Mechanisms of Augmented Segment Shortening in Nonischemic Areas during Acute Ischemia of the Canine Left Ventricle

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SUMMARY. To examine the interaction between normal and nonischemic areas of the left ventricle during acute ischemia, we implanted midwall ultrasonic segment length gauges in the ischemic zone and in nonischemic areas of the canine left ventricle. During acute ischemia, end-diastolic pressure and segment length in the nonischemic areas increased. There was no change from control in the segment length at the time of aortic valve opening and closure. Thus, in nonischemic areas, total segment shortening, as measured by the percent change in segment length from the time of end-diastole to aortic valve closure, increased. This was due to an increase in isovolumic shortening (end-diastole to aortic valve opening) with no change in ejection shortening (aortic valve opening to closure). The progressive increase in isovolumic shortening in nonischemic areas over time was directly paralleled by the progressive development of the isovolumic lengthening or bulge in the ischemic zone. Nonischemic areas, whether adjacent, on the opposite wall, or distant to the ischemic zone, all behaved similarly. Adrenergic blockade did not qualitatively alter these findings. We conclude that acute ischemia induces a mechanical disadvantage which is greater than just the loss of contractile function by the ischemic segment. Despite the apparent hyperfunction of nonischemic areas, the increased total segment shortening is expended in stretching the ischemic zone during isovolumic systole. As a result, there is no significant “compensatory” increase in ejection shortening in nonischemic areas. The results from the present study indicate that augmented total segment shortening in nonischemic areas is due to a combination of the Frank-Starling mechanism and regional intraventricular unloading of the nonischemic into the ischemic areas. (Circ Res 56: 351-358, 1985)

DURING acute ischemia of the left ventricle, an increase in systolic shortening has been measured in nonischemic areas in experimental animals by a variety of techniques, including ultrasonic segment gauges (Theroux et al., 1974, 1976, 1977; Heyndrickx et al., 1975; Molaug et al., 1983), epicardial strain gauges (Nakano, 1966; Pashkow et al., 1977), ultrasonic wall thickness gauges (Savage et al., 1981; Nakamura et al., 1982) and echocardiography (Kerber et al., 1976). Some studies using epicardial strain gauges did not find an apparent hyperfunction of nonischemic areas (Banka and Helfant, 1974; Vokonas et al., 1976; Wyatt et al., 1976), indicating that the effects may not always be reflected transmurally. An increase in systolic motion in nonischemic areas has been noted in patients by echocardiography (Corya et al., 1975; Nieminen and Heikkila, 1976) and angiography (Rigaud et al., 1979; Stack et al., 1983; Sheehan et al., 1983). The hyperfunction of nonischemic areas is thought to be due primarily to utilization of the Frank-Starling mechanism (Theroux et al., 1974; Molaug et al., 1983), although some have suggested increased sympathetic stimulation as the primary mechanism (Nakano, 1966; Pashkow et al., 1977; Rigaud et al., 1979). The increased segment shortening by nonischemic areas is thought to compensate for the loss of systolic function in the ischemic zone. This study was undertaken to clarify the mechanisms and effectiveness of the apparent hyperfunction in nonischemic areas during acute ischemia, and to define the nature of the interaction between ischemic and nonischemic segments.

Methods

Instrumentation

Ten mongrel dogs of either sex weighing between 13 and 30 kg were anesthetized with intravenous sodium pentobarbital (25 mg/kg), intubated, and respiration was supported with a Harvard respirator. The heart was exposed through a midline sternotomy and bilateral 5th interspace thoracotomy, and supported in a pericardial cradle. A 7F high fidelity micromanometer-tipped (Millar, model PC 574) catheter was advanced into the left ventricle from the left carotid artery. A 100-cm 7F fluid-filled pigtail catheter, attached to a Statham P23 DB transducer, was advanced into the left ventricle from the left femoral artery. Pressures from the two catheters were matched, then the fluid-filled catheter was withdrawn into the
FIGURE 1. Typical continuous recording from a dog with the electrocardiogram (ECG) and pressures in the aorta (AO) and left ventricle (LV), and segment length gauge signals from the anterior (ANT) apex and base, lateral (LAT) base, and posterior (POST) apex. The left panel is a control period. The middle panel at slow paper speed records 3 minutes of acute ischemia in the anterior apex, produced by occlusion of the mid-left anterior descending (LAD) coronary artery (arrow). The panel on the right is after 3 minutes of ischemia. Time scales are at the bottom. See text for discussion.

ascending aorta for measurement of central aortic pressure.

Limb leads for an electrocardiogram (ECG) were placed for monitoring. The left anterior descending coronary artery was dissected free beyond the first or second large diagonal branch. A brief 1- to 2-minute test occlusion of the coronary artery was performed while an epicardial ECG lead was used to define the location of maximal ST segment elevation. The epicardial ECG lead also was used to confirm that areas subsequently to be designated as nonischemic had no significant epicardial ST segment deviation. After release of the coronary artery occlusion, the animal was allowed to recover for at least 45 minutes.

Ultrasonic segment gauges, composed of two 5-MHz piezoelectric crystals (2 mm in diameter) were implanted through small stab wounds to a depth of 4–6 mm from the epicardial surface, approximately 1 cm apart, and oriented in the circumferential or hoop axis fiber direction (Streeter et al., 1969). Such an orientation was achieved in the anterior wall by placing the segment gauge perpendicular to the external long axis as defined by a line from the bifurcation of the left main coronary artery to the apical dimple. In the posterior wall, the external long axis was defined from the inferior pulmonary vein to the apical dimple. The external long axis of the lateral wall was defined by a line midway between the anterior and posterior external long axes and also with an end-point at the apical dimple.

In all animals, one gauge was placed in the ischemic zone of the anterior apex (in the region of maximal ST segment elevation during the test occlusion of the coronary artery), and a second gauge (pair of crystals) was placed directly opposite in the posterior apex, in a nonischemic area. Six of the 10 animals were used to determine whether the location of the nonischemic area in relation to the ischemic zone influenced its response. In all six of these animals, an additional segment gauge was placed in the lateral base, and, in four of the six animals, a fourth gauge was placed in the anterior base. All gauges in nonischemic areas were placed in areas without ST segment elevation and clearly away from visible cyanosis or dyskinesis during the trial occlusion. Gauges in the anterior base were separated from the ischemic zone (anterior apex) by at least one or two normally perfused acute diagonal branches of the left anterior descending coronary artery.

The electrocardiogram, central aortic pressure, left ventricular pressure, and ultrasonic segment length gauge signals were recorded on a forced ink (Brush Clevite) 8-channel polygraph at a paper speed of 200 mm/sec and on FM magnetic tape for subsequent playback with analog-to-digital conversion. Recordings were made with respiration transiently suspended at end-expiration during a control period and 3 and 15 minutes after coronary artery occlusion.

Experimental Protocol

In all 10 animals, regional ventricular function was measured during a control period, then continuously for 3 minutes after acute occlusion of the mid-left anterior descending coronary artery (see Fig. 1). In five animals, the coronary artery occlusion was released after 3 minutes, and the animals were allowed to recover for 45 minutes. During this recovery period, bilateral vagotomy was performed and intravenous propranolol (0.5–1.0 mg/kg) was administered. This was followed by a repeat 3-minute occlusion of the coronary artery. In four animals, the initial coronary artery occlusion was maintained for 15 minutes, and in two of these animals, it was maintained for 46 to 67 minutes.
Data Analysis

All data were played back from FM tape for analog-to-digital conversion at 5 msec intervals with at least 15 consecutive beats averaged. For purposes of timing cardiac events, end-diastole was defined by the inflection point following atrial contraction in the high gain left ventricular pressure tracing, or, if this was not obvious, from the peak of the R wave of the electrocardiogram. Aortic valve opening was defined by transposing the central aortic pressure at onset of systole onto the high fidelity left ventricular pressure tracing, thus correcting for the inherent signal delay from the fluid-filled catheter system. Similarly, aortic valve closure was defined by transposing the central aortic pressure of the dicrotic notch onto the left ventricular pressure tracing (see Fig. 1).

Total segment shortening was defined as the percent change in segment length from end-diastole to aortic valve closure. This was divided into two components. Isovolumic shortening was the percent change in segment length from end-diastole to aortic valve opening. Ejection phase shortening was calculated as the total segment shortening minus isovolumic shortening, thus measuring the change in segment length from aortic valve opening to closure.

Statistical Analysis

Changes in hemodynamic, segment length, and segment shortening measurements were compared by repeated measure analysis of variance (Winer, 1971). In all cases, a P value of less than 0.05 was considered statistically significant.

Results

Hemodynamic Measurements

Three minutes after acute occlusion of the mid-left anterior descending coronary artery, the heart rate of 122 ± 9 beats/min (mean ± 1 st) was not significantly different from the control value of 118 ± 9 beats/min. Left ventricular end-diastolic pressure increased significantly from 6.0 ± 0.8 mm Hg during control to 8.0 ± 0.7 mm Hg after 3 minutes of ischemia. There was a slight but significant decrease in mean aortic pressure from 114 ± 5 to 109 ± 5 mm Hg after 3 minutes of ischemia. In the four animals measured after 15 minutes of ischemia, there was no significant change in heart rate or ventricular pressure between 3 and 15 minutes.

Segment Lengths

In the anterior apex (ischemic zone), segment lengths throughout the cardiac cycle increased significantly 3 minutes after occlusion of the coronary artery. End-diastolic segment length of the anterior apex increased in the 10 animals, from 10.6 ± 0.9 mm to 12.2 ± 1.1 mm after 3 minutes of ischemia. The segment length at aortic valve opening increased from 10.8 ± 0.9 mm to 13.6 ± 1.2 mm and at aortic valve closure from 9.0 ± 0.8 mm to 13.5 ± 1.2 mm.

In the posterior apex (nonischemic area), the segment length at end-diastole increased significantly in the 10 animals, from a control value of 11.8 ± 1.1 mm to 12.3 ± 1.2 mm after 3 minutes of ischemia. However, there was no significant change in segment length at aortic valve opening (11.7 ± 1.1 mm control, 11.8 ± 1.2 mm after 3 minutes of ischemia) or aortic valve closure (10.5 ± 0.9 mm control, 10.6 ± 1.0 mm after 3 minutes of ischemia). There was an initial tendency for the aortic valve closure segment length to be smaller than control, but this was a transient change only during the first 10-15 seconds of ischemia (Fig. 1).

In other nonischemic areas, a similar pattern was observed. In the six animals with lateral base measurements, end-diastolic segment length increased significantly from 10.1 ± 0.6 mm to 10.4 ± 0.7 mm after 3 minutes of ischemia, but there was no significant change in aortic valve opening or closure segment lengths. In the four animals with anterior base measurements, end-diastolic segment length increased significantly from 8.4 ± 1.2 mm to 8.7 ± 1.2 mm, also without change in aortic valve opening or closure segment lengths.

In four animals, measurements were obtained during 15 minutes of acute ischemia. There were no significant changes in segment lengths in the ischemic zone (anterior apex) or nonischemic area (posterior apex) between 3 and 15 minutes. In two of these animals, segment lengths remained stable after 46 and 67 minutes of ischemia.

Regional Segment Shortening

During the control period, total segment shortening in the anterior apex (ischemic zone) of the 10 animals was 13.1 ± 3.4% and was predominantly due to shortening during the ejection phase (16.4 ± 3.0%), with little contribution by segment length changes during isovolumic systole (—2.3 ± 1.3%). After 3 minutes of ischemia, total segment shortening was replaced by total segment lengthening of —11.0 ± 3.3%, now predominantly due to lengthening during isovolumic systole (—11.4 ± 1.9%), with little contribution by segment length changes during the ejection phase (0.5 ± 1.6%). All changes in segment shortening in the anterior apex with acute ischemia were significant.

In the nonischemic posterior apex, 3 minutes of acute ischemia resulted in a significant increase in total segment shortening in the 10 animals from 10.3 ± 1.3% to 12.6 ± 1.3%, entirely due to a significant increase in isovolumic shortening from 0.4 ± 1.1% to 3.4 ± 1.0%, whereas there was no significant change in ejection phase shortening (9.9 ± 1.0% control, 9.2 ± 1.1% after 3 minutes of ischemia). These results reflect the increased end-diastolic segment length and unchanged segment lengths at aortic valve opening and closure observed in nonischemic areas (see above).

Pressure-segment length loops were drawn from digitized data obtained at 5-msec intervals (Fig. 2). In the ischemic zone, marked increases in segment length occurred throughout the cardiac cycle 3 min-
utes after coronary artery occlusion. There was segment lengthening during isovolumic systole (isovolumic bulge), with little change in segment length or akinesis during the ejection phase. In the nonischemic area, there was an increase in end-diastolic segment length 3 minutes after ischemia, due to an increase in end-diastolic pressure. However the segment length at aortic valve opening and closure were unchanged, and thus the ejection phase shortening was unchanged. Total segment shortening, measured from end-diastole to aortic valve closure, was increased, entirely due to an increase in isovolumic shortening from end-diastole to aortic valve opening. This occurred at the same time as the isovolumic bulge in the ischemic segment.

The temporal sequence of changes in shortening patterns from 30 seconds to 3 minutes is demonstrated in Figure 3 for the six animals with simultaneous measurements in the anterior apex (ischemic zone), lateral base, and posterior apex (two nonischemic areas). In all animals, the progressive isovolumic lengthening or bulge in the ischemic zone was paralleled by a progressive increase in isovolumic shortening in the nonischemic areas. There were no regional differences in the response of nonischemic areas to acute ischemia. Similar changes were seen in the lateral base, posterior apex, and in the anterior base (a third nonischemic area measured simultaneously in four of these animals).

Regional shortening patterns were stable between 3 and 15 minutes of ischemia, as examined separately in four animals. In these four animals, there was no significant change in the anterior apex (ischemic zone) from 3 to 15 minutes for total segment lengthening (−9.6 ± 3.2% to −8.9 ± 3.8%), isovolumic segment lengthening (−11.6 ± 2.8% to −11.0 ± 2.7%), or ejection phase shortening (2.0 ± 1.4% to 2.1 ± 1.5%). Similarly, in the nonischemic posterior apex, total segment shortening (13.5 ± 1.3% to 13.1 ± 1.4%), isovolumic shortening (2.8 ± 1.6% to 2.8 ± 1.4%), and ejection shortening (10.6 ± 1.9 to 10.3 ± 1.5%) did not change significantly from 3 to 15 minutes of ischemia. In two of these
animals, regional segment length changes remained stable to 46 and 67 minutes of ischemia.

In five animals, the effects of 3 minutes of ischemia were compared before and after vagotomy and intravenous propranolol. There was a 10–45% decrease in total and ejection phase segment shortening in all areas during the control period after adrenergic blockade. Nevertheless, changes in shortening patterns in response to acute ischemia were qualitatively similar, before and after vagotomy and intravenous propranolol (see Fig. 4). After 3 minutes of ischemia, there was replacement of total segment shortening with lengthening in the ischemic zone (anterior apex), primarily due to isovolumic lengthening, while there was akinesis during the ejection phase. In the nonischemic areas, there was an increase in total segment shortening due to an increase in isovolumic shortening, with no change in ejection phase shortening. Both nonischemic areas (lateral base and posterior apex) behaved similarly.

**Discussion**

During acute regional ischemia of the left ventricle, shortening in the ischemic zone decreases progressively, then is replaced by paradoxical systolic expansion, as described in the classic study by Tennant and Wiggers (1935). Nakano (1966) first described an increase in contractile force in nonischemic areas, as measured by epicardial strain gauges. Increased fiber shortening in nonischemic areas was predicted by Hood (1970a) based on postmortem measurements of animals following myocardial infarction. Theroux et al. (1974), using subendocardial ultrasonic segment gauges, demonstrated increased end-diastolic segment length, segment shortening, and work in control (nonischemic) areas during 5-minute coronary artery occlusions. Increases in segment shortening of nonischemic areas has since been shown by others (Heyndrickx et al., 1975; Kerber et al., 1976; Theroux et al., 1976, 1977; Pashkow et al., 1977; Rigaud et al., 1979; Savage et al., 1981; Nakamura et al., 1982; Molaug et al., 1983), and has been thought to represent a compensatory response produced by utilization of the Frank-Starling mechanism or by generalized increased sympathetic stimulation. The goals of the current study were, first, to clarify the mechanisms of this apparent hyperfunction response of nonischemic areas and, second, to determine its effectiveness in compensating for loss of systolic function by the ischemic zone.

The current study demonstrated a progressive replacement of systolic shortening in the ischemic zone by lengthening during isovolumic systole (isovolumic bulge), and with akinesis during the ejection phase. Increased end-diastolic length in the nonischemic areas produced increased total segment shortening by the Frank-Starling mechanism. However, this increase was entirely attributed to increased shortening during isovolumic systole, whereas ejection shortening did not change. The increase in isovolumic shortening in nonischemic areas directly paralleled the development of isovolumic bulging in the ischemic zone. Thus, part of the increased total segment shortening produced by the nonischemic areas was "dissipated" into the ischemic zone during isovolumic systole, counteracting any potential (compensatory) increase in systolic function during the ejection phase. After 2–3 minutes of ischemia, regional shortening patterns remained stable for up to 15 minutes (and in two animals for 46 and 67 minutes). The location of the nonischemic area in relation to the ischemic zone did not influence its interaction with the ischemic zone. Thus, areas within the same circumferential hoop but directly opposite the ischemic zone (i.e., the posterior apex) demonstrated the same findings as sites which were distant (lateral base) or adjacent (anterior base) to the ischemic zone. The anterior base measurements in this study were obtained in a nonischemic area separated from the ischemic zone (anterior apex) by one or two normally perfused diagonal branches of the left anterior descending coronary artery, proximal to the site of occlusion. Thus, this nonischemic area was not the same as the marginal or border segments investigated in other studies, i.e., the area directly adjacent to the ischemic zone which demonstrates a reduction in systolic function despite normal coronary artery perfusion (Theroux et al., 1974, 1976, 1977; Roan et al., 1979).
When acute ischemia was produced after removal of adrenergic influences, total segment shortening in nonischemic areas still increased, due to an increase in isovolumic shortening with no change in ejection shortening. Thus, changes in adrenergic tone may influence the extent of increase in shortening but not its distribution during systole. In these animals, the effects of an initial 3 minutes of ischemia were compared to a repeat 3-minute episode of ischemia 45 minutes later (after vagotomy and intravenous propranolol). The rationale for this protocol was based on prior studies which demonstrated full return of regional systolic and diastolic function 30–45 minutes after release of 5-minute occlusions of the coronary artery (Theroux et al., 1976), whereas abnormalities of subendocardial blood flow and function may persist for over 3 hours after release of 15-minute occlusions (Heyndrickx et al., 1975, 1978). Findings from the current study indicate that the apparent hyperfunction of nonischemic areas during acute ischemia is a mechanical phenomenon, due to a combination of utilization of the Frank-Starling mechanism and regional intraventricular unloading into ischemic segments.

The direct measurements of the current study demonstrated a significant interaction between ischemic and nonischemic segments. This interaction was envisioned by Tennant and Wiggers (1935) as "a struggle between forces causing shortening and those tending to lengthen the fibers" in the ischemic segments. Several investigators have examined the mechanical consequences of such an interaction between "weak and strong" muscles linked in series, such as with isolated strips of hypoxic and normal myocardium placed in series (Tyberg et al., 1969; Wiegner et al., 1978), ventricular aneurysms (Parmley et al., 1973; Janz and Waldron, 1978), asynchrony of ventricular contraction with pacing (Badke et al., 1980), or theoretical models of regionally ischemic ventricles (Elings et al., 1977; Laird and Vellekoop, 1977; Bogen et al., 1980). The magnitude of the mechanical disadvantage produced by the interaction of ischemic and nonischemic segments is thought to be related directly to the size and inversely related to the stiffness of the ischemic area (Elings et al., 1977; Laird and Vellekoop, 1977; Bogen et al., 1980) or of the aneurysmal tissue (Parmley et al., 1973). Although this was not systematically examined in our study, we did note that, with smaller zones of ischemia, there was less of an increase in segment shortening by nonischemic areas.

Our findings were importantly dependent on the presence of systolic lengthening in the ischemic zone, particularly during isovolumic systole. It is probable that our findings would be present for several hours beyond the period of acute ischemia studied. This hypothesis is based on the observations that the majority of changes in regional function occur in the first 5 minutes of infarction, with relatively little further change until 24 hours (Theroux et al., 1977; Roan et al., 1979), and the magnitude of aneurysmal bulging is stable for several hours (Pirzada et al., 1976; Vokonas et al., 1976; Savage et al., 1981). Indirect evidence that this interaction between ischemic and nonischemic areas is still present several hours after the acute event is provided by two clinical studies (Stack et al., 1983; Sheehan et al., 1983). After successful reperfusion of the infarcted zone with intracoronary streptokinase, as regional wall motion of the ischemic zone improved, wall motion in the nonischemic areas, which had been hyperkinetic, decreased to normal. Although our results may be applicable during the acute period of ischemia (minutes to hours), we would not extrapolate our results to the later periods (days). The increased stiffness of the ischemic zone (Hood et al., 1970b), and additional long-term compensatory mechanisms, such as hypertrophy of nonischemic areas (Theroux et al., 1977: Sasayama et al., 1981), may influence the interaction between ischemic and nonischemic areas to an uncertain extent.

The mechanical phenomena observed in the current study are probably not unique to our preparation of anterior wall ischemia. Several investigators have demonstrated an increase in nonischemic area segment shortening or wall thickening following occlusion of the left circumflex coronary artery (Heyndrickx et al., 1975; Kerber et al., 1976; Theroux et al., 1976, 1977; Savage et al., 1981; Nakamura et al., 1982). Although these investigators did not distinguish between isovolumic and ejection phase changes, the increase in nonischemic area total segment shortening in the study by Theroux et al. (1976, Fig. 3) was due primarily to an increase in isovolumic shortening.

Extrapolation of our results to the conscious animal, and, thus, the clinical application to man, is more difficult. Differences in the initial cardiac volume, shape, and contraction patterns between the conscious animal and anesthetized open-chest preparations (Rushmer, 1954; Leshin et al., 1972; Rankin et al., 1976) may influence the interaction between ischemic and nonischemic areas. Although increased nonischemic area segment shortening and wall thickening following coronary artery occlusion has been demonstrated in the conscious animal, the magnitude and time course of these changes are complex. Kumada et al. (1979) found no increase in nonischemic area segment shortening after a brief 1-minute coronary artery occlusion. Hess et al. (1982) found no change in nonischemic area wall thickening after a 2-minute occlusion, although in this study left ventricular end-diastolic pressure did not increase. In contrast, Theroux et al. (1976) found a significant increase in left ventricular end-diastolic pressure and nonischemic area segment shortening after a 2-minute coronary artery occlusion. Of note, the magnitude of these changes in this conscious dog study were less than those found in their previous study in the anesthetized dog (Theroux et al.,...
1974). Velocity of nonischemic area segment shortening has been shown to increase at 5 and 15 minutes after coronary artery occlusion (Heyndrickx et al., 1975) but not after 1 hour (Cox and Vatner, 1982). Savage et al. (1981) found a significant increase in wall thickening in the nonischemic area at 15 minutes, 24, and 48 hours after coronary artery occlusion. In a more prolonged study, Theroux et al. (1977) found an increase in nonischemic area segment shortening which was significant only at 1, 2, and 3 weeks following coronary artery occlusion. In contrast to their earlier acute study (Theroux et al., 1976), left ventricular end-diastolic pressure did not increase, which may explain the lack of increased nonischemic area shortening during the acute phase. Finally, Sasayama et al. (1981) demonstrated a tendency for nonischemic area segment shortening and wall thickening to increase after coronary artery occlusion, but only the increase in segment shortening after 3 weeks was significant. In this study, left ventricular end-diastolic pressure did not increase significantly until 2 and 3 weeks after coronary artery occlusion, which may in part explain the lack of change in nonischemic area function during the acute period of ischemia.

Acute ischemia in the conscious animal also is associated with a significant increase in heart rate (Heyndrickx et al., 1975; Theroux et al., 1976, 1977; Kumada et al., 1979; Savage et al., 1981; Sasayama et al., 1981; Hess et al., 1982), a reflex response which was blunted in our anesthetized open-chest preparation. Although such reflex changes may modify the magnitude of the interaction between ischemic and nonischemic areas, the qualitative findings in the current study were not significantly influenced by adrenergic factors. Thus, an apparent hyperfunction in the nonischemic area and regional intraventricular unloading effects during isovolumic systole were seen both before and after adrenergic blockade.

Thus, in the conscious animal, acute coronary artery occlusion may not be associated with a significant increase in nonischemic area function if the occlusion is brief (less than 2 minutes), or if left ventricular end-diastolic pressure does not increase. When an apparent hyperfunction in the nonischemic area is noted in the conscious animal, the magnitude of this change may be less than in the anesthetized preparation (Theroux et al., 1976). Furthermore, with similar periods of coronary artery occlusion, wall thickening measurements may not yield precisely the same information as segment shortening measurements (Theroux et al., 1976; Sasayama et al., 1981; Hess et al., 1982). Therefore, extrapolation of our results to the conscious animal and to more prolonged periods of ischemia must be made cautiously. The magnitude and time course of functional interactions between ischemic and nonischemic areas during isovolumic systole remain to be determined in the conscious animal.

Finally, the results from this study have implications concerning the clinical evaluation of regional ventricular function. Many methods such as echocardiography and angiography determine regional cardiac dimensions or volume at end-diastole and end-systole to calculate a regional ejection fraction. This ejection fraction is similar to the measure of total segment shortening as defined in this study, and will include changes which occur during both isovolumic systole and the ejection phase. Under normal circumstances, there is little contribution from isovolumic shortening to total segment shortening. Thus, total segment shortening will be a good approximation of ejection phase shortening. However, with acute ischemia, our results suggest that measurement of total segment shortening or the clinically used regional ejection fraction may not accurately reflect the regional contributions to the forward ejection of blood. Under these circumstances, an index of ejection phase shortening would be preferable.

In conclusion, during acute ischemia of the left ventricle, there is a reciprocal interaction between ischemic and nonischemic segments. Ischemic segments are stretched passively by pressure and volume generated from nonischemic areas during isovolumic systole. In nonischemic segments, utilization of the Frank-Starling mechanism produces increased total segment shortening. However, since most of this increased shortening is expended in stretching the dyskinetic ischemic segments during isovolumic systole, there is no true compensatory increase in ejection shortening. If the Frank-Starling mechanism is not utilized, the unloading of nonischemic segments into ischemic segments during isovolumic systole would result in a decrease in the amount of segment shortening available for ejecting blood. If these findings can be extrapolated to man, it would suggest that the immediate survival from an acute myocardial infarction will in part depend on the contractile reserve of nonischemic segments, which must be adequate to provide sufficient forward cardiac output while overcoming the mechanical disadvantages imposed by the ischemic zone.

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