length is in centimeters from the ventricular centroid. The ischemic zone is indicated by the darker solid line. A prominent mid-systolic bulge is noted.
mean number of radii falling within the infarct zones was likewise greater for the LAD group (15.3, range 10 to 22) vs the circumflex group (14.4, range 12 to 20). This difference was not statistically significant, however, indicating that the difference between these two groups was primarily in the transmural rather than the circumferential extent of infarction. When the point of maximal dyskinesis for each animal (taken as the time-weighted average) was compared to (1) the total number of radii showing evidence of dyskinesis, (2) the total number of radii within the infarct zone, or (3) the infarct area expressed as a percentage of the slice area, no relationship could be demonstrated either in the entire group of animals taken together or in the LAD and circumflex groups individually.

While the infarct density or transmural extent of infarction did not appear to affect the timing of maximal dyskinesis, it did appear to influence the percentage of the radii within the infarct zone that were dyskinetic. Thus, when infarct density defined as percentage slice area infarcted/percentage circumferential infarct was examined the animals within each group (LAD and circumflex) in which all radii within the infarct zone were dyskinetic had the greatest infarct density. In the LAD group, while there was a clear separation in infarct densities between animals in whom all radii in the infarct zone were dyskinetic (mean 1.29, range 1.19 to 1.59) and those in whom only a portion of the radii in the infarct zone were dyskinetic (mean 0.82, range 0.44 to 1.00), the number of samples was too small to allow determination of statistical significance. In the circumflex group, however, there was a significant difference (p < .05) between the mean infarct density for animals in whom all radii in the infarct zone were dyskinetic (mean 0.78, range 0.66 to 0.88) vs those showing showing heterogeneous contraction (mean 0.49, range 0.33 to 0.59).

Relationship of the temporal pattern of contraction to heart rate and blood pressure. Heart rate for the total group of animals varied from 100 to 120 beats/min, with an average systolic ejection period of 203 msec. Within this range, there was no correlation between heart rate and timing of maximal dyskinesis. Likewise, there was no relationship between either peak (mean 114 mm Hg, range 100 to 120) or mean blood pressure (92.5 mm Hg, range 85 to 100) and timing of maximal dyskinesis.

Factors affecting persistence of dyskinetic motion to end-systole. Finally, we examined why dyskinetic motion, once established, persisted along certain radii to end-systole, while along others, it was evident only during the early portion of systolic contraction. The major determinant appeared to be the amplitude of initial systolic dyskinetic motion. Thus, the maximal outward motion for radii that remained dyskinetic to end-systole was $-29.8 \pm 13\%$ compared with only $-11.4 \pm 7\%$ for radii showing no dyskinesis at end-systole ($p < .001$).

Discussion

The results of this study demonstrate that (1) there is marked temporal and spatial variability in the abnormal wall motion that characterizes acute myocardial ischemia, (2) the maximum degree of abnormal motion is most often found in the first half of the systolic contraction period rather than at end-systole, and (3) by end-systole, more than 60% of the radii that show dyskinetic motion early in the contraction period are no longer moving paradoxically. These findings have important implications for all echocardiographic analyses of abnormal wall motion and may be extrapolated to similar studies in which other imaging methods are used. They suggest that, since the maximal outward movement along radii selected from within ischemic zones occurs during the first half of the normalized contraction sequence, simple analysis of end-diastolic and end-systolic frames may fail to reflect the major quantitative wall motion abnormalities that occur in the acute phase of myocardial infarction. This is emphasized by our observations that only 1% of dyskinetic radii showed their maximum outward motion at end-systole and that less than 40% of the radii that moved paradoxically early in the contraction sequence were still dyskinetic at the end of the systolic contraction period.

Unfortunately, despite the tendency for the maximal motion abnormality to occur in the second quartile of the normalized contraction sequence, the fact that at most only 34% of all radii showed their maximal motion abnormality within any given decile suggests that no fixed temporal point in the contraction sequence can be arbitrarily selected that will consistently allow determination of the maximal degree of abnormal motion either for all radii within an individual animal or across animals.

These data also indicate that within ischemic zones the size of the dyskinetic area varies with time during contraction. As indicated in figure 5, just under half of dyskinetic radii show some outward motion in the initial frame after the onset of systolic contraction. This dyskinetic wave front then gradually expands along its margins to reach a maximum during the fourth decile of the normalized contraction sequence and, having reached its maximum, gradually recedes to a mean size

Vol. 70, No. 1, July 1984
at end-systole that is slightly less than that in the initial systolic frame.

Thus, correlations between infarct size and any quantitative descriptor of wall motion, such as dyskinesis, will vary markedly based on the point in the contraction sequence at which these measurements are made.

Finally, even within zones of infarction, all dyskinetic radii do not show evidence of paradoxical motion at any given point in the contraction sequence. Thus, of a total of 168 radii that showed dyskinesis at some point in the contraction sequence only 141 or 84% were all moving dyskinetically at the point at which the dyskinetic wave front was at its maximum. Here again, while the initial conclusion might be that selection of the fourth decile of the contraction sequence would provide the optimal descriptors of both the extent and degree of abnormal motion, there is sufficient variation along individual radii to preclude such arbitrary selection. Consideration of this dyskinetic motion in terms of a wave front, however, seems reasonable since all dyskinetic radii within the infarct zones were contiguous and their overall pattern of motion suggested phasic expansion and contraction as systole progressed.

The basic observation that functionally and temporally disordered ventricular contraction occurs in response to myocardial ischemia/infarction is well established and the detection of such abnormal patterns of myocardial contraction in man has become an accepted criterion for inferring the presence of myocardial ischemia, infarction, or scarring.13-32

Of the different patterns of abnormal contraction that have been described, dyskinesis or paradoxical systolic bulging of a myocardial segment is the most clearly defined and its mechanisms have been extensively studied.25, 27, 33 The timing in systole of such paradoxical bulging has received less attention, although significant variation has been noted during frame-by-frame analysis of angiographic studies.25, 30, 34, 35 In such studies in man, predominant early systolic paradoxical or dyskinetic motion has been observed in patients with critical coronary lesions both with and without prior infarction.13, 14, 15, 30 The dyskinetic motion in these abnormal segments has been associated with an increase in wall curvature consistent with an aneurysmal bulge15 and in many cases, wall motion in the affected region has been noted to return toward normal by end-systole.13, 15, 16, 30 While these angiographic findings appear to confirm the temporal pattern of contraction noted in our study of acute ischemia, direct comparison is difficult since they generally represent data derived from heterogenous populations of patients with established coronary artery disease, including many with evidence of old myocardial infarction or with angiographic evidence of critical coronary narrowing without total coronary occlusion.

Careful examination of studies in which other techniques were used in the experimental preparation of acute ischemia, however, reveals similar findings. Bawka and Helfant,36 for example, using epicardial segment length gauges, demonstrated a roughly 120% increase in segmental length in the ischemic zone at 1 hr after coronary occlusion, which their figures suggest reached a peak midway between the onset of isovolumetric segment lengthening and initial systolic relaxation (i.e., during the first half of systole).

Theroux et al.,18, 19 using implanted sonomicrometers, and Kerber et al.,20 using M mode echocardiography, likewise noted holosystolic myocardial expansion in ischemic regions immediately after occlusion. Inspection of their data suggests that the maximal ischemic segment lengthening occurred roughly 40% of the way between the onset and termination of systole.

The sonomicrometric measurements reflect the distance between fixed points within the ischemic zone, and as such appear to correspond more closely to our data concerning the number of radii showing dyskinesis at each point in the normalized contraction sequence than to the maximal degree of dyskinesis. Likewise, the fact that both the M mode echocardiographic and sonomicrometric measurements showed segmental lengthening persistent to end-systole in all probability reflects selection of the center of the infarct zone for the sampling area. In our tomographic method, in contrast, all radii that fall within the infarct zone are used, not just those intersecting the infarct center. Significantly, in our series, both the maximal dyskinetic motion along individual radii and the tendency of radii to remain dyskinetic to end-systole was uniformly most obvious in the infarct center.

The temporal pattern of dyskinetic motion noted in this study appears to be related to the timing and sequence of peak tension and pressure development in the left ventricle.37, 38 It is well established that as muscle tension rises in the ischemic ventricle, the underperfused area is unable to build up sufficient local tension to maintain the radius of curvature demanded by contraction. It therefore assumes a shape of smaller radius that will support intracavitatory pressure, which results in the initial formation of an aneurysmal bulge.25 While the mechanism by which the aneurysmal bulge forms is understood, the factors that affect the amplitude and timing of radially directed motion
within the ischemic region are less well defined. The net motion of any point along the endocardial interface at any interval in time should be determined by the residual tension that can be developed by the ischemic muscle, the stress on the wall in the affected area (which is proportional to the intracavitary pressure and the local radius of curvature of the involved segment), and the passive mechanical motion imparted to the region by the contraction of normal adjacent myocardium. In the normal ventricle, wall stress drops during ejection despite the continued increase in intracavitary pressure due to the decrease in local radius of curvature that accompanies the diminishing chamber volume.\(^37\) The ischemic segment, however, is already operating at a diminished radius of curvature at the onset of ejection due to the aneurysmal bulge and wall stress in this region should be more dependent on the effects of intracavitary pressure during the initial phase of ejection. The result is that the aneurysmal segment may continue to expand in some cases after stress in the remaining areas of the ventricle has begun to fall. Furthermore, since the mechanical effects of contraction in surrounding areas will have a varying effect on different portions of the ischemic zone, the sum of forces acting at any given point in the ischemic zone is complex and constantly changing, which undoubtedly accounts for the individual radial variability noted in this study. Despite this variability, the maximal distending and expanding forces appear to occur along the majority of radii at a point at which cavity pressure and local radius of curvature combine to produce maximal wall stress in the ischemic segment.

In comparing the methods and results of this study to those of others, it is of particular importance to consider the fiducial points used to define end-diastolic and end-systolic volume and its diameter. Since the majority of data concerning the temporal sequence of left ventricular contraction is based on frame-by-frame analysis of angiographic studies, we have used the angiographic precedent assuming that the frame with the largest cavity area represents end-diastole and that with the smallest cavity area, end-systole.\(^39\)\(^-\)\(^43\) In using these references, we believe that we have included both the isovolumetric and ejection phases of systolic contraction. This assumption is based on the expected changes in ventricular shape that occur during isovolumetric contraction. Rushmer\(^44\)\(^-\)\(^46\) and Hawthorne\(^47\) have shown that, in the open-chest animal, the shape of the ventricle tends to become more spherical during isovolumetric contraction, while in the closed-chest dog the ventricle shifts toward a more elliptical configuration. They have further demonstrated that these changes in shape relate to ventricular volume, with the ventricle becoming more spherical during isovolumetric systole at lower volumes and more elliptical with increasing ventricular volume. Since the open-chest animal is relatively volume depleted, sphericalization is noted in that preparation. In man there appears to be a general agreement that the transverse diameter of the endocardial cavity decreases during the pre-ejection phase of systolic contraction,\(^48\)\(^-\)\(^50\) while the epicardial transverse diameter increases because of muscular thickening.\(^45\) Although the model used in the present series of experiments cannot be considered a pure closed-chest preparation, the animals were studied well after the initial thoracotomy, at a point when volume loading should have been normal. We therefore assume that there would be minor dimensional shortening, rather than sphericalization, during the isovolumetric phase of contraction. Thus, by selecting the frame before the onset of initial inward motion as end-diastole, we included the isovolumetric contraction phase.

Furthermore, by choosing the frame with the smallest cavity area to represent end-systole, we included the period of systole up to end-ejection, but not isovolumetric relaxation. This is consistent with the data of Ruttley et al.\(^42\) and Marier and Gibson,\(^31\) which show a slight, but significant, increase in left ventricular chamber diameter and angiographically measured volume during the isovolumetric phase of ventricular relaxation.

There are several limitations to our method that may have affected our results. First, precise registration of anatomic and echocardiographic sections is extremely difficult despite the use of external markers and internal references since the echocardiographic radii are plotted when the ventricle is volume distended and contracting while those that intersect the infarct are defined from an excised fixed heart section that is typically shrunken and slightly deformed. In addition, the plotted centroid for the formalin-fixed anatomic slice will not correspond exactly to the calculated center for the echocardiographic image and thus the ray position will vary slightly. Thus, some radii at the margins of the infarct zone that, in vivo, actually transect zones of infarction may, in the postmortem alignment process, be defined as falling outside the infarct zones, while others that fall within the more normal regions may be included within what is presumed to be the TTC-defined area of infarction. Because of our dual reference system, however, we would anticipate this number to be very small and, given the consistency of our data, to have little effect on our overall results. Second, our method of defining dyskinesis is
clearly arbitrary. This method was chosen since it has become obvious in studying numerous animals that all radii do not move synchronously at the onset of contraction and it is common both in the normal and abnormal ventricle to see scattered outward or dyskinetic motion in the initial frame after the onset of contraction. Thus, we felt it important to eliminate this random initial outward movement from our definition of dyskinetic motion. It was likewise apparent in the digitization process that occasional random fluctuations in tracing the endocardial border resulted in sporadic outward movements throughout both the normal and ischemic zones in an individual frame. Thus, we believed that the inclusion of outward motion for only one field generated meaningless data, and as a result, we have defined dyskinesis as outward motion present during two consecutive fields along the same radius not including the first frame. Third, it is possible that the preparation itself might have induced some of the abnormalities that we noted. Here again, in each study control recordings were obtained that showed symmetrical contraction around the ventricle in each animal before coronary ligation. In each animal for each ray, a correlation was plotted between the motion along each individual ray around the 360 degree circumference of the ventricle with a recognized contraction slope derived from pooled normal data. In no experiment did control contraction fall outside the 95% confidence limits for this correlation. Thus, we are confident that the preparation does not introduce artifacts of motion in the control setting. The loss of pericardial constraint, however, might permit more outward motion during the ejection phase than would be noted were the pericardium intact. The same problem, however, would be encountered in all open-chest animal experiments, including those using strain gauges, sonomicrometers, and M mode echocardiography. The angiographic observation that predominant outward motion occurs early in the systolic contraction phase in the ischemic human ventricle with an intact pericardium again suggests that the opened pericardiums of the dogs did not significantly affect our data. Likewise, the similarity between data from the anterior wall infarct group, in which the myocardium was totally free to expand, and that from the posterior wall group, in which the ischemic myocardium rested against and was partially restrained by the posterior surface of the thorax, suggests that lack of pericardial constraint did not play a major role in these observations. To test this further, we performed three additional experiments in intact, anesthetized animals in which coronary occlusion was produced by inflation of a balloon-tipped catheter placed within a coronary artery under fluoroscopy. In each of these animals a clearly defined area of dysnergy was noted and a total of 24 dyskinetic radii were identified at 1 hr after occlusion. Of these 24 radii, 50% (12), 25%, 12.5%, and 12.5% showed maximal dyskinetic motion in the fifth through eighth deciles of the normalized contraction period, respectively. Thus, in a totally different preparation with an intact pericardium and at significantly different heart rates, it was still apparent that maximal dyskinesis occurred in the middle of the contraction sequence rather than at end-systole.

The effects of time after ligation on the pattern of temporal and spatial heterogeneity should be considered. Although data are presented here only for the 1 hr period after ligation, we also obtained samples, as part of the current protocol, at 10 min and 2, 4, and 6 hr after coronary ligation. In this acute phase after coronary ligation we noted no difference in the temporal sequence of contraction and have thus elected to present the data for only the 1 hr period.

Finally, the effects of left ventricular pressure and heart rate on the timing of contraction must be considered. Since it was our purpose to determine the natural history of abnormal wall motion after acute coronary ligation, no attempt was made to vary either heart rate or left ventricular pressure. The M mode echocardiographic studies of Kerber and Abboud, however, suggest that increasing heart rate did not significantly alter the amplitude of the aneurysmal bulge in the center of the infarct or alter systolic wall excursion. In their studies, the elevation of blood pressure to approximately equal levels by administration of different drugs produced varying effects. These were related to the nature of the pressor used and its individual effect on myocardial contractility and on end-diastolic left ventricular diameter. Further studies are therefore necessary to determine precisely the effects of variations of preload and afterload on the temporal and spatial pattern of dyskinetic motion within ischemic segments.

Our results demonstrate that there is significant temporal and spatial heterogeneity in both the timing and extent of maximal dyskinesis within ischemic zones in the immediate postinfarction period. Maximal dyskinesis or aneurysmal bulging is most commonly observed during the fourth decile of the normalized contraction period. The maximum breadth of the dyskinetic zone, as reflected by the absolute number of radii showing dyskinesis at any point in the contraction sequence, also occurs at this temporal point. Simple measurement of contraction from end-diastole to end-
systole may therefore miss the maximal functional abnormality associated with acute myocardial ischemia and an alternate method of integrative analysis needs to be developed that takes into account both variations in space and time.

References


24. Harrison TR: Some unanswered questions concerning enlargement and failure of the heart: Am Heart J 69: 100, 1965


41. Hamby RI, Aintablian A, Tabrah F, Reddy K, Wisoff G: Late
44. Rushmer RF: Physical characteristics of myocardial performance. Am J Cardiol 18: 6, 1966
47. Hawthorne EW: Dynamic geometry of the left ventricle. Am J Cardiol 18: 566, 1966
49. McDonald IG: The shape and movements of the human left ventricle during systole: a study by cineangiography and by cineradiography of epicardial markers. Am J Cardiol 26: 221, 1970
Importance of temporal heterogeneity in assessing the contraction abnormalities associated with acute myocardial ischemia.

A E Weyman, T D Franklin, Jr, R D Hogan, L D Gillam, P S Wiske, J Newell, E F Gibbons and R A Foale

Circulation. 1984;70:102-112
doi: 10.1161/01.CIR.70.1.102

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1984 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/70/1/102