Postsystolic Shortening of Acutely Ischemic Canine Myocardium Predicts Early and Late Recovery of Function After Coronary Artery Reperfusion

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Postsystolic shortening and thickening of ischemic and postischemic myocardium are well-recognized phenomena, but their significance is controversial. To discover whether postsystolic shortening and thickening might represent an active process and to establish their place as possible predictors of functional recovery during and after recovery from ischemia, we examined correlations in severely ischemic dyskinetic myocardial segments in 14 open-chest anesthetized dogs (90 minutes' ischemia, n = 9; 180 minutes' ischemia, n = 5) between the magnitudes of postsystolic shortening and thickening during ischemia and either the magnitudes of systolic shortening and thickening in the same segments before coronary occlusion or the magnitudes of shortening and thickening at 30–60 minutes and at 2–3 weeks after reperfusion. We found positive correlations between preocclusion shortening and postsystolic shortening (r = 0.44, n = 33 myocardial segments; p < 0.02) and between preocclusion thickening and postsystolic thickening (r = 0.73, n = 13 segments; p < 0.01), both measured at 5 minutes after onset of ischemia. Strong correlations were found also between postsystolic shortening and thickening measured immediately before reperfusion and systolic shortening and thickening measured after recovery at 2–3 weeks (r = 0.73, n = 28; p < 0.001 for shortening; r = 0.79, n = 12; p < 0.01 for thickening). Significant but less-exact correlations were found between postsystolic shortening and thickening measured immediately before reperfusion and early recovery of shortening and thickening at 30–60 minutes after reperfusion (during the "stunned myocardium" period). Postsystolic shortening and thickening persisted early after reperfusion in dogs that had had 90 minutes of ischemia, and this predicted further significant return of function at 2–3 weeks. However, dogs that had had 180 minutes of ischemia did not have postsystolic shortening or thickening during early recovery and showed no further return of function at 2–3 weeks. The magnitudes of postsystolic shortening and thickening immediately before reperfusion were better predictors of late return of function than the histological appearance of the ischemic segments at 2–3 weeks or the magnitude of their blood flow during ischemia (15 ± 3 μm microspheres). From correlations made immediately before reperfusion with those at functional recovery after reperfusion, we conclude that postsystolic shortening and thickening of dyskinetic myocardial segments are markers of their potential for recovery. Correlations between preocclusion shortening and thickening and the postsystolic changes at 5 minutes after occlusion further suggest that postsystolic shortening and thickening represent active contraction; probably because of delay in relaxation caused by acute ischemia. Persistence of the postsystolic changes after reperfusion shows that prolonged contraction continues into the postischemic period. (Circulation 1988;78:994–1007)

It is well known that acutely ischemic canine myocardium has latent contractile function, as evidenced by improvement of systolic shortening after administration of inotropic drugs or paired pacing in hypokinetic1 or dyskinetic2 myocardial segments. Moreover, preservation of latent function can be used as an index of potential for
recovery after coronary reperfusion in patients. We have described a relation between the magnitude of postsystolic shortening, defined as early diastolic shortening beyond the previous end-diastolic length in acutely dyskinetic ischemic myocardial segments, and the magnitude of shortening both before the onset of ischemia and after restoration of perfusion. These findings suggested that postsystolic shortening was a marker of potential for recovery after reperfusion and that it represented latent contractile function, implying an active process. Return of function in these experiments, however, was followed for no more than 3 hours of reperfusion after periods of coronary occlusion of 60 or 90 minutes. Thus, the presence of myocardial "stunning" made it inappropriate for us to extrapolate from our data on early functional recovery to assess the value of postsystolic shortening for prediction of long-term functional recovery and the severity of myocardial infarction.

The present experiments were done to follow the functional changes resulting from 2 or 3 weeks of reperfusion after 90 or 180 minutes of coronary occlusion in open-chest, anesthetized dogs. Results confirm that the occurrence of postsystolic shortening and thickening during acute ischemia is a marker for both early and late recovery of function after reperfusion.

Materials and Methods

Preparation

Nineteen mongrel dogs weighing 19–32 kg (average, 24 kg) were sedated with an injection of 0.05 ml/kg i.m. Innovar-Vet (Pittman-Moore, Washington Crossing, New Jersey) containing 0.4 mg/ml fentanyl and 20 mg/ml droperidol. Anesthesia was induced with oxygen and halothane, and dogs were intubated with a cuffed endotracheal tube and ventilated with a Harvard volume-cycled respirator at rates that maintained the blood pH at 7.4 ± 0.5. Anesthesia was maintained with approximately 70–80% oxygen, 10–20% nitrous oxide, and 1% halothane. Arterial pressure was monitored by an 8F catheter placed in the right femoral artery via the saphenous artery to allow ligation at completion of the sterile study. The chest was painted with 0.5% chlorhexidine after shaving; with full aseptic technique, a left thoracotomy was performed through the fifth intercostal space and the heart suspended in a pericardial cradle.

The left anterior descending coronary artery (LAD) was dissected free and a 2-0 silk snare was placed between the first and second diagonal arteries for subsequent occlusion. A high-fidelity micromanometer-tipped catheter (Millar, Houston, Texas, or Koenigsberg Model P22, Pasadena, California) for measurement of left ventricular pressure and its first derivative (dP/dt) was inserted into the left ventricle through the left atrial appendage and mitral valve or through a stab incision at the ventricular apex. A short 6F fluid-filled silastic catheter or 7F balloon-tipped angiographic catheter (Berman, Tampa, Florida) was also inserted into the left ventricle to obtain zero pressure reference and to calibrate the micromanometer when the Koenigsberg P22 manometer was used. A 6F catheter was placed in the left atrium for injection of radioactive microspheres.

Length changes in left ventricular segments were measured with sonomicrometry, with placement of crystals in a manner identical to that used in our previous experiments. Two pairs of ultrasonic crystals made from sheets of 1.5-mm thick crystal were inserted into the subendocardium of the potentially ischemic zone of the anterior wall (ABCD; Figure 1). The position of the ischemic margin was estimated to be midway between the first and second diagonal arteries, and the first pair of crystals (AB) was placed parallel to and approximately 5 mm within the potentially ischemic zone at a separation of 15–20 mm (16 ± 2 mm). The second pair (CD) was placed parallel to AB and an additional 15–20 mm (17 ± 4 mm) toward the center of the potentially

![Figure 1. Drawing showing position of the ultrasonic crystals relative to the ischemic zone (stippled area). Matrix of four subendocardial crystals (A–D) was positioned to measure segment length parallel to and perpendicular to the ischemic margin, defined as the midpoint between occluded and unoccluded diagonal arteries. Wall thickness in the ischemic zone was measured by crystal pair EF, while crystal pair GH lay in the subendocardium of the normal zone. Cross-hatching and spotting indicates position of the tissue specimens taken for histological and myocardial blood flow measurements. Block for histological examination was sectioned along the face of crystal insertion. Myocardium at the center of the ABCD matrix was discarded. LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery.](http://circ.ahajournals.org/content/95/2/80.full)
ischemic zone. With considerable care taken to orient the crystals so that an optimum acoustic signal was seen on an oscilloscope, it was possible to make recordings both parallel to and perpendicular to the ischemic margin. Wall thickness was measured in the ischemic zone with a further pair of crystals (EF) in the position shown in Figure 1. A track was made with an 18G needle at 45° to the epicardium, and one crystal was directed into the subendocardium. The epicardial surface crystal, 4 mm in diameter, was positioned at the minimum distance (10 ± 2 mm) from the inner crystal. A pair of subendocardial crystals (GH) were also placed in the normal myocardium adjacent to the ischemic zone, parallel to and 2–3 cm above the ischemic margin.

After completion of the initial measurements, the ultrasound crystals were removed and the site of each crystal was marked by 5–0 prolene sutures. The micromanometer-tipped catheter, the left atrial catheter, and the femoral arterial catheter were removed with appropriate hemostasis. These instruments were taken out of the dogs to avoid possible infection and to facilitate exercise. The pericardium was closed loosely, the chest was closed over a drainage tube, and the dogs were placed in a recovery pen for 12 hours. Antibiotics were given according to the following regimen: 1 ml/10 kg s.c. Penstrep LA forte (250 mg procaine benzyl penicillin and 80 mg dihydrostreptomycin, Glaxo, New Zealand) before surgery and every 48 hours after surgery for 10 days and Tribactral 80 (90 mg trimethoprim and 400 mg sulphadiazine) twice daily for 10 days.

At 2 or 3 weeks after the first surgical procedure, the dogs were reanesthetized with the same anesthetic regimen and the chest was reopened without asepsis for repeat measurements of hemodynamics and regional wall motion. The ultrasound crystals were reinserted with considerable care to reposition them in the tracks made at the first study. Because of severe fibrosis, it was sometimes necessary to separate hard tissue with mosquito forceps. Recordings were made of left ventricular pressure, left ventricular dP/dt, and segment length changes between pairs of crystals. The dogs were then killed with an overdose of pentobarbital. The hearts were removed with the ultrasound crystals in place and immersed in 10% formalin solution for 48 hours. After fixation, the myocardium between each pair of subendocardial crystals was removed and subdivided perpendicular to the epicardium into two blocks for either histological assessment or measurement of myocardial blood flow (MBF) (Figure 1). To facilitate orientation for sectioning in the plane of subdivision, the blocks for histology were marked with Indian ink on their opposite face. The blocks for measurement of MBF were divided into approximately equal epicardial and endocardial halves of about 0.5 g (0.45 ± 0.02 g). Similar samples were taken between crystals EF and GH. The previously occluded arteries were also removed for histological examination. The study was approved by the hospital Animal Ethics Committee.

**Measurements**

Regional myocardial function was measured by a two-channel dimension gauge. The propagation time of acoustic signals traveling at an assumed speed of 1.568 × 10^5 m/sec between two piezoelectric crystals was measured at a repetition rate of 1,800/sec. A voltage proportional to the propagation time was derived and calibrated against signals of known duration. The electrical drift was less than 0.1 mm/5 hr. Recordings of left ventricular pressure, segment length of two crystal pairs, and dP/dt were made simultaneously on a four-channel Gould recorder at 100 mm/sec. A standard length scale was preset for each crystal pair to measure changes in end-diastolic segment length. In addition, an electrically independent magnified scale was used to amplify the signal. The magnified recording was arbitrarily positioned to allow more accurate measurement of systolic and end-diastolic length changes.

Regional blood flow was measured by the radioactive microsphere technique in all dogs. Microspheres were suspended in 10% dextran containing 0.01% Tween 80 solution and agitated by vibration for 6 minutes to ensure uniform suspension before injection. Approximately 10^6 microspheres (15 ± 3 μm) labelled with 57Co or 113Sn (New England Nuclear, Boston, Massachusetts) were injected through the left atrial catheter over approximately 10 seconds. A reference sample of blood was withdrawn via the femoral artery catheter, beginning immediately before each injection and continuing for 3 minutes at a withdrawal rate of 7 ml/min. Myocardial samples were counted for 200 seconds in a gamma well counter with appropriately selected energy windows. Counts were corrected for background and energy crossover and compared with the reference blood sample to obtain flow as milliliter per minute per 100 grams tissue. Because the microspheres were 15 μm in diameter, no correction was made for late loss from the myocardium over the next 2–3 weeks.

Measurements of end-diastolic length were taken at the onset of the rapid upstroke in left ventricular pressure, and end-systolic length was defined 15 msec before peak negative dP/dt. Systolic shortening was the difference between end-diastolic and end-systolic length; if the magnitude of systolic shortening was between 0% and 66% of baseline shortening, the myocardial segment was considered to be hypokinetic, while dyskinesia was considered present when end-systolic length was greater than end-diastolic length. Postsystolic shortening in hypokinetic segments was defined as any shortening after end-systole. In dyskinetic segments, which show holosystolic bulging during ischemia, post-systolic shortening was measured from end-diastole (Figure 2). Similar measurements were made of systolic thickening and postsystolic thickening. All measurements of systolic shortening and postsys-
Systolic shortening were expressed as a percentage of end-diastolic length (EDL).

Recordings were made at a paper speed of 1 or 25 mm/sec on preset standard length scales and again at 100 mm/sec on the electrically independent magnified scale. The recorded data were measured and averaged over at least five cardiac cycles.

All tissue for histological examination was processed and embedded in paraffin wax with a Tissue-Tek Vacuum Infiltration Processor (Miles Scientific, Naperville, Illinois) and sectioned at 6 μm. The occluded artery was subdivided into a sequential series of blocks 2-mm thick before processing. These blocks were subsequently sectioned at three levels for microscopic examination, the sections stained with hematoxylin and eosin (H&E), phosphotungstic acid–hematoxylin (PTAH), and elastic Van Gieson. Sections cut from the full transmural face of each block of myocardium in the plane of the pair of crystals were stained with H&E, PTAH, and Masson's trichrome. After microscopic examination, the percentage of apparently viable muscle in each section was calculated with an electronic digitizer (Hipad, Houston Instrument Division of Bausch and Lomb, Austin, Texas) attached to a Rainbow computer.

Protocol
The LAD was occluded for 90 minutes in 11 dogs (group 1) and for 180 minutes in eight dogs (group 2). Left ventricular pressure, dP/dt, and segment length and thickness changes on standard and magnified scale were recorded at 5 minutes before LAD occlusion, at slow speed (1 mm/sec) during occlusion, and at 15, 30, 60, and 90 minutes after occlusion, with additional measurements at 120, 150, and 180 minutes after occlusion in group 2 dogs. To avoid reperfusion arrhythmias, partial reperfusion for the first 5 minutes was achieved by removal of a 20-gauge cannula that had been included in a ligature around the LAD. Lidocaine (1 mg/kg) was given immediately before occlusion in five dogs and immediately before reperfusion in all dogs. Segment length measurements were repeated at 30 and 60 minutes after reperfusion in both groups, and the recording showing the greatest degree of shortening was taken as representative of early recovery. Myocardial blood

FIGURE 2. Side panels of recording show the length changes for ischemic segments AC and BD together with left ventricular pressure and left ventricular dP/dt before (left) and at 5 minutes after (right panel) occlusion of the left anterior descending coronary artery, recorded at a paper speed of 100 mm/sec. SS, systolic shortening; PSS, postsystolic shortening; EDL, end-diastolic length. Center panel: At a paper speed of 1 mm/sec, the effects of left anterior descending coronary artery occlusion, comprising a slight fall in left ventricular pressure and a rise in end-diastolic pressure with a corresponding fall in peak positive and negative dP/dt and a more marked but transient fall in negative dP/dt. EDL increases, SS falls (with minimal dyskinesis in segment A–C), and PSS develops. (See text for discussion.)
flow was measured at 55 minutes after LAD occlusion and again at 55 minutes after reperfusion.

Remeasurement of segment length and hemodynamics was undertaken at 2 weeks in the first two dogs and at 3 weeks in the remaining dogs.

Statistical Analysis

Hemodynamic measurements after LAD occlusion and subsequent reperfusion were compared with analysis of variance. Comparisons between segment length measurements before and during occlusion and after reperfusion were made with Student's t test. Results were expressed as mean ± SEM. Correlation coefficients and regression lines were calculated with the least-squares method.

Results

In group 1, the first study was completed in all 11 dogs, but two dogs became ill with classic symptoms of distemper and had to be killed on the 5th and 7th days, leaving only nine survivors for the second study. Of the eight group 2 dogs, three developed ventricular fibrillation shortly after LAD occlusion and could not be reverted to sinus rhythm. Another dog developed ventricular fibrillation at 2 hours after occlusion but was successfully reverted, and the results are included in the analysis. The second study was undertaken successfully in the surviving five dogs.

Hemodynamic Changes

Table 1 shows the sequential changes in heart rate, left ventricular systolic and diastolic pressures, and peak positive and negative dP/dt for dogs of both groups during occlusion, up to 60 minutes after reperfusion and at 3 weeks after reperfusion. There was a rise in left ventricular end-diastolic pressure and a fall in peak positive dP/dt that continued into early reperfusion. At 3 weeks after reperfusion, hemodynamics were not significantly different from the preocclusion values.

Segment Length Changes Before Coronary Occlusion

Data on segment length and thickness before and during coronary occlusion were available from 16 dogs, each providing a possible four segments for length analysis and one segment for thickness analysis (Figure 1). Of 64 length segments, 54 were technically satisfactory. All 16 thickness segments provided technically satisfactory recordings.

Segments perpendicular to the diagonal artery (AC, BD; n=25; Figure 1) showed greater total baseline shortening (19.0±1.0% of end-diastolic length) than segments parallel to the diagonal artery (AB, CD; n=29; 14.7±1.0%; p<0.05). Baseline systolic thickening was 16.3±2.6% of end-diastolic thickness. Minimal postsystolic shortening was often seen after normal systolic shortening, more commonly in segments perpendicular to the diagonal artery (16 of 25) than in those which were parallel to it (six of 29; p<0.01). Moreover, postsystolic shortening had greater magnitude (10% of total shortening) in segments AC and BD than in segments AB and CD (1% of total shortening; p<0.001). Similarly, postsystolic thickening was present in six out of 16 segments on baseline recordings with an average magnitude of 10% of total baseline thickening.

Changes After Coronary Occlusion and Reperfusion

After LAD occlusion, four segments lost adequate recording for measurement, 33 segments showed dyskinesia, and 17 showed hypokinesia. Of 16 wall thickness measurements, 13 segments were dyskinetic (showing systolic thinning) and three were hypokinetic.

Recordings from a typical experiment with length traces from two segments, left ventricular pressure, and dP/dt taken before, during, and after LAD occlusion are shown in Figure 2. Recordings taken at slow speed during occlusion show hypokinesis beginning to develop at 10–15 seconds after occlusion, with subsequent development of dyskinesis.
during early systole. Postsystolic shortening is seen from approximately 25 seconds after occlusion. Systolic pressure and peak positive dP/dt decline slightly, while diastolic left ventricular pressure rises. Peak negative dP/dt shows a marked fall between 15 and 60 seconds after occlusion and then stabilizes at a slightly lower level than before occlusion. This transient fall in negative dP/dt bears no temporal relation to the development of postsystolic shortening. It is thought to be related to transient regional inhomogeneity caused by the interaction between late systolic shortening in the ischemic segment and accelerated lengthening of the adjacent normal myocardium.9,10

**Dyskinetic Segments**

As we found previously,4 the magnitude of postsystolic shortening and thickening was maximum at 5 minutes after LAD occlusion, averaging 49±4% and 31±6% of baseline shortening and thickening, respectively. Correlation of the magnitude of baseline systolic shortening with the magnitude of postsystolic shortening at 5 minutes in each dyskinetic segment was found to be significant (r = 0.44 for 33 segments; p < 0.02). Similarly, baseline systolic thickening correlated with the magnitude of postsystolic thickening at 5 minutes (r = 0.73 for 13 segments, p < 0.01); these results are shown in Figure 3. There was no correlation between postsystolic shortening and thickening and the extent of dyskinesia within each segment measured at end systole (r = 0.08; n = 33 for postsystolic shortening; r = 0.36; n = 13 for postsystolic thickening). Although the correlations are weaker than those we found previously,4 these results support our previous findings, suggesting that the magnitude of postsystolic shortening and thickening is related to the magnitude of active systolic shortening before the onset of ischemia.

Temporal changes in end-diastolic length and thickness, systolic shortening and thickening, and postsystolic shortening and thickening are shown in Figure 4. End-diastolic length increased by approximately 10% during ischemia and end-diastolic thickness fell by 10%. End-diastolic length returned to control levels with reperfusion, but thickness increased above control after 180 minutes of ischemia, presumably because of tissue edema formation. Dyskinesia (systolic lengthening and thinning) was present, usually during the total period of ischemia. There was recovery of systolic function [from −22±6% to 8±7% of baseline shortening (p<0.001) and from −30±10% to 1±7% of baseline thickening (p<0.1)] in group 1 segments at 30–60 minutes after reperfusion. There was no significant recovery in group 2 segments. However, there was marked variation in recovery in both groups of segments; of 33 segments that had been dyskinetic during ischemia, 15 remained dyskinetic at 30–60 minutes, 17 became hypokinetic, and one lost adequate recording.

Postsystolic shortening and thickening, which were maximal at 5 minutes after occlusion (49±4% and 31±6% of baseline shortening and thickening),

**FIGURE 3.** Plots of correlations between baseline preischemic systolic shortening (left) or thickening (right) and postsystolic shortening or thickening measured at 5 minutes after left anterior descending coronary artery occlusion.
declined by 32% and 52%, respectively, during 90 minutes of ischemia in group 1 segments and by 45% and 82%, respectively, during 180 minutes of ischemia in group 2 segments. The postsystolic changes did not decline further after 30–60 minutes of reperfusion in group 1 segments. Postsystolic shortening remained at a significantly higher level at 30–60 minutes after reperfusion (23 ± 6% of baseline shortening) than it had been before coronary ligation (8 ± 2% of baseline shortening; p < 0.01). Similarly, postsystolic thickening at 30–60 minutes after reperfusion was 22 ± 5% of baseline thickening compared with 2 ± 2% of baseline thickening before coronary occlusion (p < 0.01). However, in group 2 segments, the postsystolic values after 30–60 minutes of reperfusion were not significantly different from baseline. On reinsertion of the crystals at 3 weeks after reperfusion, end-diastolic lengths and thicknesses were similar, confirming that the crystals had been reinserted close to their previous sites. Regional wall motion of the normal segments (GH, Figure 1) was insignificantly less than at the first study (10.9 ± 1.1% vs. 12.7 ± 1.7% of end-diastolic length; n = 13, p = 0.26), suggesting that baseline conditions were comparable. Systolic shortening and thickening had improved significantly in group 1 segments (shortening from 9 ± 7% to 42 ± 11% of baseline shortening (p < 0.05) and thickening from 1 ± 7% to 56 ± 17% of baseline thickening (p < 0.01)). However, there was no significant improvement in either shortening or thickening of group 2 segments. Postsystolic shortening and thickening had declined further but were still present at an insignificantly higher level in group 1 segments comparing the magnitude at 3 weeks after reperfusion with the magnitude before occlusion [12 ± 5% vs. 8 ± 2% (p = 0.35) for length and 8 ± 4% vs. 2 ± 2% (p = 0.09) for thickness]. There was no significant increase in postsystolic shortening or thickening above baseline at 3 weeks in group 2 segments, which had had 180 minutes of ischemia.

**Hypokinetic Segments**

End-diastolic length of the 17 hypokinetic segments increased by 6% during coronary occlusion and returned to control levels with reperfusion. Systolic shortening was 34 ± 6% of baseline after 90 minutes of ischemia (group 1) and 29 ± 13% after 180 minutes of ischemia (group 2) and returned to 64 ± 11% of baseline during early reperfusion and 64 ± 13% of baseline at 3 weeks in group 1 segments and to 40 ± 13% at early reperfusion and 62 ± 14% at 3 weeks in group 2. Postsystolic shortening declined

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**FIGURE 4.** Plots of time-course of changes in end-diastolic length (EDL), systolic shortening (SS), and postsystolic shortening (PSS) (left) and end-diastolic thickness (EDT), systolic thickening (ST), and postsystolic thickening (PST) (right) before coronary occlusion, during 90 minutes (closed circles; group 1) or 180 minutes (open circles; group 2) of coronary occlusion, and after reperfusion for 30–60 minutes and 3 weeks.
from $34 \pm 4\%$ to $27 \pm 3\%$ of baseline shortening between 5 and 90 minutes of ischemia (group 1 and 2 segments, $n=17$) and to $23 \pm 5\%$ after 180 minutes of ischemia (group 2; $n=5$). There was no or minimal persistence of postsystolic shortening in hypokinetic segments either early or at 3 weeks after reperfusion.

**Correlation Between Postsystolic Shortening of Dyskinetic Segments Before Reperfusion and Their Functional Recovery After Reperfusion**

To test the hypothesis that postsystolic shortening and thickening when present immediately before reperfusion were markers of potential for recovery of function after reperfusion, we correlated their magnitude after 90 and 180 minutes of ischemia with the magnitude of systolic shortening and thickening that were present at 30–60 minutes and at 3 weeks after reperfusion. In testing these correlations, we assumed that an increased degree of myocardial stunning after 180 minutes as compared with 90 minutes of ischemia would alter the relation between postsystolic shortening and thickening and early recovery for group 2 segments as compared with group 1 segments. However, after 3 weeks of reperfusion, kinetic abnormalities would be attributable entirely to myocardial necrosis, so the relation between postsystolic changes during ischemia and recovery of function should be the same regardless of the duration of ischemia. Accordingly, we attempted these correlations individually for group 1 and group 2 segments at 30–60 minutes after reperfusion, but we pooled the results from both groups for the 3-week comparisons.

Results of these correlations are shown in Figures 5 and 6, and a representative example is shown in Figure 7. The plots show that postsystolic shortening and thickening is better for predicting late recovery at 2–3 weeks ($r=0.73$, $n=28$, $p<0.001$ for postsystolic shortening; $r=0.79$, $n=12$, $p<0.01$ for postsystolic thickening) than for predicting early recovery at 30–60 minutes ($r=0.63$, $n=21$, $p<0.01$ for group 1 segments; $r=0.52$, $n=11$; $p=\text{NS}$ for group 2 segments). Correlations between postsystolic thickening and early recovery were not carried out because insufficient data were available for analysis (eight group 1 segments and five group 2 segments).

Because postsystolic shortening, which was still present to a significant degree at 30–60 minutes after reperfusion in group 1 segments (Figure 4), might be additive to systolic shortening as an index of the capacity of the previously ischemic segment to contract, we repeated the comparison between postsystolic shortening during ischemia and early recovery of systolic shortening (Figure 5A), but this time we added the magnitude of postsystolic postsystolic shortening to the magnitude of systolic shortening. This improved the correlation for group 1 segments (Figure 5A) from $r=0.63$ to $r=0.79$. 

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**Figure 5.** Plots of correlations between postsystolic shortening of dyskinetic segments at 90 minutes (left; group 1 segments) or 180 minutes (right; group 2 segments) after left anterior descending coronary artery occlusion and subsequent recovery of systolic shortening over 30–60 minutes of reperfusion.
Myocardial Blood Flow

Values for myocardial blood flow during ischemia and after 55 minutes of reperfusion are shown in Table 2. Flow during ischemia was lower in dyskinetic segments (9 ± 2 ml/min/100 g myocardium) than in hypokinetic segments (20 ± 7 ml/min/100 g). Each segment group showed restoration of tissue flow during reperfusion, although there was considerable variation in individual results.

Histologic Changes at 3 Weeks After Ischemia

The relative proportions of viable myocardium in group 1 and group 2 segments are shown in Table 3. Necrosis was more extensive in dyskinetic segments than in hypokinetic segments and in the endocardial half of the wall than in the epicardial half. For both dyskinetic and hypokinetic segments, the extent of necrosis was greater after 180 minutes than after 90 minutes of ischemia, being nearly complete in the subendocardial portion of most dyskinetic segments after 180 minutes of ischemia. All arteries appeared patent throughout.

Correlations Among Indexes of Viability of Dyskinetic Segments

Correlations among the four variables comprising magnitudes of postsystolic shortening and thickening before reperfusion, recovery of shortening and thickening after 3 weeks, histological damage at 3 weeks, and myocardial blood flow during ischemia are shown in Table 4. Because the effects of flow reduction were clearly time-dependent, correlations involving myocardial blood flow were performed separately for groups 1 and 2. Recovery of function of these severely ischemic segments correlated more strongly with the magnitude of postsystolic shortening and thickening before reperfusion than with either the histological appearance of the posts ischemic segments or with impairment of their blood flow during ischemia. Correlations involving myocardial blood flow were inconsistent, four of the six correlations failing to achieve statistical significance.

Discussion

The present results confirm and extend our previous findings. Postsystolic shortening and thickening are sensitive indexes of ischemia, appearing in both dyskinetic and hypokinetic segments and persisting in the stunned myocardium after reperfusion. As in our earlier study, we found the magnitude of postsystolic shortening and thickening to be considerable, reaching 49% and 31% of baseline shortening and thickening, respectively, in dyskinetic segments at 5 minutes after coronary occlusion. Maximum postsystolic shortening occurred after the return of left ventricular pressure to its diastolic level (Figure 2), indicating that the peak of shortening and thickening occurred after mitral valve opening and during the early rapid phase of ventricular filling. We observed that the slight degree of postsystolic shortening that was present in some segments before coronary occlusion (more in long-axis than in short-axis segments) appeared to be balanced by more rapid relaxation in other segments. Presumably, this was a manifestation of normal regional inhomogeneity of myocardial fiber shortening; alternatively, it could have been a nonspecific abnormality associated with the anesthe-
tized open-chest preparation. However, as supported by our previous findings,\(^4\) we do not believe that the much greater extent of postsystolic shortening that occurred during ischemia and after reperfusion could be explained simply in terms of transmission of forces attributable to accelerated relaxation of the normal myocardium to the ischemic or postischemic myocardial segment. Also in accord with our previous findings, postsystolic shortening and thickening could not be explained in terms of elastic recoil of dyskinetic segments because both phenomena occurred in hypokinetic as well as in dyskinetic segments, both persisted when dyskinetic segments became hypokinetic after reperfusion, and there was no correlation between the magnitude of dyskinesia and the magnitude of postsystolic shortening or thickening.

Evidence for an active component of postsystolic shortening and thickening was adduced in our earlier study from positive correlations in dyskinetic segments between the magnitude of postsystolic shortening and thickening (measured either at 5 minutes after coronary occlusion or immediately before reperfusion) and either the magnitude of systolic shortening and thickening before coronary occlusion or recovery of systolic function early after reperfusion. However, our earlier experiments were terminated after 3 hours of reperfusion. Thus, the present data extend our previous observations by showing that the predictive value of postsystolic shortening and thickening during ischemia extends to the late recovery phase when myocardial function is in a steady state,\(^{11,12}\) with myocardial stunning no longer present. Stunning was a prominent feature in the present experiments after 90 minutes of LAD occlusion, as shown by the marked degree of functional recovery after 3 weeks (Figure 4), but in agreement with other investigators,\(^{11}\) this did not

**Figure 7.** Recordings of left ventricular pressure (LVP) and segment length changes (AB and CD) and left ventricular dp/dt (LV dp/dt) taken at baseline, after 5 minutes of left anterior descending coronary artery occlusion, immediately before reperfusion, and after 60 minutes and 3 weeks of reperfusion in two representative experiments. Dotted lines indicate the beginning and end of systole. Panel A: One dyskinetic segment (CD) and one hypokinetic segment (AB) are shown. Postsystolic shortening is prominent in both segments 5 minutes after occlusion and immediately before reperfusion; it persists in CD but not in AB after 60 minutes of reperfusion. After 3 weeks of reperfusion, there is partial return of function in CD, although AB is hypokinetic relative to baseline. Panel B: Dyskinetic segment CD shows postsystolic shortening at 5 minutes after occlusion, which has almost disappeared immediately before reperfusion. There is no recovery of function after 60 minutes of reperfusion and minimal recovery after 3 weeks.
occur after 180 minutes of occlusion. Although the correlations we found between postsystolic shortening and baseline systolic shortening and between postsystolic shortening and shortening during early recovery were less exact than those we had found previously, it was of interest that the correlation between postsystolic shortening during ischemia and early recovery was better when total shortening of group 1 segments (systolic shortening plus postsystolic shortening) was used as the descriptor of recovery \((r=0.79)\) than when postsystolic shortening alone was used as the descriptor \((r=0.63)\). Moreover, postsystolic shortening was still present to a significant degree after 90 minutes of ischemia with reperfusion (group 1) and systolic shortening improved further after 3 weeks, while neither of these events happened after 180 minutes of ischemia with reperfusion (group 2). This would have been expected if postsystolic shortening is a manifestation of the potential ability of dyskinetic myocardial segments to contract.

Neither myocardial blood flow during ischemia nor the extent of histological necrosis at 3 weeks after ischemia correlated as closely with functional recovery of dyskinetic segments as did the magnitude of postsystolic shortening measured immediately before reperfusion (Table 4). This is at first sight surprising because both myocardial blood flow and histological necrosis have been regarded by many as gold standards for assessing the severity of myocardial infarction.\(^{13,14}\) However, previous comparisons of contractile function, blood flow, and histological changes\(^{15,16}\) have correlated the whole gamut of functional impairment (from mild hypokinesia to dyskinesia) with deficient blood flow and histological damage, whereas correlations in the present study deal with the more narrow range of severely ischemic dyskinetic segments. Moreover, there are inherent inaccuracies and limitations in methods for assessing myocardial blood flow and structural damage. Measurements of flow are inaccurate at very low flow rates when under 400 microspheres are contained in a tissue sample,\(^{17}\) while leaching of microspheres over 3 weeks and tissue edema can reduce the number of microspheres artifactually\(^{18,19}\) and tissue scarring and shrinkage can increase it.\(^{19}\) Blood flows during reperfusion in the present experiments (Table 2), while confirming that reperfusion had occurred, showed an apparent reversal in previously dyskinetic segments of endocardial flow: epicardial flow ratios in the 90-minute occlusions compared with the 180-minute occlusions. There was also an apparent depression of flow in the normal segments during reperfusion, even though the other hemodynamic indexes were unchanged (Table 1). Presumably, some depression of myocardial blood flow resulted from the prolonged anesthesia, although experimental variation is another possible cause. These reperfusion blood flows do not

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</tr>
<tr>
<td>Dyskinetic segments ((n=38))</td>
</tr>
<tr>
<td>Transmural</td>
</tr>
<tr>
<td>Endocardial</td>
</tr>
<tr>
<td>Epicardial</td>
</tr>
<tr>
<td>Hypokinetic segments ((n=15))</td>
</tr>
<tr>
<td>Transmural</td>
</tr>
<tr>
<td>Endocardial</td>
</tr>
<tr>
<td>Epicardial</td>
</tr>
<tr>
<td>Normal segments ((n=13))</td>
</tr>
<tr>
<td>Transmural</td>
</tr>
<tr>
<td>Endocardial</td>
</tr>
<tr>
<td>Epicardial</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

<table>
<thead>
<tr>
<th>Table 3. Histological Assessment at 3 Weeks After Reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viable myocardium (%)</td>
</tr>
<tr>
<td>Transmural</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>90-minute occlusions (group 1)</td>
</tr>
<tr>
<td>Dyskinetic segments ((n=25))</td>
</tr>
<tr>
<td>Hypokinetic segments ((n=9))</td>
</tr>
<tr>
<td>180-minute occlusions (group 2)</td>
</tr>
<tr>
<td>Dyskinetic segments ((n=16))</td>
</tr>
<tr>
<td>Hypokinetic segments ((n=6))</td>
</tr>
</tbody>
</table>

Values are mean±SEM.
affect the correlations shown in Table 4 and discussed above. With regard to histological assessment, although scar tissue does not show contractility, the presence of normal contractile function cannot necessarily be inferred from a normal histological appearance of the myocytes. Furthermore, we examined the histology only in the plane of insertion of the crystals; tethering from adjacent myocardial segments could have influenced shortening independent of the functional performance of the segment under consideration. Overall, it is not surprising that an indicator of contractile function, postsystolic shortening, should be a better predictor of functional recovery than an indicator based on either structure or single estimates of low flow rates.

Postsystolic shortening has been described by many authors with varying nomenclature. Delayed relaxation of myocardial fibers after release of a coronary ligature in dogs was observed by Sayen et al in 1958. Prolongation of tension development and relaxation was noted both in isolated mammalian ventricular muscle during hypoxia and in intact dog hearts after ischemia by Bing et al, while postsystolic shortening in conscious dogs with severe ischemia was described by Vatner et al. In the context of mild ischemia, Foex and coworkers have described postsystolic shortening as an early abnormality of wall motion when critical coronary constriction is produced by gradual tightening of a snare and have shown that it is increased by halothane anesthesia and calcium channel-blocking drugs and is reduced by infusions of calcium chloride. These observations, together with our own, show that postsystolic shortening and thickening are not specific for myocardial ischemia because they occur in the postsischemic myocardium and with administration of cardiac-depressant drugs.

The mechanism of production of postsystolic shortening is not addressed by the present or previous studies. However, in the total context of its occurrence in severe and mild ischemia and in postsischemia, the most likely mechanism appears to be delay in myocardial relaxation. From the standpoint of muscle physiology, systole can be said to extend into the phase of rapid ventricular filling because the active process of myocardial relaxation extends into this phase of the cardiac cycle. This corresponds with the proportion of the cardiac cycle occupied by postsystolic shortening in the present and previous studies. The concept that tension prolongation leads to an imbalance between imposed force and developed contractile force beyond the time of usual end systole (Figure 8) was proposed as the basis for active post-systolic shortening. Tyberg et al used hypoxic and normal muscle strips in series and Wiegner et al used a computer model of an hypoxic and a normal segment in series to show active postsystolic shortening attributable to tension prolongation in the hypoxic muscle.

The value of postsystolic shortening and thickening for prediction of recovery of function has considerable clinical significance. Although reperfusion is clearly of clinical benefit, it is not known what time-window is available for reperfusion or whether reperfusion will be of value in any particular patient. Gibson and colleagues have described prolonged inward movement of the ischemic segment during isovolumic relaxation in cineventriculograms of patients at 3.5 ± 1.2 hours after onset of myocardial infarction; this phenomenon is attributed to residual contractility of the ischemic segment. Again, we have seen postsystolic shortening in areas of hypo-

### Table 4. Correlations Among Indexes of Viability of Ischemic Dyskinetic Segments

<table>
<thead>
<tr>
<th>Variables correlated</th>
<th>Comparisons</th>
<th>Correlation coefficient</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS:ST (3W) vs. PSS:PST (before reperfusion)</td>
<td>28 (PSS)</td>
<td>0.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>12 (PST)</td>
<td>0.79</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>40 (PSS+PST)</td>
<td>0.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SS:ST (3W) vs. percent viable myocardium (3W)</td>
<td>40</td>
<td>0.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SS:ST (3W) vs. MBF (during ischemia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>20</td>
<td>0.21</td>
<td>NS</td>
</tr>
<tr>
<td>Group 2</td>
<td>14</td>
<td>0.78</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Percent viable myocardium (3W) vs. PSS:PST</td>
<td>40</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(before reperfusion)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent viable myocardium (3W) vs. MBF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>23</td>
<td>0.29</td>
<td>NS</td>
</tr>
<tr>
<td>Group 2</td>
<td>16</td>
<td>0.46</td>
<td>NS</td>
</tr>
<tr>
<td>MBF (during ischemia) vs. PSS:PST (before reperfusion)</td>
<td>20</td>
<td>0.23</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>0.53</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

SS, systolic shortening; ST, systolic thickening; PSS, postsystolic shortening; PST, postsystolic thickening; W, weeks; MBF, myocardial blood flow.
kinesia or akinesia in cineventriculograms of patients with chronic myocardial ischemia. Whether surgical revascularization for such patients would be of value for restoration of normal contractile function remains to be determined. Also of interest would be the relation of postsystolic shortening to the abnormalities of diastolic function that are prominent in ischemia\textsuperscript{34,35} and that may be the earliest manifestation of it.\textsuperscript{36} Clearly, further work is necessary to assess the importance of postsystolic shortening and thickening in the context of clinical myocardial ischemia and reperfusion.

Acknowledgments

We are grateful to Robin W. Easdale and Philip V. Lacey for technical assistance and to Mrs. Janice Pillinger for secretarial assistance in the preparation of this manuscript.

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KEY WORDS • postsystolic shortening • myocardial ischemia • reperfusion • diastolic function
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Circulation. 1988;78:994-1007
doi: 10.1161/01.CIR.78.4.994

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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