LABORATORY INVESTIGATION
CORONARY ARTERY DISEASE

The natural history of regional dysfunction in a canine preparation of chronic infarction

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ABSTRACT We used a canine preparation of experimental infarction to study the natural course of echocardiographically defined regional wall motion abnormalities in the 6 weeks after acute coronary ligation. Eight dogs underwent serial short-axis echocardiographic evaluation and microsphere blood flow determinations at control, and 30 min, 48 hr, 1 week, 3 weeks, and 6 weeks after acute coronary artery ligation. Wall motion analysis and blood flow calculations were applied to 10 degree radial segments of the left ventricle (short axis) and correlated to the size and extent of infarction as defined histologically at 6 weeks. All animals had at least 50% transmural histologic infarction. The ratio of flow in infarcted tissue vs noninfarcted myocardium fell to 0.40 ± 0.13 for endocardium and 0.56 ± 0.13 for epicardium at 30 min after ligation, but recovered to 0.83 ± 0.15 for endocardium and 1.12 ± 0.11 for epicardium by 6 weeks. The maximum circumferential extent of abnormal regional wall motion was observed at 48 hr after infarction (mean circumferential extent = 51%), but was resolved to a significant extent by 6 weeks (circumferential extent = 21%, p < .0001). Four animals had virtually normal wall motion by 6 weeks after infarction. Segment-by-segment regional dysfunction correlated highly with the regional transmural reduction in blood flow of 20% (r = .89, p = .0001) for the experiment as a whole, but the echocardiogram tended to underestimate the size of the histologic infarct at 6 weeks. We conclude that the natural history of regional dysfunction in a canine preparation of chronic infarction is characterized by significant resolution of abnormal contraction in the area of the infarct and occurs concomitantly with normalization of transmural blood flow.


A NUMBER OF cross-sectional echocardiographic studies2-7 have examined the relationship of abnormal segmental wall motion to infarct size in acute experimental myocardial infarction. These studies uniformly indicate that cross-sectional echocardiography can be used to identify regions of acute ischemia/infarction with use of traditional methods of wall motion analysis and that the extent of dysfunction consistently overestimates the histologic span of the infarct as defined at postmortem examination. Surprisingly little is known, however, about the natural history of these regional wall motion abnormalities beyond the acute phase of the infarction process.

Hemodynamic data indicate that global left ventricular function begins to improve within the first week after acute coronary ligation8-10 and is virtually normal 4 to 6 weeks after experimental infarction in the dog.11 Sonomicrometric studies of chronic infarction12-13 suggest that areas that are dyskinetic in the early infarct period tend to become akinetic by 4 weeks and that the circumferential extent of infarction tends to shrink over time during the process of scar formation and contraction.

It is not clear, however, whether the observed improvement in global left ventricular function is the result of the conversion of areas of dyskinesis to regions manifesting lesser degrees of dysfunction or to compensatory hyperfunction of noninfarcted muscle. Although cross-sectional echocardiography appears to be ideally suited to the confirmation of the pace and character of the recovery of left ventricular function,14,15 its role in assessing these phenomena is as yet undocumented. The purpose of the present study, therefore, was threefold: (1) to define the natural history of regional wall motion abnormalities over the 6 weeks after experimental canine infarction by use of cross-sectional echocardiography, (2) to correlate these regional wall motion abnormalities with simultaneously determined microsphere blood flow data, and
(3) in so doing, to further validate a method of quantitative wall motion analysis that integrates both the spatial and temporal variations in regional motion.

Materials and methods

Animal preparation. A total of 25 mongrel dogs were used to provide a net number of 12 dogs with complete sets of data; 13 dogs either died or had technically inadequate studies in one or more time periods. A standardized closed-chest preparation tailored to facilitate long-term echocardiographic imaging was employed. Under general anesthesia, a left lateral thoracotomy was performed, approximately 8 cm of the anterior fifth and sixth ribs was resected, and a pericardial cradle was fastened to the chest wall. A silk snare with a Teflon occluder was placed around the left circumflex coronary artery (five dogs) or the left anterior descending artery (three dogs) or sham snared (four dogs) and a silicone rubber catheter was placed in the left atrium. The snare and left atrial catheter were tunneled under the skin to a pouch at the posterior nape of the neck. The thorax was then closed, the pneumothorax was evacuated, and the animal was allowed to recover.

Two to four days later the dogs were reanesthetized, intubated, and ventilated with oxygen-enriched air, the concentration of which was adjusted according to arterial blood gas measurements. The anesthetic agent used was \( \alpha \)-chloralose (60 mg/kg). A femoral arterial line was placed for blood pressure monitoring and fixed-rate arterial blood sampling. Baseline echocardiographic images were recorded and time 0 microsphere injections were made for preocclusion blood flow determination. The previously placed coronary snare was then tightened to achieve complete occlusion in the eight experimental animals. At intervals of 30 min, 48 hr, 1 week, 3 weeks, and 6 weeks thereafter, the echocardiographic examination and radioisotope microsphere injections were repeated. Immediately after the 6 week injection, the animals were killed with an overdose of sodium pentobarbital.

Acquisition of data

Echocardiography. Cross-sectional echocardiographic images were obtained with an ATL Mark III mechanical sector scanner and a 3.5 MHz transducer and were stored for subsequent analysis on \( \frac{1}{2} \) inch videotapes. A standard midpapillary muscle short-axis view was used for all wall motion analysis, with use of internal cardiac landmarks as points of triangulation to ensure continuity of long-term serial study.

Histologic definition of infarction. At the end of the experiment, the hearts were excised in their entirety, formalin fixed, dissected free from the right ventricle, and sectioned transversely into 2 cm sections. Concordance between the midpapillary muscle anatomic section and the echocardiographic imaging plane was established by morphologic similarity. After fixation and sectioning, the slices were oriented to a radial coordinate platform and stained with hematoxylin-eosin and Masson trichrome and the extent of infarction was defined by whole-mount mock-up maps oriented to the previously defined radial coordinates (figure 1).

Radioisotope-microsphere measured blood flow. Established techniques were used for determination of regional blood flow. Specifically, determinations in the control period and subsequent time periods were made with the use of 10 ± 2 \( \mu \)m microspheres (3M Company) labeled with \(^{103}\)Ru, \(^{141}\)Ce, \(^{85}\)Cr, \(^{95}\)Nb, \(^{46}\)Se, or \(^{113}\)Sn; for each measurement, 4 to 6 million microspheres suspended in Tween 80 and dextrose were mechanically agitated and injected into the left atrial catheter; the catheter was then flushed with heparinized Ringer's lactate solution. Beginning 30 sec before the injection and continuing for 2 min thereafter, blood for reference flow was withdrawn through the femoral line at a rate of 2.9 ml/min.

The formalin-fixed slice that corresponded to the echocardiographic imaging plane was subsequently subdivided for microsphere counting. Guided by the gross appearance of scarring, regions that appeared to be homogeneously infarcted were identified, and the initial cuts were made at the margins of the infarct. The 30 degree segments on either side of the infarcted region were considered border zones. The remaining opposite myocardial wall was considered normal. Each zone was then divided into radial wedges, each weighing approximately 2 g, and each wedge was subsequently subdivided into endocardial and epicardial pieces. In this way, each transverse slice produced 15 to 20 pieces for counting. By standard techniques, 16

FIGURE 1. Map of radial coordinate system for alignment of echocardiographic, histologic, and blood flow data. For each set of data, the radius that bisects the interpapillary chord is oriented in the 0 degree position (bold line) and data are calculated for each of 36 10 degree rays. Top, Uniform contraction in all 36 rays. Bottom, Wall motion abnormality from rays 29 to 5 (shaded) and frank dyskinesis from rays 32 to 1.
myocardial and reference blood samples were counted in a Packard 9000 series multichannel analyzer. A computer-assisted modification of the spectral stripping technique was used to separate counts emitted from the six isotopes, to calculate decay and adjust for specific activity over experimental time period, and thereafter to calculate myocardial blood flow according to the relationship

$$MBF = \frac{STA \times BSW}{BA \times SW}$$

where MBF = myocardial blood flow (ml/g/min); STA = specific tissue activity (cpm corrected); BSW = blood sample withdrawal rate (ml/min); SW = sample weight (g); BA = blood activity (cpm corrected).

**Data analysis**

**Echocardiography.** Systolic cycles with optimal endocardial visualization were selected for digitization using a FS video digitizing system interfaced with a DEC VAX 11/780 computer. The digitized fields were then manipulated to fix a calculated endocardial center of area and to rotate the endocardial outline, when necessary, to center the 0 degree reference point (midpoint between the papillary muscles) to the 3 o'clock position of radial coordinates. An average center of area for all digitized fields was computed and the fields were tracked for analysis with use of this average center.

Endocardial target motion along 10 degree incremental rays emanating from the predefined average center were then examined.

The circumferential extent and degree of dyskinesis were defined according to a derived method of analysis that integrates the entire course of systolic radial motion. The details of and justification for use of this method have been previously described. The upper plot (figure 2, A) was constructed with data from the control period in one of the study dogs. Motion around the circumference is uniformly similar to composite normal ray motion and the r values for all rays near unity, in this situation. After coronary occlusion, however, a plot such as in figure 2, B, is obtained. As before, the r values for the normal rays (in this example 0 to 210 degrees) were near unity. When the infarcted portion of the ventricle (210 to 340 degrees) is approached, however, there is an abrupt fall in correlation coefficient, with values, as in this case, generally becoming negative.

The circumferential extent of infarction for each experimental time point was defined as the span of radii outside the 95% confidence intervals of the baseline normal radii. An estimate of the degree of abnormal wall motion was defined by the area under the 95% confidence intervals (shaded area on figure). Thus, while the circumferential extent of infarction gives the span of abnormality, it gives no estimate of the degree of abnormal wall motion. The estimate of the degree of abnormal wall motion comes from the integrated area under the curve of the experimental wall motion plot. The importance of this distinction will become clear in specific examples.

**Histologic extent of infarction.** To allow comparison with microsphere-determined blood flow and wall motion abnormality, the transmural and circumferential extent of infarction were calculated for each of the 36 10 degree segments around the circumference of the ventricle. The transmural extent was defined by planimetry of the histologic sections for each 10 degree segment of 6-week-old infarcts, and the circumferential extent was defined as the number of 10 degree rays with any histologic evidence for infarction.

**Regional perfusion.** Transmural flow for each ray was derived with a computer-smoothing method that uses the endocardial center of mass to compute transmural flow at 10 degree increments around the ventricular circumference. This integrative computer method produces an area-weighted computation of flow from the raw microsphere flows by taking into account the position and overlap of the 1 g pieces of tissue in the map of radial coordinates. This allows the calculation of endocardial, epicardial, and transmural flow in 10 degree increments. Normalization of derived flow was then achieved by two sequential calculations.

In the first adjustment, flow for a particular region of interest was normalized to flow in the nonjeopardized position of ventricle. Thus, for animals in whom posterior infarcts were produced by occlusion of the left circumflex artery, an area of 50 degrees in the anterior wall (left anterior descending distribution) was chosen, and a similar-sized area in the posterior wall was chosen for the anterior infarcts.

In the second adjustment, scar contraction causing elevation of microsphere concentrations was taken into account, as in the method of Reimer and Jennings. To introduce this correction, endocardial and epicardial pieces for a particular region were normalized to the opposite wall as stated above (first adjustment). A flow ratio calculated from time 0 control microsphere blood flows was then calculated and applied inversely (second adjustment) to account for microsphere increase resulting from

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**FIGURE 2.** An idealized representation of the correlation plot method of wall motion analysis. This method plots the correlation coefficients of observed against ideal wall motion (endocardial excursion) throughout systole for 37 endocardial points. The circumferential extent (CE) and degree of abnormal wall motion (shaded area) are illustrated; see text for details.
scar contraction at the 30 min, 48 hr, and 1 week time periods. Thus, normalized blood flow was calculated as

\[
\frac{\text{Absolute endo or epicardial flow (infarct)}}{\text{Absolute endo or epicardial flow (normal)}} \times \frac{\text{Time 0 flow (normal)}}{\text{Time 0 flow (infarct)}},
\]

The circumferential extent of reduced blood flow was then defined as the number of 10 degree rays demonstrating normalized blood flow of 80% of normal.

**Data correlations and statistical methods.** The relationship between the time-dependent alteration of blood flow in the region of infarction and echocardiographic wall motion abnormality was examined with standard techniques of linear regression. In the comparison of circumferential extent of infarction between time periods the Student t test for paired comparisons was used. In the evaluation of circumferential extent of wall motion abnormality for infarct vs control wall motion the “correlation plot” method with the Fisher Z transformation was used to define the 95% confidence intervals from the derived plots of correlation.

**Results**

**Histologically defined circumferential extent of infarction.** All eight experimental animals demonstrated histologic evidence of infarction with greater than 50% transmural involvement in four or more 10 degree rays. The average percentages of transmural involvement expressed as the average histologic radial involvement are listed in table 1, along with the circumferential extent of each infarct. No sham animal showed histologic evidence of infarction.

**Radiolabeled microsphere assessment of perfusion.** In the control period, no significant regional differences in blood flow were noted. Normalized, adjusted blood flow for noninfarcted endocardial regions was 110.5 ± 4.1 ml/min/100 g and that for subsequently infarcted endocardial regions was 107.7 ± 4.7 ml/min/100 g before occlusion. Noninfarcted epicardial flow averaged 103.8 ± 5.9 ml/min/100 g and subsequently involved regions of epicardium had preocclusion flows averaging 106.7 ± 4.5 ml/min/100 g. The flow ratio of infarcted to control tissue flow fell at 30 min to an average of 0.40 ± 0.13 for endocardial pieces and to 0.56 ± 13 for epicardial pieces. By the 6 week determination, the flow ratio had recovered to 0.83 ± 0.15 for endocardial regions and to 1.12 ± 0.11 for epicardial regions. No significant differences in flow ratios were observed over the 6 week period in the four sham-ligated animals. The circumferential extent of reduced flow (normalized flow <0.80) at all time points is summarized in table 2.

**Echocardiographically defined extent of abnormal wall motion.** The circumferential extent of abnormal wall motion was assessed in each of the eight experimental animals for each of the six experimental time periods. The serial plots of correlations (as described in Methods) for two representative circumflex distribution infarctions are presented in figure 3 for dogs 1 and 4. For each of the series of plots, the region of abnormal wall motion is clearly defined, reproducible from time period to time period, and can be seen to shrink significantly from 30 min to the end of the experiment at 6 weeks. A histologic map of percentage of transmural infarction for each of the matched 10 degree rays is illustrated at the top of each series; it is evident that the center of each infarct closely matches the center of maximal wall motion abnormality in the early experimental time points.

Table 2 includes data from all of the animals and outlines the circumferential extent of abnormal wall

**TABLE 2**

<table>
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*Number of 10 degree rays with flow less than 80% control normalized flow (flow), or number of 10 degree rays with abnormal wall motion (awm).*

LCX = left circumflex artery; LAD = left anterior descending coronary artery.
FIGURE 3. Serial wall correlation plots of motion abnormalities for dogs 1 and 4. Correlation plots registered to identical radial coordinates here demonstrate both radial shrinkage in the span of abnormal wall motion and diminution of the magnitude of abnormality. For further details, see text.

motion at each of the time points, as determined by the 95% confidence limits calculation.

Figure 4 graphically summarizes the pooled data of circumferential extent of abnormal wall motion for all time points. When the span of circumferential extent for each time period was compared with the 30 min span, paired t tests demonstrate that at 48 hr, the span of abnormal wall motion was significantly greater, thereafter began to shrink and become significantly smaller by 3 weeks, and was again smaller by more than 50% at 6 weeks (p = .001).

Moreover, when individual animal trends were plotted, it could be seen that the circumferential extent of abnormal wall motion (figure 5, A) shrank for all animals, but to a much greater degree for some animals than for others. If the same trends are examined, but abnormal wall motion is expressed as the degree of dyskinesis (or area under the curve of circumferential extent), far more dramatic resolution of abnormal wall motion becomes evident (figure 5, B) and is indistinguishable from normal in four animals. This analysis resolves, to a large degree, the discrepancy between deficit of flow and wall motion abnormality that appears for individual cases in table 2. In particular, those dogs with minor wall motion abnormalities by 6 weeks had minor, albeit statistically significant (80% normal), flow deficits; those with major wall motion abnormalities, defined by the area under the correlation plot curve, had large flow deficits. Dog No. 5, which had a minor flow deficit, had no detectable wall motion abnormality.

Circumferential extent of abnormal wall motion vs microsphere-derived flow. The circumferential extent of abnormal wall motion for the experimental time points correlated highly (r = .89, p = .0001) with the circumferential extent of reduction in transmural blood flow of greater than 20% (figure 6).

When pooled data for each of the experimental time points were examined separately (figure 7) it was evident that the same high correlation existed up to 3 weeks, but at 6 weeks, when abnormal wall motion had significantly resolved, the echocardiographically determined abnormal wall motion span underestimated the degree of reduction in blood flow, and likewise, the extent of histologic infarction.

Comparison of the correlation method with end-diastolic-end-systolic radial change. When circumferential extent of abnormal wall motion is defined by the more traditional method of calculating end-diastolic–end-systolic radial change less than the arbitrary value of 0.20, a poorer correlation with reduction in blood flow of less than 20% is evident (figure 8). Even so, the trend in reduction of circumferential extent of abnormal wall motion over time is the same for the end-diastolic–end-systolic radial change method (data not shown), which overestimates the circumferential ex-
tent of abnormal wall motion when compared with the correlation methods ($r = .71$).

Discussion

This study suggests (1) that the integrative method of wall motion analysis provides an accurate assess-

![FIGURE 5. Left, Abnormal wall motion (number of 10 degree rays) for individual dogs at 30 min, 48 hr, and 6 weeks showing progressive return toward normal in all dogs. Right, Abnormal wall motion expressed as the degree of dyskinesis, or area under the correlation plot curve, for the same time intervals shows even more dramatic improvement, with virtually no abnormality detectable by 6 weeks in four animals.](image)

![FIGURE 6. Circumferential extent of abnormal wall motion by correlation plot (number of abnormal 10 degree rays) is plotted (y axis) against the number of 10 degree rays at the same experimental time point with a reduction in transmural blood flow of at least 20% below that of the normal opposite wall (x axis).](image)

ment of infarct size, as judged by simultaneously derived blood flow data, up to and including the 3 week period after canine infarction, (2) the extent and degree of abnormal wall motion reaches a maximum near 48 hr after infarction and resolves significantly but variably over the 6 weeks thereafter, and (3) by 6 weeks after infarction, the functional consequences of infarction are no longer present in some animals. In these instances, wall motion analysis underestimates the size of the chronic infarct scar.

The natural history of wall motion abnormalities after infarction in the dog has not heretofore been defined through the 6 week recovery period. Canine dyskinetic motion has been shown to convert to akinetic motion in sonomicrometry studies, and the improvement in systolic shortening has been shown to occur concomitantly with a fall in left ventricular end-diastolic pressure toward normal by 4 weeks after infarction; other parameters of left ventricular function have been shown to be normalized by 4 weeks as well.

Our study confirms the inference regarding segmental recovery made by these investigations and extends the documentation. All eight dogs in our study, whether undergoing infarction of the distribution of the left anterior descending or left circumflex artery, had significant wall motion abnormalities immediately after coronary ligation, and had even more extensive circumferential extent of abnormality at 48 hr after ligation. However, even when the infarct encompassed
more than 50% of the circumferential extent of the ventricle, wall motion abnormalities were significantly resolved by 6 weeks after infarction. There appeared to be no "break point" of circumferential extent above which significant recovery was impossible.

It is particularly intriguing that four dogs, all with left circumflex ligations, had little or no detectable wall motion abnormality at the end of the experiment. Because of the small numbers of dogs in the recovered (mostly left circumflex) and nonrecovered (primarily left anterior descending) groups, we were unable to define statistically significant differences between them with respect to circumferential extent of infarction, percent transmural extent of infarction, or degree of reduction in transmural blood flow. On the other hand, it is significant that in dogs with large infarcts in the circumflex distribution recovery of wall motion was complete by 6 weeks after infarction. This observation lends further support to the recent discovery that infarcts of the left anterior descending coronary artery are larger, for a given occluded bed size, than corresponding infarcts of the left circumflex artery, and perhaps reflects differential collateral support for the two arterial distributions.

Karsner and Dwyer studied the pathologic correlates of canine infarctions up to 70 days after infarction and described a process of dense scarring and infarct contraction from day 18 to day 61 after infarct. Importantly though, they described significant variation in the rate of maturing of infarct scar during the time up to 70 days: some dogs still had necrotic tissue organizing into scar by 61 days. For this reason, we cannot state unequivocally whether the variation we see in recovery of wall motion at 6 weeks represents the variation in rate of maturation of scar, or is a fixed deficit at 6 weeks.

**FIGURE 8.** Abnormal wall motion defined as the number of 10 degree rays with end-diastolic–end-systolic change of less than 20% radial shortening (y axis) also correlates with reduction in transmural blood flow (x axis) in our dogs. The correlation is less good than the correlation plot method, and the estimate of abnormality is, in general, greater than that by the correlation method.
**Scar contraction.** The issue of scar contraction raises several questions both in the interpretation of flow and wall motion data and in the interpretation of the meaning of recovery. Reimer and Jennings have eloquently cautioned us about the risks of interpreting regional perfusion and functional changes over time after infarction because, they argue, the anatomic reference base on which regional definition depends changes as compensatory left ventricular mechanisms and scar contraction progress. In other words, the posterior wall we define at the beginning of the experiment has an entirely different composition at 1, 3, and 6 weeks after infarction, even though we have assigned the same radial coordinates to the remodeling tissue.

It is with this problem in mind and based on the histologic natural history of canine infarctions that we have applied the normalization adjustments to the 0 time, 30 min, 48 hr, and 1 week flow data. We realize that since the flow data is regionally calculated at the 6 week time point, after whatever anatomic shifts of expansion or contraction have taken place, the assigned radial flows may be inaccurate by whatever factor the infarct shrinks circumferentially. It is likely, however, that we have in part counteracted this error by applying our investigation of regional flow and wall motion to 10 degree rays rather than larger areas of myocardium. Our method of computing segmental flow not only calculates flow for the piece of tissue in question, but integrates the rate of change of flow from one piece of tissue to the next such that transition zones, should they occur near the junction of two separate pieces of tissue, are accounted for in the calculation.

The determinants of scar contraction or infarct expansion remain undiscovered. In acute infarction in the dog, there is a poor correlation between the size of an infarct (circumferential extent) and expansion of the infarct within 24 hr, even though the greater transmural extent of infarct, the greater the tendency of the infarct to expand. Reimer and Jennings have shown in reperfusion experiments that for a given perfusion bed in the dog, length of occlusion increases only the transmural extent, not the circumferential extent, of reperfused infarct. Thus, we infer that additional metabolic or anatomic factors play a significant role, over and above the histologic topology, in determining infarct expansion and scar contraction.

**Regional flow and regional wall motion.** Despite these uncertainties in defining regions, we have been able to demonstrate a good correlation for each experimental time period between the regional wall motion perturbation and reduction in transmural blood flow for those same regions. This correlation is only satisfactory, however, up to 3 weeks after infarction. At 6 weeks, when recovery of wall motion has been dramatic, the wall motion analysis underestimates the degree of transmural blood flow deficit, and certainly underestimates the size and presence of the infarct scar. The wall motion analysis does not underestimate transmural flow more, perhaps, because by 6 weeks the infarct has shrunk at least 50% radially and the calculated transmural flow represents predominantly viable epicardial flow.

Recent sonomicrometer studies by Gallagher et al. indicate that wall thickening is predominantly a phenomenon of the inner wall, and thus endocardial myocardium. These authors demonstrate that coronary stenosis, which predominantly affects endocardial blood flow, has profound effects on wall motion precisely because wall thickening is perturbed in the region in which it is most significant. It may be that in our experiment with chronic infarction the rate of recovery of wall motion in the region of the infarct depended in part on the ability of the epicardial viable myocardium to assume the contractile properties of endocardial myocardium. If this is so, then in non-transmural infarction wall motion recovery may reflect this epicardial functional remodeling in which scar contraction may likely be a passive phenomenon.

**Integrative wall motion analysis.** The method of analyzing regional wall motion throughout systole and correlating radial motion with normal patterns was first used to analyze angiographic ventriculograms. We have applied this method in a modified fashion using a fixed center of endocardial area for the short-axis echocardiographic midpapillary muscle view of the left ventricle. The superiority of this method of analysis over the more traditional end-diastolic-end-systolic radial change method is reflected in a better correlation of results with regional blood flow deficit. The integrative method takes into account what, in practice, is abnormal wall motion early in systole in infarcted segments of myocardium; these segments frequently recover near-normal patterns of contraction later in systole, but may still have a lengthened end-diastolic radius. The degree to which radial shortening approaches normal in linearity is reflected in the integrative method, but not in the radial change method. Overall then, as this study demonstrates, the radial change method, in practice, overestimates the size of blood flow deficit and results of its use correlate less well with blood flow deficit than do results obtained by the integrative method.

Our computer-assisted integrative method by neces-
sity also calculates not only the correlation coefficient of the experimental fractional radial change compared with the fractional change of pooled normal data, but also the slope of fractional change as a function of time. We have found that plots of radial slope give a less clear picture of abnormal wall motion, even though they roughly outline regions of hypercontractility in noninfarcted muscle. We therefore have found it most useful to use correlation coefficient plots for 36 endocardial targets in which linearity is independent of the slope of hypercontractile regions and in which normal, noninfarcted muscle is clearly demarcated from abnormally contracting muscle.

We therefore conclude that the natural history of isolated coronary ligation is to produce infarctions that are significant in size but not uniformly transmural. Regional wall motion in infarcted hearts significantly improves over the 6 weeks after infarction, and in some cases is completely recovered. We propose that the end point of regional dysfunction is highly variable, and that studies that set out to demonstrate conservation of regional function by interventions that limit infarct size must take into account the variability in recovery inherent in the natural history of such wall motion abnormalities.

References

9. Hood WB: Experimental myocardial infarction III: recovery of left ventricular function in the healing phase; contribution of increased fiber shortening in noninfarcted myocardium. Am Heart J 79: 531, 1970
The natural history of regional dysfunction in a canine preparation of chronic infarction.
E F Gibbons, R D Hogan, T D Franklin, M Nolting and A E Weyman

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