Analysis of Regional Ischemic Left Ventricular Dysfunction by Quantitative Cineangiography

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SUMMARY The ability of left ventricular angiography to detect regional ischemic dysfunction was assessed in 10 closed-chest dogs during the course of acute balloon occlusion of the anterior descending coronary artery. During the 2-minute period of occlusion, serial cineangiography revealed a sequence of wall motion abnormalities over the anteroapical region almost identical to that observed using directly implanted gauges. This sequence consisted of progressive reduction in regional systolic shortening with eventual replacement by systolic expansion. These changes preceded both electrocardiographic ST-segment and hemodynamic alterations, and were readily observed by gross subjective inspection of the cineangiograms, but with an intraobserver variability of 22%. Frame-by-frame motional analysis of the ventricular perimeter relative to its centroid of mass allowed more precise characterization of regional dysfunction. These data are consistent with previous studies demonstrating that regional wall motion abnormalities are both sensitive and specific markers of acute ischemia, and support the use of computerized left ventricular angiography for the quantitative assessment of clinical ischemic dysfunction.

REGIONAL ABNORMALITIES of left ventricular function have been demonstrated both during the course of acute coronary occlusion and graded reduction in coronary blood flow in the experimental animal by using a variety of analog techniques. The changes are best characterized as a sequence that begins as late systolic outward motion and ends with total replacement of active shortening by passive expansion. Such a sequence is highly specific for regional ischemia and invariably precedes electrocardiographic ST-segment shifts. It has been postulated that these alterations of regional function are directly analogous to qualitative angiographic contraction patterns such as "hypokinesis" and "dyskinesis." If this is the case, clinical left ventriculography might be used as a quantitative measure of regional ischemia. It is not known, however, if angiographic techniques reveal a similar sequence of altered regional function in response to acute ischemia, nor if such changes are detectable by qualitative inspection. The present study was designed to determine the effect of acute coronary occlusion on regional and global cardiac performance assessed by angiography in the closed-chest animal, and to correlate subjective qualitative angiographic assessment with quantitative analysis of a computerized two-dimensional analog representation.
Methods

Studies were performed in 10 closed-chest mongrel dogs that weighed 22–32 kg. The dogs were anesthetized with intravenous pentobarbital, 20 mg/kg after premedication with morphine sulfate, 30 mg subcutaneously. Respiration was maintained via intubation using a Harvard respirator. The left ventricle was catheterized by way of the left carotid artery using a 50-cm #8F angiographic Teflon catheter. An additional #7F NIH catheter was placed in the left ventricle by way of the femoral artery for pressure recording and was attached to a Statham P23dB transducer. The frequency response of this system was determined in vitro by gas flame rupture of an attached saline-filled latex balloon, as ±10% from 0–20 Hz. Left ventricular pressure was recorded simultaneously with three precordial electrocardiographic leads throughout the experimental procedure. During the data collection periods, the respirator was temporarily turned off at end-expiration. A #2F polyethylene balloon-tipped catheter was introduced into the left anterior descending coronary artery via the right carotid artery, under fluoroscopic control. The position of the catheter was documented by hand injection of a small amount of Renografin-76 (meglumine diatrizoate). A control left ventriculogram was obtained in the left lateral projection by power injection of 6 ml Renografin-76 at 14 ml/sec using a Cordis automatic injector attached to the left ventriculographic catheter. The ventriculogram was recorded on 35-mm film at 50 frames/sec and simultaneously on videotape. This procedure produced adequate visualization of the left ventricular chamber for at least three cardiac cycles and elicited no premature ventricular complexes. Acute coronary occlusion was effected by inflation of the intracoronary balloon with 0.4–0.6 ml of Renografin-76. The completeness of occlusion was documented by observing the elongation of the balloon against the arterial wall during inflation. Left ventriculography was repeated after coronary occlusion at intervals of 5, 10, 30, 60 and 120 seconds, after which time the balloon occlusion was relieved. Each angiogram was viewed on a Vanguard projector by three experienced observers who were asked to characterize subjectively the motion of the anterior, apical and inferior regions. For this purpose, a six-point grading system was used: 5 — hyperkinetic; 4 — normal; 3 — dysyneretic; 2 — hypokinetic; 1 — akinetic; and 0 — dyskinetic. For each region, the three observations were totaled. A score of 12 represented subjectively normal regional contraction. The hemodynamic influence of this method of sequential ventriculography was evaluated separately on six more dogs without coronary occlusion during the 2-minute period after the first ventriculogram.

Cineangiograms were digitized, frame-by-frame, using a sonic digitizer pen interfaced with a Xerox Sigma-3 computer. The ventricular area was then calculated for successive frames by the following algorithm: The outline of the ventricle was defined by a series of points in the first quadrant of the xy plane. Assuming the first and last points to be adjacent yields n pairs of adjacent points, P1 and P2. For each of these pairs, a triangle was defined by P1 and P2 and the origin. The area was calculated by the following equation:

\[ A = \frac{X_{P2}Y_{P1} - Y_{P2}X_{P1}}{2} \]

The sum of the positive and negative areas is equal to the area enclosed by the n points. Using a model that assumes the left ventricle to be elliptical in shape, left ventricular volume was then calculated by the following equation:

\[ V = 8A^2/3\pi L \]

where L is the length of the long axis and A is the area of the ventricular cavity as calculated above. The long axis was determined as the line connecting the midpoint of the aortic root with the most distant point on the digitized cardiac perimeter. End-diastole and end-systole were defined as those frames with the maximum and minimum calculated volumes, respectively. The period of ejection was defined as the time between these two extremes.

To calculate segmental wall motion, each digitized perimeter was divided into 50 equal-length segments. By visual inspection, the anterior region was defined by segments 4–18; the apical region, by segments 18–28; and the inferior region, by segments 28–48. The midpoint of each segment was then determined and used as a discrete reference point for the measurement of segmental wall motion. A centroid for each frame, defined as the center of gravity of the ventricular wall, was computed and distance was measured from this center point to the wall segment midpoints of the frame. The magnitude of the motion between the two frames is the difference between the distance (Dn) from the centroid of frame I to the nth midpoint (Pn) on frame I and the distance (D0) from the centroid of frame I + 1 to the nth point (P0) on frame I + 1. This difference was interpreted as the wall motion for segment n between the respective frames. The calculation was then repeated for each frame in the cycle to describe continuous motion throughout that cardiac cycle.

Statistical comparisons were performed by analysis of variance.

Results

Hemodynamic and Electrocardiographic Response to Coronary Occlusion

Acute occlusion of the left anterior descending coronary artery produced hemodynamic and electrocardiographic abnormalities in all dogs (fig. 1). The most prominent change was in left ventricular ejection fraction, which fell within 5 seconds from 60 ± 2% to 47 ± 4% (p < 0.01). Only a minimal further fall was observed by 10 seconds and thereafter a slight increase was observed by 30 seconds. Left ventricular end-
diastolic pressure (LVEDP) increased from 6 ± 1 mm Hg before coronary occlusion to 10 ± 2 mm Hg by 30 seconds and to 11 ± 3 by 60 seconds (p < 0.01).

Changes in the ST segment appeared less rapidly than hemodynamic alterations. No significant ST-segment changes were recorded at 5 seconds of left anterior descending occlusion and only minimal (0.02 ± 0.01 mV) ST elevation was recorded at 10 seconds. By 30 seconds, the ST segment was substantially elevated (0.19 ± 0.05 mV) and continued to increase, reaching a maximum of 0.32 ± 0.05 mV by 120 seconds after left anterior descending occlusion (p < 0.001).

Left ventricular end-diastolic volume increased significantly over the 2-minute period of occlusion, from 66 ± 2 ml to 74 ± 3 ml (p < 0.001). In the six dogs prepared similarly to the 10 described above, but without coronary occlusion, there was no significant change in ejection fraction, LVEDP or the ST segment. As with the occlusion dogs, we noted a significant increase in left ventricular end-diastolic volume, from 56 ± 4 ml at control to 64 ± 4 ml at 2 minutes (p < 0.01).

Segmental Wall Motion Response to Coronary Occlusion

Figure 2 shows the magnitude of systolic inward motion for each region of the left ventricle. Before occlusion, mean systolic inward motion of all segments was 6.7 ± 1.4 mm. The anterior, inferior and apical regions all exhibited a similar magnitude of inward systolic motion. After left anterior descending occlusion, inward systolic movement in the anterior and apical segments decreased rapidly. Within 5 seconds of anterior occlusion, inward movement had decreased significantly to 57 ± 12% of control values (p < 0.001). The decrease in inward systolic motion was essentially complete by 10 seconds, before any important change in either left ventricular end-diastolic pressure or the ST segment. From 1–2 minutes, slight, statistically insignificant recovery of inward motion was observed. The change in apical motion had a similar temporal sequence but was more profound, as inward systolic motion was completely replaced by outward systolic motion in all dogs. In contrast, inferior wall motion increased significantly (p < 0.01) after coronary occlusion, but had a different time course. The earliest change in inferior wall motion, at 5 seconds after occlusion, was a small decrease, after which an increase to 140 ± 16% of control values at 30 seconds, and to 123 ± 16% at 2 minutes, was observed.

Figure 3 illustrates the mean magnitude of segmental wall motion in all dogs, plotted as a function of time after coronary occlusion. There was a smooth transition from normal inward motion in areas proximal to the coronary occlusion, to markedly diminished inward motion at the apex. We saw a similar smooth increase in the number of anterior segments with diminished inward motion and in the number of inferior segments with increased inward systolic motion with increasing time after occlusion. Figure 4 summarizes these data in a conventional left ventriculographic format. Anterior segments 6–18 and apical-inferior segments 23–32 showed significant reduction of wall motion compared with control.
Segments 36–42 of the inferior wall, on the other hand, showed significant increase in wall motion compared with the control state.

The Morphology of Segmental Wall Motion Changes

Figure 5 illustrates the morphology of change in the motion of two anterior segments (10 and 11) after coronary occlusion in a single dog, as recorded by the left ventriculogram. Below these segments is illustrated the simultaneous motion of an inferior segment (no. 40). Before occlusion, all segments showed inward motion throughout systole; 10 seconds after coronary occlusion, reduction in the magnitude of systolic shortening appears anteriorly accompanied by the development of late systolic outward motion. By 30 seconds systolic shortening has been replaced by holosystolic outward motion, while the inferior segment has increased systolic inward motion.

**Figure 3.** Magnitude of systolic shortening of each segment of the left ventricular perimeter relative to the centroid of mass before and after acute coronary occlusion. Segments 4–18 represent the anterior wall; 18–28, the apex; and 28–48, the inferior wall. Each symbol represents the mean \( \pm \text{SEM} \) for 10 dogs.

**Figure 4.** Ventriculographic representation of altered regional systolic shortening 5 and 60 seconds after acute coronary occlusion. The shaded areas represent segments demonstrating statistically significant changes in the magnitude of systolic motion, measured along a line joining the midpoint of a segment on the end-diastolic perimeter and the centroid of mass. The dashed perimeter represents the average end-systolic configuration of the left ventricle after occlusion. The solid perimeters are the average control end-diastolic and end-systolic configurations.

**Figure 5.** Morphologic alterations in segmental wall motion after acute coronary occlusion. See text for discussion. ED = end-diastole; ES = end-systole.
Visual Analysis of Left Ventricular Segmental Wall Motion

Three experienced observers carefully analyzed all 60 left ventriculograms from the 10 occlusion dogs (fig. 6). All readily designated wall motion in the anterior and apical segments as already abnormal at 5 seconds but none could describe the precise morphologic pattern of wall motion (e.g., the early onset of late systolic outward motion or the transition from this pattern to holosystolic outward motion), and in only four dogs was the presence of hypercontraction of the inferior wall noted. The variability between readers was significant. Of 540 total readings, only 249 (46%) were in complete agreement, and in 117 instances (22%) at least one reader disagreed upon an assigned score. In 30 cases (6%) there was complete disagreement between readers.

Discussion

Since the classic description of ischemic dysfunction after acute coronary occlusion by Tennant and Wiggers, a number of studies in both animals and man have suggested that regional segmental left ventricular dysfunction is a sensitive and specific marker of ischemia, and that the observed pattern of regional dysfunction bears a semiquantitative relationship to the magnitude of ischemia. After acute reduction in coronary blood flow a specific reproducible sequence of regional dysfunction occurs. This invariable pattern is observed at both the endocardium using ultrasonic crystals and at the epicardium using mercury-in-silastic length gauges. The first change recorded is late systolic outward motion, which is perceived by subjective angiographic analysis as “dyssyneresis.” As the magnitude of ischemia increases, the onset of outward motion begins earlier in systole, progressively encroaching upon inward motion, producing segmental “hypokinesis.” Eventually shortening is abolished and when ischemia is most severe, holosystolic outward motion is observed. The subjective correlates of these latter changes are “akinesis” and “dyskinesis.”

Clinical analysis of regional ischemic dysfunction currently remains limited largely to subjective interpretation of the left ventricular cineangiogram, a format which is subject to a relatively high degree of intrasubject variation. In this study, for instance, three experienced angiographers completely agreed upon their subjective interpretations in only 46% of instances, and partially agreed in an additional 32%. Although computer techniques for analysis of ventriculographic volumetric data are now widely available, little attention has been paid to a similar detailed analysis of regional wall motion. The results of the present study support the view that left ventriculography provides a clinically applicable method for quantitative interpretation of regional ischemic left ventricular dysfunction. The pattern of wall motion abnormality observed was essentially identical to that previously described using directly implanted epicardial length gauges, endocardial ultrasonic crystals and noninvasive cardiokymography. The sensitivity of these changes to ischemia is indicated by the fact that they are observed to occur within 5 seconds of acute coronary occlusion, or graded reduction in resting coronary blood flow to approximately 50% of control, and by the fact that they almost invariably precede electrocardiographic, metabolic and hemodynamic markers of ischemia.

An internal reference system was used to analyze the angiographic data in this study. This system is analogous to that used for analysis of length-gauge and ultrasonic-crystal data and does have a major disadvantage of an external reference system — that rotational and translational cardiac motion is added to regional motion as an artifact. The disadvantage of the internal reference system, however, is that it is not directly analogous to clinical subjective interpretation and to other noninvasive measures of regional wall motion as provided by echocardiography and cardiokymography. In addition, the algorithm for calculating segmental wall motion does not align the long axes colinearly. As a result, segmental wall motion may be artificially attenuated in the anterior segments and intensified in the corresponding inferior segments by superimposed intrathoracic movement. Consequently, a variable but systematic bias has been introduced into the calculations. Nevertheless, the method corresponded well with visual analysis, since a similar magnitude of anterior dysfunction was identified subjectively. Moreover, the augmentation in inferior function observed in this study corresponds to that detected clinically in the presence of old inferior myocardial infarction by echocardiography and by other algorithms for computerized ventriculography.

One must extrapolate the findings in this study to the clinical state only with caution. Acute coronary ischemia as produced in this study is potentially analogous to the syndrome of acute coronary spasm or to acute myocardial infarction, but not necessarily
to chronic ischemic heart disease. Some data suggest, however, that the acute occlusion model has clinical relevance. First, exercise studies in free-running dogs with partial coronary occlusion and normal resting ventricular function reveal similar patterns of induced ischemic dysfunction. Second, clinical exercise studies using left ventriculography, technetium-99m gated blood pool scintigraphy and cardiovymography also reveal similar patterns of induced ischemic segmental left ventricular dysfunction. Therefore, it is likely that acute regional dysfunction that occurs in the face of chronic coronary artery disease is analogous to that observed in the experimental animal during acute occlusion and graded reduction in coronary blood flow.

In summary, quantitation of the pattern of regional left ventricular function by angiography in this study appears to be both a sensitive and specific marker for detection and evaluation of the effects of acute ischemia on left ventricular performance. Clinical application of the method offers promise of more precise characterization of the effects of ischemia on cardiac performance.

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