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Regional Myocardial Function in the Conscious Dog During Acute Coronary Occlusion and Responses to Morphine, Propranolol, Nitroglycerin, and Lidocaine

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SUMMARY **Regional myocardial function following occlusions of the circumflex coronary artery was studied in unanesthetized dogs using miniature ultrasonic crystal pairs implanted subendocardially within the left ventricle for measurement of control, marginal, and ischemic lengths. As early as five beats after coronary occlusion, reduced function was apparent in ischemic zones, and an increase in heart rate occurred (78 to 115 beats/min) at an average of 25 sec. In the control zones, shortening initially increased from a constant end-diastolic length, but later end-diastolic length also increased by 7.5%. Shortening in the marginal zones was reduced by 50% at 90 sec as holosystolic expansion developed in the ischemic zones. On reperfusion, systolic function returned to normal within a few minutes while protodiastolic abnormalities persisted for up to 45 min. With coronary occlusions longer than two minutes most dogs exhibited arousal and further tachycardia; this reaction was prevented by morphine. During two minute occlusions morphine also decreased the heart rate increase by 37%, and marginal segment shortening was improved by 40%. Prior administration of propranolol also decreased heart rate during coronary occlusion and produced similar improvement in marginal segment function; however, in contrast to morphine, there was depression of contraction in the control segments. Nitroglycerin given during coronary occlusion caused decreases in end-diastolic length of all segments and increased shortening in the marginal segment by 28%. Lidocaine administered during coronary occlusion produced a mild depression of myocardial function in all regions of the heart.**

THE REGIONAL NATURE of the contractile responses of the myocardium after experimental coronary occlusion has been recognized since the work of Tennant and Wiggers.[1] However, the dynamic shortening and lengthening characteristics of various regions of the left ventricle and the responses to various forms of treatment have not been defined in the conscious animal. An understanding of these characteristics could have considerable importance in assessing therapy designed to improve myocardial performance during ischemic episodes, or to reduce ischemic damage after acute coronary occlusion in man. The present study extends our previous observations in the anesthetized, open-chest dog[2] to an analysis of regional myocardial function during acute coronary occlusion in the unanesthetized animal. Our primary purposes were to define acute hemodynamic changes in relation to the dynamic alterations in function of the normal myocardium and the marginal and central ischemic zones, as well as the reproducibility of these responses with a second coronary occlusion. In addition, the studies were designed to study the responses to several therapeutic agents commonly used in the management of myocardial ischemia (nitroglycerin, propranolol) and acute myocardial infarction (morphine, lidocaine), with a particular view to assessing differences in the responses of normal and ischemic regions of the left ventricle to these drugs.

Methods

Dogs were prepared for study at surgery under general anesthesia. Following left thoracotomy and pericardiotomy, a high fidelity pressure micromanometer (Konigsberg, P-22) and a silastic fluid-filled catheter of 0.5 mm inner diameter were inserted into the left ventricular chamber through the ventricular apex and secured in position with intramyocardial sutures. The circumflex coronary artery was dissected free near its origin and a hydraulic cuff placed around it. Three pairs of small ultrasonic crystals were then implanted in the left ventricular wall in a circumferential plane close to the endocardium and as near the left ventricular

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minor equator as possible, each pair being separated by 1 to 1.5 cm, as previously described.[2, 3] Although precise myocardial fiber angles at the sites of crystal implantation could not be obtained, the depth of the crystals (1 to 3 mm from endocardium), their orientation transversely to the long ventricular axis, and their proximity to the minor equator make it likely that each pair lay generally parallel to the muscle fibers in that region.[4] One pair of crystals was placed in a region termed the ischemic segment, near the base of the posterior papillary muscle in the distribution of the circumflex artery; one pair was placed in a control, normal segment in the anterior wall of the left ventricle and one pair in a marginal segment in the lateral wall at the edge of the ischemic zone. In two-thirds of the animals during a brief coronary occlusion a margin could be clearly identified between myocardium of normal color and the cyanotic region and the crystals were placed across this margin. In the remaining dogs, epicardial ECG mapping during a brief coronary occlusion was used to identify normal myocardium (ST-segment elevation < 2 mV) and the crystals were placed toward the ischemic zone, just inside the normal region.[2] In implanting the crystals, a small tract was created with an 18 gauge needle, a teflon tubing was placed around the wire leading from the crystal to provide support, and the crystal was then pushed to the desired depth (about 8 mm from the epicardium) as marked by a ligature on the wire. After positioning, the teflon tube was removed and the adequacy of the acoustical signal at the receiver crystal was verified by observation on an oscilloscope. No further maneuvers were necessary to stabilize the crystals. The pericardium was left open and all wires and tubing were passed subcutaneously to the back of the animal and brought through the skin between the scapulae.

The ultrasonic technique for studying regional wall motion[3] employs pairs of 5 MHz piezoelectric crystals, one of which is excited by 0.2 μsec, 200 volt impulse at 1 KHz repetition rate; the resultant sound travels through the myocardium to the opposing crystal in a time proportional to the separation of the crystals. A voltage proportional to the sonic transit time is developed. This measured transit time is calibrated against an accurate standard by substituting for the sonically derived signals a signal of precisely known duration derived from a stable crystal controlled oscillator. Multiple myocardial segment dimensions are derived from several pairs of transducers by separating the pulses to the projecting crystals of each pair by 250 μsec. The resolution capability of the instrument is a small fraction of the wave length of the sonic signal (less than 0.08 mm). The over-all functional stability is limited by the extent to which the transducers faithfully follow the movement of the myocardium in which they are embedded; however, the reproducibility of the measurements during repeated brief occlusions (table 1), the constancy of the measurements from day to day, and histologic examinations which showed the crystals to be held in place by a thin fibrous rim[2] indicate that over-all system stability approached the measured electronic stability.

Studies were conducted in 20 dogs at least ten days postsurgery when the animals were healthy and trained to lie quietly in an unsedated state. The effects of a short, 2 min coronary occlusion were first recorded in each dog. This short duration of occlusion was chosen in order to avoid the excitement reaction (perhaps associated with pain) which usually occurred at about 2 to 4 min after coronary occlusion. In ten dogs, the changes during two successive short coronary occlusions separated by an interval of 60 min of unobstructed flow were compared. In eight other dogs, a control coronary occlusion was induced and its effects compared with those of a second coronary occlusion 45 min after pretreatment with morphine (5 mg i.v. and 15 mg subcutaneously), given one hour after the release from the first, control coronary occlusion. A brief period of nausea occurred in most dogs after morphine, which was often followed by light sleep from which they were easily aroused. The effects of propranolol were studied in the same way in nine dogs on another occasion. One hour after release of the first coronary occlusion, propranolol was administered (0.5 mg/kg i.v.); 5 min later the coronary artery was occluded again and the effects compared with those of the first occlusion. In 15 dogs studied on a different day, the responses to a bolus of lidocaine (40 mg i.v.) at 2 min of coronary occlusion were determined. The effects of nitroglycerin administered as a bolus (0.4 mg i.v.) at 2 min after coronary occlusion were also recorded in ten dogs.

Recordings were made during each experiment on a Brush forced ink oscillograph and also on magnetic tape for subsequent analysis. The three segment lengths and left ventricular pressures derived from both the micromanometer and the fluid filled catheter were recorded simultaneously; variables analyzed included peak systolic and diastolic left ventricular pressures, dP/dt, segment dimensions and their first derivatives and analog calculations of peak segment power, average power and segment work per beat.[2] The pressure recorded through the tube was calibrated against a mercury manometer attached to a Statham P-23 Db strain gauge transducer; zero pressure was set at the mid-chest level. The micromanometer was calibrated to match the pressure obtained with the catheter. Heart rate was derived from the pressure signal using a cardiotachometer. End-diastolic and end-systolic lengths were readily identified on the recording (fig. 1), and active segment shortening was calculated as the difference between these two lengths; the values for end-diastolic length and extent of shortening were then normalized to a 10 mm initial segment length by dividing the end-diastolic length and the extent of shortening by the control end-diastolic length, and multiplying by ten. This method of normalization of segment dimensions was chosen because the distance between each pair of crystals was variable and arbitrary (1 to 2 cm) in relation to the actual circumference of each heart. Therefore, this method makes it more convenient to compare segmental responses among different dogs during serial interventions. Since in each dog the data are related by a constant fraction of the end-diastolic segment length, the relative changes are no different than if the actual end-diastolic length had been employed.

The first derivatives of the left ventricular pressure (dP/dt) and of the segment lengths (dL/dt) were obtained using an active differentiating circuit with a break point at 700 Hz and calibrated against a triangular wave of known slope. Three analog multipliers were used to obtain the instantaneous product of left ventricular pressure and the

TABLE 1. *Effects of Coronary Occlusion on Regional Left Ventricular Function*

	No.	HR (beats/min)	LVP (mm Hg)	LVEDP (mm Hg)	Control segment EDL (mm)	Control segment ΔL (mm)	Control segment dL/dt (cm/sec)	Control segment Seg W (dynes-cm)
Control	20	78 ± 2	119 ± 2	6.6 ± 0.3	10	2.26 ± 0.12	1.87 ± 0.10	2.89 ± 0.30 (10^4)
CO (2 to 3 min)	20	115 ± 6	120 ± 3	15.2 ± 1.5	10.28 ± 0.03	2.43 ± 0.12	1.96 ± 0.11	2.75 ± 0.32 (10^4)
*P**		<0.001	NS	<0.001	<0.001	<0.001	<0.05	NS
Release of CO (1 to 2 min)	18	95 ± 3.1	119 ± 2	5.5 ± 0.7	9.90 ± 0.05	1.98 ± 0.12	1.68 ± 0.10	2.38 ± 0.39 (10^4)
P†		<0.001	NS	NS	NS	<0.001	<0.01	<0.01
ΔCO	9	+30 ± 5	−3	+6.3 ± 0.9	+0.36 ± 0.06	+0.30 ± 0.15	+0.16 ± 0.18	−0.27 ± 0.12 (10^4)
ΔCCO	9	+28 ± 3	0	+6.8 ± 1.1	+0.29 ± 0.08	+0.20 ± 0.18	+0.06 ± 0.16	−0.22 ± 0.19 (10^4)
P‡		NS	NS	NS	NS	NS	NS	NS

All values are mean ± SEM.
All *P* values derived by the paired Student's *t*-test.
NS = non ignificant.
*Comparison of CO values to control values.
†Comparison of release of CO values to control values.
‡Comparison of the changes during a coronary occlusion (ΔCO) to the changes during a second control coronary occlusion one hour later (ΔCCO).
Abbreviations: No. = number of dogs studied; HR = heart rate; LVP = peak left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; EDL = end-diastolic length; ΔL = systolic shortening; dL/dt = maximal velocity of segmental shortening during ejection; Seg W = segment work; control = basal recording before coronary occlusion; CO = 2 to 3 min after sustained coronary occlusion; Release of CO = 1 to 2 min after reperfusion; ΔCO = changes induced by a first coronary occlusion; ΔCCO = changes induced by a second control coronary occlusion.

velocity of shortening for each segment. The products were integrated during each beat by use of three analog integrators, resetting to zero at the beginning of positive dP/dt. Thus, indices of instantaneous power and work per stroke for the different segments of the myocardium were obtained simultaneously. These products and their integrals were calibrated against an electronic output corresponding to known inputs of pressure in dynes/cm² and velocity in cm/sec corrected to a 10 mm initial segment length. Dynamic pressure-length loops (x-y plots) were recorded using an oscilloscope.

The position of the crystals in the myocardium was examined at the end of each experiment and their subendocardial location verified. Histological studies were also done in each experiment and showed a rim of approximately 1 mm of fibrous tissue surrounding the site of crystal implantation and extending along the wire tract within the muscle, but there was no additional evidence of damage in the myocardium between the crystals. In three animals, not included in the study, the sites of crystal implantation showed histologic evidence of an infectious process extending into the surrounding tissue.

All data were recorded at a paper speed of 100 mm/sec and averaged over ten cardiac cycles to account for respiratory variations. They were then analyzed by the paired Student's *t*-test and expressed as mean ± standard error of the mean (SEM).

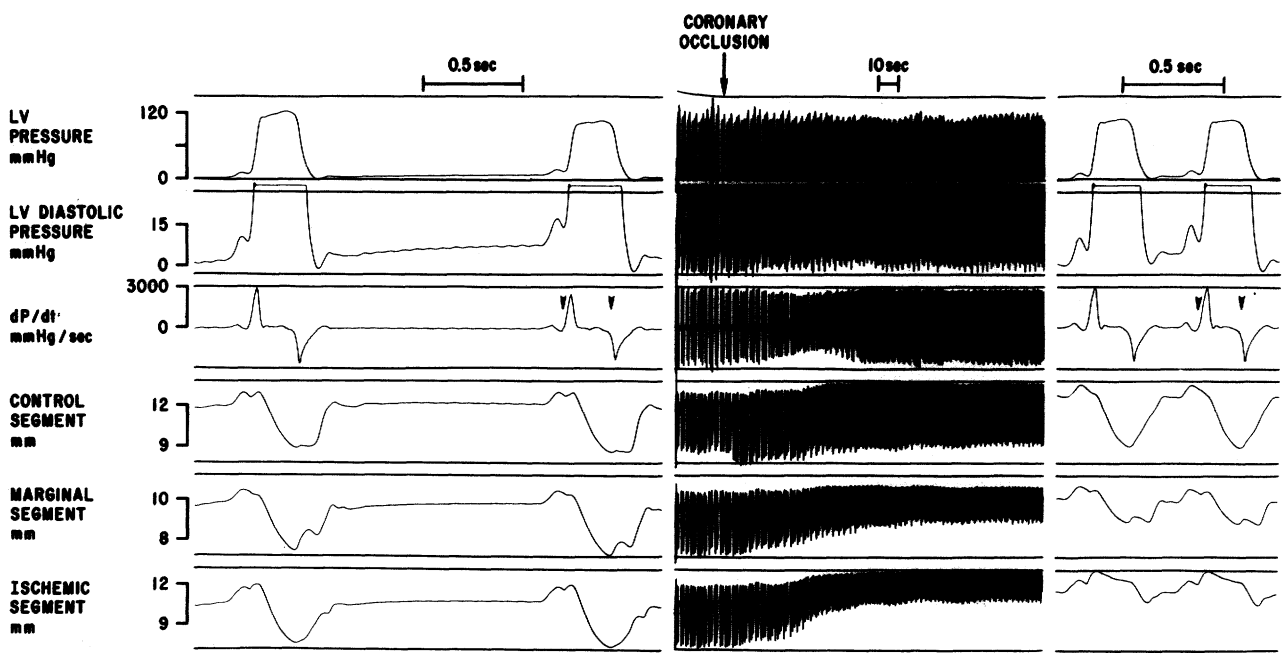

FIGURE 1 *Representative direct recording from a resting unanesthetized dog. Left ventricular pressure and three segment dimensions are recorded simultaneously. Control tracings before coronary occlusion are shown on the left. The changes induced by a rapid cuff inflation (indicated by the arrow at coronary occlusion) are shown at slow paper speed in the center panel. On the right are tracings obtained at the same paper speed as the left panel about 2 min after the occlusion, during the tachycardia. Measurements of end-diastolic dimensions were taken at the nadir of pressure following atrial contraction (at the time dP/dt crossed zero). End-systolic dimensions were taken 20 msec prior to the nadir of negative dP/dt. These points are indicated by arrows.*

Marginal segment				Ischemic segment			
EDL (mm)	ΔL (mm)	dL/dt (cm/sec)	Seg W (dynes-cm)	EDL (mm)	ΔL (mm)	dL/dt (cm/sec)	Seg W (dynes/cm)
10	2.16 ± 0.15	1.77 ± 0.17	1.95 ± 0.18 (10^4)	10	1.84 ± 0.12	1.77 ± 0.15	2.34 ± 0.26 (10^4)
10.37 ± 0.06	1.09 ± 0.16	1.00 ± 0.12	0.97 ± 0.12 (10^4)	10.46 ± 0.06	−0.27 ± 0.06	0.39 ± 0.05	0.25 ± 0.06 (10^4)
<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
9.91 ± 0.06	2.1 ± 0.2	1.62 ± 0.21	1.86 ± 0.23 (10^4)	9.96 ± 0.06	1.75 ± 0.11	1.61 ± 0.19	2.22 ± 0.30 (10^4)
NS	NS	NS	NS	NS	NS	NS	NS
+0.35 ± 0.06	−1.06 ± 0.22	−0.74 ± 0.24	−1.02 ± 0.50 (10^4)	0.46 ± 0.09	−2.27 ± 0.30	−1.50 ± 0.26	−2.47 ± 0.41
+0.38 ± 0.1	−1.06 ± 0.21	−0.73 ± 0.25	−0.97 ± 0.51 (10^4)	0.50 ± 0.09	−2.02 ± 0.24	−1.39 ± 0.22	−2.28 ± 0.38
NS	NS	NS	NS	NS	NS	NS	NS

Results

Effects of Acute Coronary Occlusion

Rapid inflation of the cuff around the circumflex coronary artery in a conscious unsedated dog produced abrupt changes in the measured variables (fig. 1). Changes in shortening characteristics were observed as early as five beats following the occlusion, and within one to two minutes a steady-state was reached in all experiments. The reproducibility of the effects of the initial occlusion was assessed by inducing a second coronary occlusion 60 min after the first coronary occlusion. The hemodynamic and segment length changes were not significantly different during these two short coronary occlusions (table 1).

Hemodynamic Changes

Between 20 and 45 sec (ave 25 sec) after coronary occlusion, heart rate increased from the control, basal value of 78 beats/min to 115 beats/min, and left ventricular end-diastolic pressure began to rise (fig. 2). This heart rate response was observed whether or not the dogs were somnolent, as was frequently the case, or were fully awake; the animals did not appear to be aware of the coronary occlusion. Peak systolic left ventricular pressure was reduced by about 7% at 1 min after coronary occlusion but returned to control shortly thereafter. A conspicuous transient decrease in peak negative dP/dt, by an average of 40%, with a broadening of the waveform occurred during the first minute of coronary occlusion; peak positive dP/dt also dropped by

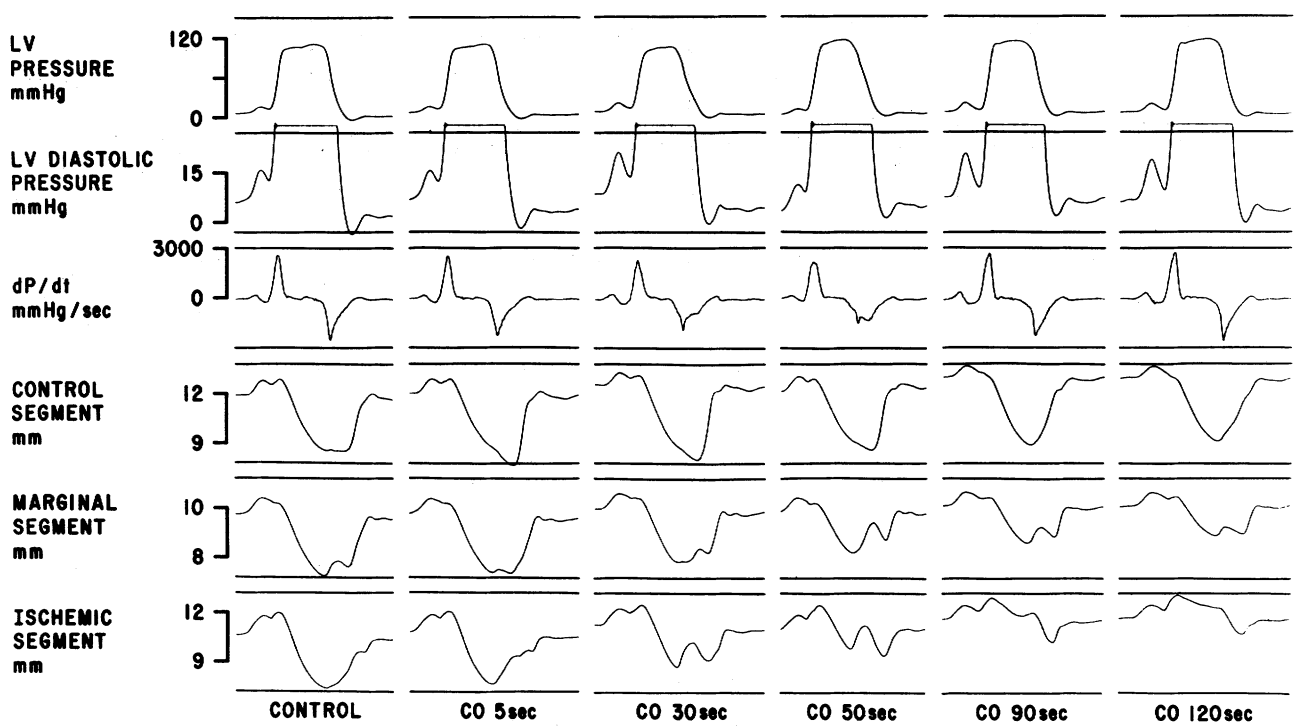

FIGURE 2 *The progression of changes during acute coronary occlusion (CO) are illustrated by selected beats displayed at rapid paper speed, taken from the experiment shown in figure 1. The control segment shows an initial increase in the extent of shortening from a constant end-diastolic length (5 sec) followed by an increase in both end-diastolic length and extent of shortening (90 sec). In the ischemic segment there is an early abbreviation of the extent and duration of active shortening (5 sec), the late systolic expansion is first shown at 30 sec. As the extent and duration of active shortening progressively diminish, holosystolic expansion replaces shortening, most evident in the ischemic segment at 120 sec. The peak rate of fall of left ventricular pressure (dP/dt) is prolonged and reduced (30 sec, 50 sec) and then returns to near the pre-occlusion value (120 sec). The marginal segment shows reduced extent and duration of shortening, and a small late systolic expansion.*

an average of 20% at that time. Subsequently, both positive and negative dP/dt were slightly depressed, but the change was not significant. During the steady-state, heart rate remained elevated and left ventricular end-diastolic pressure, which began to rise at 20 to 30 sec, remained higher than control.

Segment Length Changes

In the ischemic segment, the first observed change after coronary occlusion was a decrease in systolic segment shortening accompanied by a small late systolic elongation that began at an average of 7 sec postocclusion (fig. 2). By 60–90 sec this abnormal motion, accompanied by progressive reduction in the duration and extent of shortening, encompassed all of systole in a paradoxical expansion. At 2 min of coronary occlusion, only a slight shortening was generally observed during the ejection phase, the end-diastolic length was increased by 4.6%, and segment work per beat was reduced by 90%.

In the marginal segment, at 2 min of coronary occlusion the end-diastolic length was increased by 3.7% while shortening was decreased by 50%, velocity of shortening fell by 40% and segment work was reduced by 50%.

In the control segment, between 5 and 25 sec after coronary occlusion there was an increase in shortening by an average of 35% without a significant change in end-diastolic length. Subsequently, at about 25 sec after coronary occlusion, end-diastolic length began to increase, and at 2 min after the occlusion it was 2.8% higher than control, shortening had increased by 7.5% and the maximum velocity of shortening by 4.5%, segment work was unchanged.

The variations occurring during the development of ischemia were also studied by observing individual cardiac cycles as pressure-length loops (fig. 3). This allowed a comparison of the relative sequence of shortening and elongation among the three segments using phasic pressure as the common parameter. During control the loops were similar to those derived by other dimension or volume measuring techniques. Prior to coronary occlusion (panel A) all loops rotated counterclockwise during ventricular systole, with a small clockwise loop during atrial systole. The patterns during the isovolumetric phases were similar in all three segments. Within ten seconds following occlusion (panel B), there were major alterations in the pressure-length loops of all segments. In the marginal and ischemic segments, shortening during ventricular ejection decreased, and the segments elongated late in systole as ventricular pressure fell. In the ischemic segment, the loop became a figure of eight, shortening slightly early in systole, then lengthening as the pressure increased; during the maximum pressure, a small amount of shortening occurred, and during late systole length was longer than at end-diastole. In the control segment, additional shortening occurred as systolic pressure declined. The elongation during late systole in both the ischemic and marginal segments coincident with further shortening of the control segment is compatible with regional unloading of the control segment during the initial response to coronary occlusion. As the response progressed to a stable level (panel C) the control segment loop resumed its initial general form with a somewhat increased area (work). The marginal segment shortened less during maximum systolic pressure, with additional shortening as pressure fell, and the area within the loop was smaller than control. The ischemic segment displayed a total loop area near zero, suggesting passive deformation. The isovolumetric components of the marginal and ischemic loops were reversed from the control segment in that during isovolumetric contraction the marginal and ischemic segments lengthened and they shortened during the isovolumetric relaxation phase. In all segments there was an exaggerated, clockwise loop during atrial systole.

Release of Coronary Occlusion

The values during recovery from ischemia, one to two minutes after release of a 2 to 3 min coronary occlusion, were compared to the control, pre-occlusion values (table 1). Heart rate was by then slower than during the occlusion but remained significantly faster than control. Peak left ventricular pressure was unchanged from control; end-diastolic pressure was slightly lower and peak positive dP/dt was significantly less than control. The end-diastolic dimensions of the three segments were not significantly reduced from control (less than 1%). In the control segment, the extent of shortening was 12% less than control, the velocity of shortening 10% less and the stroke work less by 17.6%; these changes were significant compared to the control, pre-occlusion values. By contrast, in the marginal and ischemic segments, the values were not significantly different from control; in the marginal segment extent of shortening was reduced by only 2%, velocity by 8% and stroke work by 4.6%, and in the ischemic segment, the extent of shortening was less by 5%, the velocity by 9% and the stroke work by 5%.

Despite this very rapid recovery to near normal values, abnormal wall motion characteristics persisted for some time in the marginal and ischemic segments during the early left ventricular relaxation period, after peak negative dP/dt. Five minutes after release of the occlusion, abnormal shortening of 0.4 ± 0.02 mm was observed in the ischemic segment and 0.2 ± 0.01 mm in the marginal segment ($P < 0.01$). At 15 min in the marginal segment a slight degree of lengthening had reappeared (0.05 ± 0.01 mm, $P < 0.01$) but abnormal shortening persisted (0.025 ± 0.1 mm, $P < 0.01$) in the ischemic segment. At 30 min, these values were back to control in the marginal segments, but a slight degree of shortening persisted in the ischemic segment (0.08 ± 0.05 mm, $P < 0.01$). By 45 min, motion during the relaxation period had returned to a normal pattern in all three segments. Thus, while active contraction returned to normal by two minutes after release of occlusion, late abnormal shortening during ventricular protodiastole persisted in previously ischemic zones for up to 45 min.

Effects of Therapeutic Agents

Morphine (table 2, figs. 4, 5)

In the basal state, before the coronary artery occlusion, morphine decreased heart rate from 95 to 83 beats/min ($P < 0.02$); dP/dt was also decreased from 3299 to 2990 mm Hg/sec ($P < 0.05$). The average end-diastolic dimensions in

the three segments increased from 9.9 ± 0.04 to 9.98 ± 0.03 mm ($P < 0.05$). The extent of shortening was not significantly changed (1.73 ± 0.12 mm before and 1.69 ± 0.1 mm after morphine).

With control coronary occlusions before morphine was given, each of the eight dogs studied was basal; four were dozing or asleep, and four were resting quietly. No changes in the attitude of the dogs could be detected during the first two minutes after the coronary occlusion. The hemodynamic and segment length changes shown on table 2 were calculated at this time. However, at two to four minutes of coronary occlusion, six of the eight dogs exhibited an excitement reaction. In two dogs this reaction was characterized mainly by moaning, while in the other four dogs there was marked agitation and struggling. An example of the hemodynamic accompaniments of this reaction is illustrated in figure 4. The reaction was characterized by a marked increase in the heart rate to above 200 beats/min, an increase in peak left ventricular pressure and in peak positive dP/dt, and in some animals an increase in left ventricular end-diastolic pressure to abnormally high levels (25 to 40 mm Hg in four dogs; in two dogs, it decreased slightly). Shortening in the marginal segments deteriorated in four dogs, while in two dogs it slightly increased. Ventricular premature beats

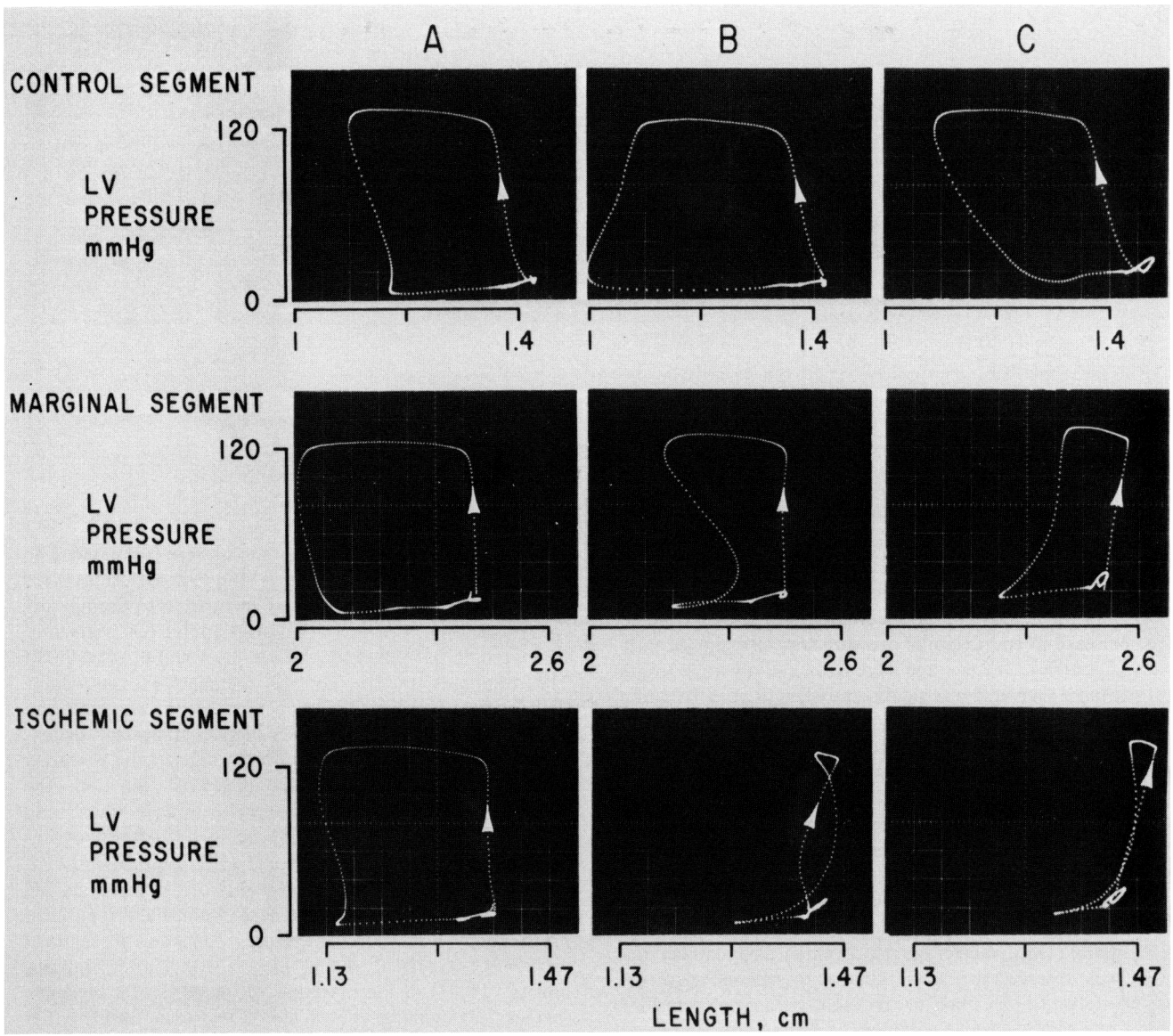

FIGURE 3 *Pressure-length loops of the three segments: A) the control state, B) early after coronary occlusion (about 10 sec); and C) the steady state during coronary occlusion (about 2 min). In A, the normal loops rotate counterclockwise. In B, reduced systolic shortening and a marked lengthening during the isovolumetric relaxation phase are apparent in the marginal and ischemic segments; this is more marked and gives rise to a figure-of-eight inscription of the loop in the ischemic segment, and the late systolic length is larger than that at end-diastole. Also in B, the control segment shows a relatively normal shortening pattern until late in systole, then additional shortening occurs coincident with the lengthening in the other two segments; thus, unloading is apparent in the control segment. In C, during the fall in LV pressure, both ischemic and marginal segments shorten, whereas the control segment lengthens. Work (the area within the loop) in the ischemic segment is near zero.*

TABLE 2. *Effects of Therapeutic Agents on Response to Coronary Occlusion*

	No.	HR (beats/min)	LVP (mm Hg)	LVEDP (mm Hg)	dP/dt (mm Hg/sec)	Control segment EDL (mm)	ΔL (mm)	dL/dt (cm/sec)	Seg W (dyne-cm)
A) Morphine									
Control	8	86 ± 4	123 ± 1	10.8 ± 0.7	3141 ± 238	10	2.28 ± 0.19	1.94 ± 0.21	2.83 ± 0.65
CO	8	124 ± 5	122 ± 4	15.3 ± 0.4	2916 ± 200	10.25 ± 0.07	2.52 ± 0.21	1.9 ± 0.18	2.55 ± 0.65
C′	8	95 ± 6	127 ± 4	10.6 ± 0.8	3299 ± 255	9.9 ± 0.08	2.2 ± 0.22	1.89 ± 0.18	2.77 ± 0.65
Morphine	8	83 ± 4	120 ± 3	11.3 ± 1.1	2990 ± 210	10 ± 0.07	2.2 ± 0.21	1.8 ± 0.15	2.64 ± 0.55
P		<0.02	NS	NS	<0.05	NS	NS	NS	NS
Morphine CO	8	103 ± 4	116 ± 3	13.1 ± 0.8	2979 ± 203	10.15 ± 0.07	2.4 ± 0.21	1.78 ± 0.16	2.58 ± 0.6
P′		<0.01	NS	<0.02	NS	NS	NS	NS	NS
B) Propranolol									
Control	9	81 ± 4	118 ± 2	6.7 ± 0.4	2767 ± 167	10	2.2 ± 0.3	1.7 ± 0.18	2.15 ± 0.6 (10^4)
CO	9	114 ± 4	115 ± 3	12.5 ± 1.2	2528 ± 153	10.21 ± 0.06	2.4 ± 0.2	1.75 ± 0.2	1.9 ± 0.5 (10^4)
C′	9	83 ± 5	119 ± 3	7.6 ± 0.8	2645 ± 122	9.96 ± 0.03	2.28 ± 0.36	1.68 ± 0.18	2.07 ± 0.5 (10^4)
Prop	9	78 ± 3	121 ± 4	8.4 ± 0.8	2477 ± 149	10.1 ± 0.03	2.1 ± 0.33	1.5 ± 0.17	2.2 ± 0.6 (10^4)
P		<0.05	NS	NS	NS	NS	<0.05	<0.05	NS
Prop CO	9	101 ± 3	120 ± 5	14 ± 0.8	2400 ± 126	10.37 ± 0.8	2.3 ± 0.24	1.57 ± 0.2	1.9 ± 0.5 (10^4)
P′		<0.02	NS	NS	NS	NS	NS	NS	NS
C) Nitroglycerin									
Control	10	70 ± 4	124 ± 2	9.9 ± 0.8	2908 ± 212	10	2.15 ± 0.31	1.87 ± 0.24	3.12 ± 0.71 (10^4)
CO	10	106 ± 7	126 ± 4	15.6 ± 1.3	2975 ± 278	10.33 ± 0.07	2.43 ± 0.29	1.97 ± 0.24	3.0 ± 0.71 (10^4)
Ntg	10	140 ± 9	104 ± 3	8.6 ± 1.4	3230 ± 344	9.89 ± 0.14	2.56 ± 0.34	2.4 ± 0.3	2.67 ± 0.6 (10^4)
P		<0.001	<0.001	NS	<0.02	NS	NS	<0.01	NS
D) Lidocaine									
Control	15	80 ± 3	118 ± 2	6.7 ± 0.5	2760 ± 197	10	2.37 ± 0.19	1.95 ± 0.16	2.7 ± 0.36 (10^4)
CO	15	114 ± 5	118 ± 4	13.5 ± 1.3	2456 ± 162	10.36 ± 162	2.57 ± 0.17	2.0 ± 0.17	2.5 ± 0.33 (10^4)
Lido	15	121 ± 5	113 ± 4	16.1 ± 1.3	2149 ± 149	10.4 ± 0.08	2.4 ± 0.19	1.85 ± 0.18	2.17 ± 0.30 (10^4)
P		<0.001	<0.05	<0.01	<0.001	NS	<0.01	<0.01	<0.001

All values are mean ± SEM. All values derived by paired Student's *t*-test. NS = nonsignificant.

A) Morphine: C′ = control after the first occlusion (CO) and before morphine; Morphine CO = coronary occlusion after morphine; *P* = comparison of the values after morphine to the values before morphine (C′) without coronary occlusion; *P′* = comparison of the changes induced by the coronary occlusion after morphine to the changes induced by the control coronary occlusion.

B) Propranolol: C′ = control after the first occlusion and before propranolol; Prop = values after propranolol; Prop CO = coronary occlusion after propranolol; *P* = comparison of the values before propranolol to the values after propranolol without coronary occlusion; *P′* = comparison of the changes induced by the coronary occlusion after propranolol to the changes induced by the control coronary occlusion.

C) Nitroglycerin: CO = coronary occlusion prior to nitroglycerin; Ntg = values after nitroglycerin was injected during CO; *P* = comparison of effects of CO before and after Ntg.

D) Lidocaine: CO = coronary occlusion prior to lidocaine; Lido = values after lidocaine was injected during CO; *P* = comparison of effects of CO before and after lidocaine.

Abbreviations: No. = number of dogs studied; HR = heart rate; LVP = peak left ventricular pressure; LVEDP = left ventricular end-diastolic pressure; dP/dt = peak positive dP/dt; EDL = end-diastolic length; ΔL = extent of systolic shortening; dL/dt = maximal velocity of segment shortening; Seg W = segment work; CO = coronary occlusion.

commonly occurred during the reaction.*

When coronary occlusion was performed after morphine, seven dogs were sleeping at the time of coronary occlusion and one was quiet but awake. At approximately two minutes of coronary occlusion, the increase in heart rate was 37% less than in the control coronary occlusion ($P < 0.01$) and the increase in end-diastolic pressure was also significantly less ($P < 0.02$). The average increase in end-diastolic length of the three segments was significantly less (0.18 ± 0.03 mm after and 0.30 ± 0.04 mm before morphine, $P < 0.05$). In the control segment, the extent and velocity of shortening were slightly but not significantly less. However, in the marginal segment, the extent and velocity of shortening were improved by 40% and 33%, respectively, compared to the control occlusion. In the ischemic segment, significantly more shortening was observed after morphine during the ejection phase of systole; the velocity of shortening during ejection increased and segment work increased by 80% ($P < 0.05$). Thus, an average improvement in dynamic function was observed in the marginal and ischemic segments after morphine. In none of the eight coronary occlusions after morphine was an excitement reaction observed two to four minutes after the coronary occlusion.

*Because we presume that this reaction is related to the occurrence of pain, and because the first three dogs with extended coronary occlusions fibrillated during extreme agitation, we now administer morphine routinely prior to any coronary occlusion that is to exceed two minutes in duration. Since the initiation of this procedure, two of 30 dogs have fibrillated within 2 hours during occlusion and all of these dogs exhibited negligible or no agitation as judged subjectively.

Propranolol (table 2, fig. 5)

The effects of coronary occlusions produced before and after the administration of propranolol were compared. The hemodynamic changes induced by the two occlusions were similar, except that the increase in heart rate during coronary occlusion was less after propranolol (24 beats/min compared to 33 beats/min before propranolol, $P < 0.02$). The responses in the control segment did not differ significantly between the two occlusions although the average end-diastolic length was slightly longer and the extent of shortening less after propranolol. In the marginal segment, propranolol partially preserved function, the magnitude of the decrease in the extent of shortening produced by coronary occlusion being less after propranolol (1.3 mm decrease before and 0.95 after [$P < 0.01$]). Similarly, the reduction in the velocity of shortening during coronary occlusion was 0.89 cm/sec before and 0.64 after propranolol ($P < 0.01$). The average decrease in segment work was 1.05 $(10)^4$ dyne-cm before and 0.78 after propranolol ($P < 0.01$) in the marginal segments. In the ischemic segment, no significant shortening was present during either of the two occlusions.

Nitroglycerin (table 2, figs. 6, 7)

Administration of nitroglycerin during coronary occlusion significantly increased heart rate and decreased peak left ventricular systolic and end-diastolic pressures. The end-diastolic dimensions tended to fall (4.2%) in the control segment (NS), fell 5.3% in the marginal segment ($P < 0.02$),

Marginal segment				Ischemic segment			
EDL (mm)	ΔL (mm)	dL/dt (cm/sec)	Seg W (dyne-cm)	EDL (mm)	ΔL (mm)	dL/dt (cm/sec)	Seg W (dyne-cm)
10	1.87 ± 0.17	1.71 ± 0.11	2.13 ± 0.45	10	1.6 ± 0.19	1.75 ± 0.12	2.09 ± 0.35
10.27 ± 0.08	0.90 ± 0.16	0.86 ± 0.13	0.99 ± 0.21	10.38 ± 0.04	−0.11 ± 0.06	0.39 ± 0.09	0.25 ± 0.09
10 ± 0.05	1.88 ± 0.14	1.8 ± 0.14	2.32 ± 0.05	9.8 ± 0.09	1.58 ± 0.17	1.8 ± 0.14	1.99 ± 0.3
10.04 ± 0.04	1.88 ± 0.13	1.88 ± 0.1	2.22 ± 0.4	9.92 ± 0.04	1.56 ± 0.16	1.85 ± 0.12	2.02 ± 0.25
NS	NS	NS	NS	NS	NS	NS	NS
10.16 ± 0.07	1.26 ± 0.18	1.15 ± 0.1	1.37 ± 0.2	10.18 ± 0.07	0.01 ± 0.07	0.95 ± 0.09	0.45 ± 0.1
<0.02	<0.01	<0.01	<0.01	<0.02	<0.01	<0.05	<0.05
10	2.0 ± 0.24	1.5 ± 0.1	1.5 ± 0.3 (10^4)	10	1.6 ± 0.14	1.56 ± 0.14	1.6 ± 0.32 (10^4)
10.4 ± 0.07	0.7 ± 0.3	0.61 ± 0.1	0.45 ± 0.14 (10^4)	10.34 ± 0.06	0	0.39 ± 0.11	0.25 ± 0.08 (10^4)
10.1 ± 0.05	1.9 ± 0.12	1.5 ± 0.13	1.5 ± 0.2 (10^4)	10.09 ± 0.05	1.53 ± 0.14	1.37 ± 0.13	1.5 ± 0.26 (10^4)
10.19 ± 0.04	1.75 ± 0.12	1.3 ± 0.12	1.46 ± 0.3 (10^4)	10.17 ± 0.04	1.43 ± 0.12	1.25 ± 0.13	1.47 ± 0.32 (10^4)
<0.05	<0.02	<0.05	NS	<0.05	NS	NS	NS
10.5 ± 0.05	0.85 ± 0.2	0.66 ± 0.1	0.68 ± 0.1 (10^4)	10.45 ± 0.06	0.05 ± 0.12	0.4 ± 0.09	0.32 ± 0.1 (10^4)
NS	<0.01	<0.01	<0.01	NS	<0.01	<0.05	<0.01
10	2.01 ± 0.23	1.72 ± 0.21	2.2 ± 0.17 (10^4)	10	1.78 ± 0.2	1.78 ± 0.25	2.65 ± 0.5 (10^4)
10.45 ± 0.24	1.26 ± 0.29	0.71 ± 0.16	1.1 ± 0.17 (10^4)	10.5 ± 0.2	0	0.45 ± 0.08	0.25 ± 0.1 (10^4)
9.9 ± 0.19	1.62 ± 0.29	1.62 ± 0.24	1.1 ± 0.11 (10^4)	10.1 ± 0.2	0	0.84 ± 0.14	0.33 ± 0.13 (10^4)
<0.02	<0.001	<0.01	NS	<0.05	NS	<0.01	NS
10	2.0 ± 0.27	1.77 ± 0.3	1.7 ± 0.26 (10^4)	10	1.8 ± 0.12	1.8 ± 0.16	1.77 ± 0.2 (10^4)
10.42 ± 0.07	0.90 ± 0.24	0.9 ± 0.22	0.79 ± 0.18 (10^4)	10.47 ± 0.08	0	0.4 ± 0.06	0.17 ± 0.05 (10^4)
10.56 ± 0.8	0.67 ± 0.19	0.73 ± 0.15	0.56 ± 0.13 (10^4)	10.54 ± 0.09	0	0.32 ± 0.04	0.12 ± 0.05 (10^4)
<0.02	<0.05	<0.05	<0.02	<0.01	NS	<0.02	<0.01

and 3.8% in the ischemic segment (NS). The average shortening increase (5.3%) in the control segment was not significant, but shortening increased by 28% ($P < 0.001$) in the marginal segment. Nitroglycerin had no significant effect on shortening in the ischemic segment. The velocity of shortening during ejection increased by 22% in the control segment and by 125% in the marginal segment. Work tended to fall in the control segment, but the changes were not significant. No significant changes in segment work occurred in other segments.

Lidocaine (table 2)

A bolus injection of lidocaine during coronary occlusion increased heart rate by 7 beats/min, peak left ventricular systolic pressure fell by 5 mm Hg, peak positive dP/dt dropped by 12.5%, while end-diastolic pressure increased by 2.6 mm Hg. The end-diastolic dimensions of the three segments increased slightly by an average of 0.8%, extent of shortening fell by 6.6% in the control segment and by 22% in the marginal segment; velocity of shortening decreased by 7.5% in the control segment, by 19% in the marginal seg-

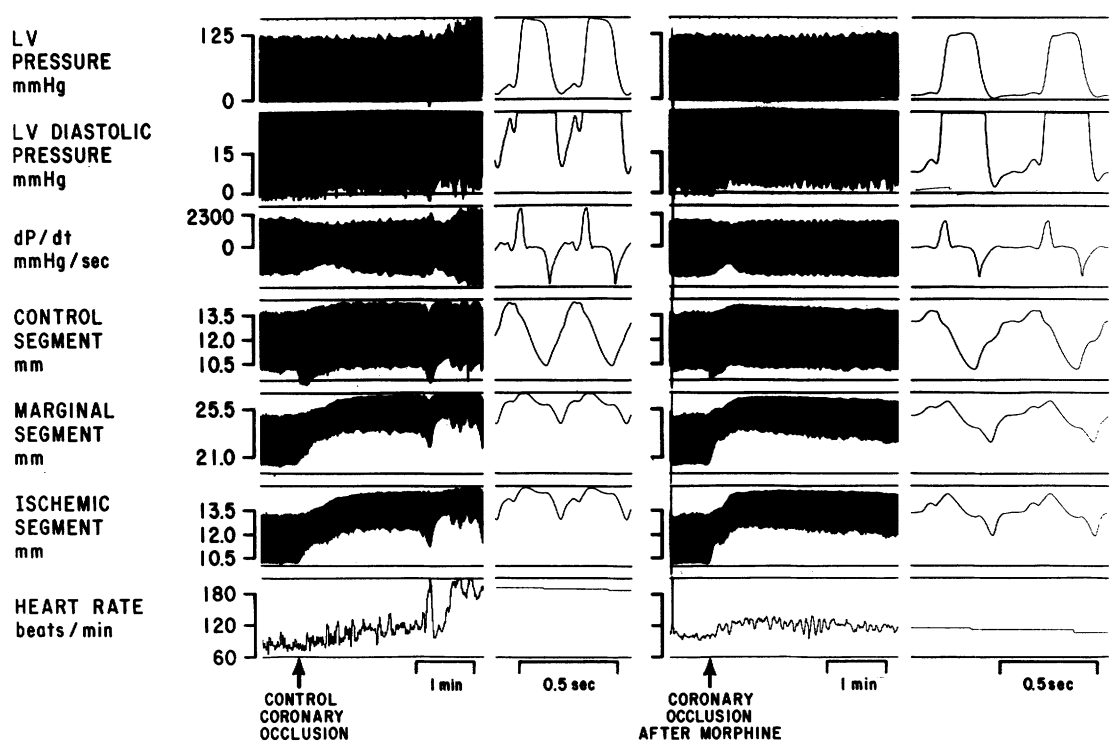

FIGURE 4 *Comparison of the changes induced by a control coronary occlusion (left-hand panels) and a coronary occlusion after prior administration of morphine sulfate (right-hand panels) in an unanesthetized dog. The fast paper tracings were taken at 3 min after the occlusions. The fast speed tracing on the left illustrates sympathetic activation.*

ment and 20% in the ischemic segment. All of these changes indicate that lidocaine produced a mild depression of function in all zones of the heart during coronary occlusion.

Discussion

Since the description by Tennant and Wiggers of bulging during systole in the ischemic zone following coronary occlusion[1] many investigators, employing a variety of techniques, have studied local myocardial function and identified systolic expansion in the ischemic zone in anesthetized animals.[2, 5-11] In the present investigation, we have used methods which have allowed direct measurement of the dynamic responses to coronary occlusion simultaneously in several intramyocardial segments of the left ventricle in the unanesthetized dog. The ultrasonic approach employed has several advantages over previous methods for measurements in conscious animals: the implantation of crystals is relatively atraumatic, minimal strain is placed on the subtended or adjacent myocardial regions,[12] there are no sutures to interfere with coronary blood flow, and the dimension measurements are reliable and stable over long periods of time.

The results of this study in the awake dog differ in several respects from those previously reported in the anesthetized, open-chest animal.[2] One of the most striking differences was the agitation, possibly due to pain, which usually occurred in the conscious dog if the coronary occlusion was maintained for more than two minutes. Therefore, the responses were calculated during the first two minutes of ischemia, when the animals remained quiet or sleeping. Under such conditions, and prior to any agitation, a substantial increase in heart rate was observed in the unanesthetized dog (from 86 to 115 beats/min), whereas in the unanesthetized, open-chested dog no significant increase in heart rate was observed after occlusion of the left anterior descending coronary artery. The fact that the dogs apparently were not aware of the coronary occlusion at this time suggests that it was reflex in origin; the tachycardia occurred within the first minute, as the left ven-

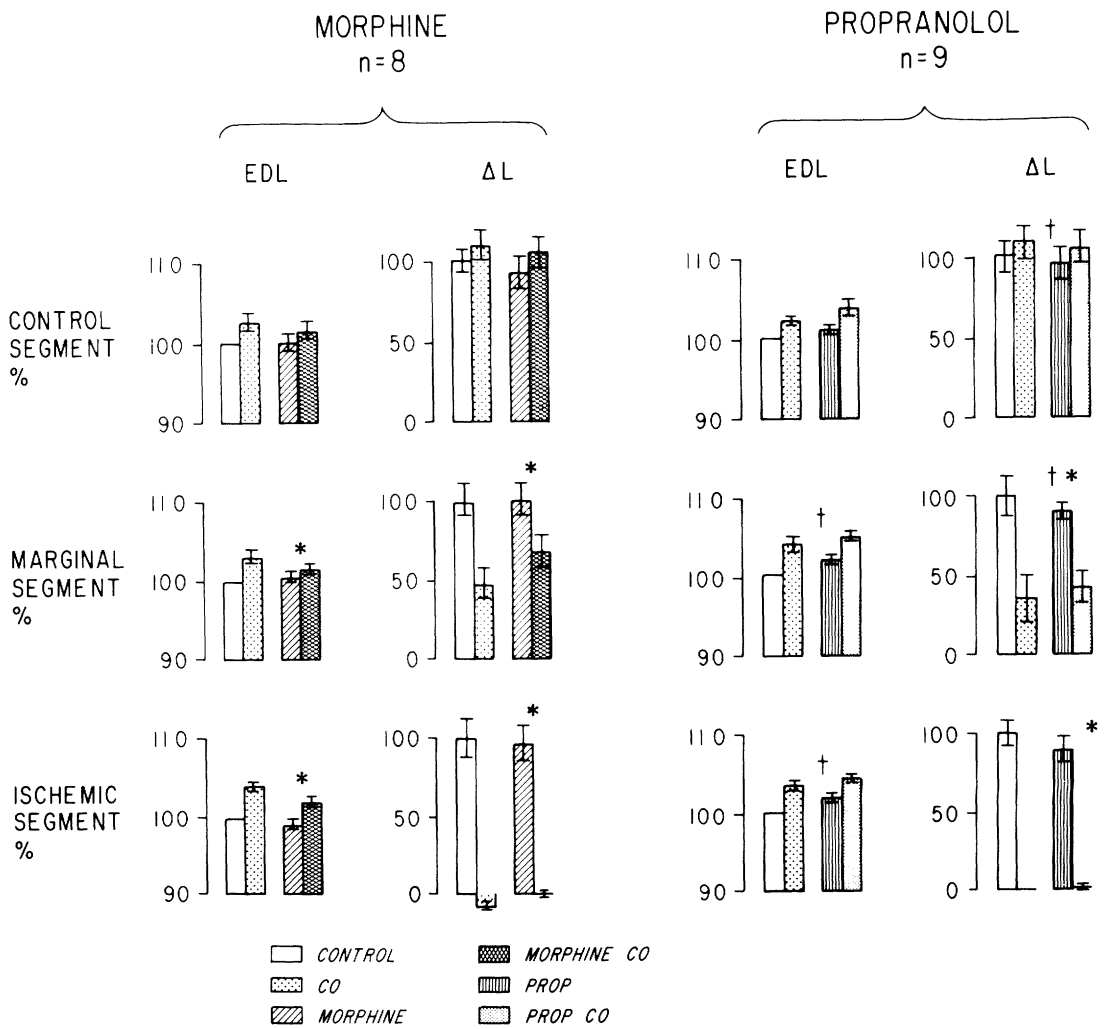

FIGURE 5 *Graphic representation of the effects of morphine and propranolol on the regional myocardial responses to coronary occlusion (see table 2). The effects of a control occlusion on end-diastolic length (EDL) and systolic shortening (ΔL) are compared with the effects of occlusion following administration of the drug. * indicates a significant difference between the change induced by coronary occlusion prior to the drug and the change induced by the coronary occlusion after the drug. † indicates a significant difference between the preocclusion unmedicated value and the preocclusion medicated value.*

tricular end-diastolic pressure was rising, but whether or not intrathoracic or carotid-aortic stretch receptors might have been involved will require further study. Other differences between the anesthetized and unanesthetized animal include a more marked increase in the left ventricular end-diastolic pressure in the conscious dog, and the lack of significant change of peak left ventricular pressure and peak positive dP/dt, both of which fell in the anesthetized dog. The agitation response in the conscious dog led to studies on the effects of giving morphine prior to the coronary occlusion, and this drug proved to have favorable effects which are discussed more fully subsequently.

The response of the ischemic segment differed from that observed during anterior descending coronary artery ligation in the open-chest dog[2] in that the increases in end-diastolic length were substantially less (4.6%, compared to 11% in the anesthetized dog). This difference could be explained in part by the fact that the operating end-diastolic transmural pressures were higher in the awake animal, with a negative intrapleural pressure, and therefore these segments were operating on a steeper part of the diastolic pressure-length curve. Other possible factors include the more marked increase in heart rate observed in the conscious dog, and the different location and greater size of the ischemic area due to circumflex coronary artery occlusion. Pericardial restriction can probably be excluded as a factor, since the pericardium was left open at the operation, and none of the pressure tracings suggested a constrictive pattern during diastole. The dyskinetic motion in the ischemic segment appeared just as rapidly (within a few beats) in the unanesthetized as in the open-chest dog.[2] During the development of this paradoxical expansion, a fall in segment work was observed which reached a negative value, and then became approximately zero in the steady-state. This finding suggests that the ischemic segment was exhibiting passive elongation during ventricular systole, followed by elastic recoil. Using a mercury-in-rubber gauge to plot epicardial segmental pressure-length loops, other investigators have reported negative values during ischemia slightly later in the steady-state;[11] this discrepancy might be explained in part by differences in the instrumentation,[12] differing segmental dynamics in the subendocardial and epicardial regions, variations related to the anesthetized versus the unanesthetized state, as well as differences in the duration of coronary occlusion.

As in the open-chest dog,[2] the control segment immediately after coronary occlusion showed an increase in shortening from a constant end-diastolic length. This phenomenon, illustrated on the pressure-length loop (fig. 3), was synchronous with the initial late systolic bulge observed in the ischemic segments (see fig. 2, 30 and 50 sec). Therefore, the ischemic zone expanded during late systole, presumably because of inability to sustain active tension development; this expansion could have caused a regional

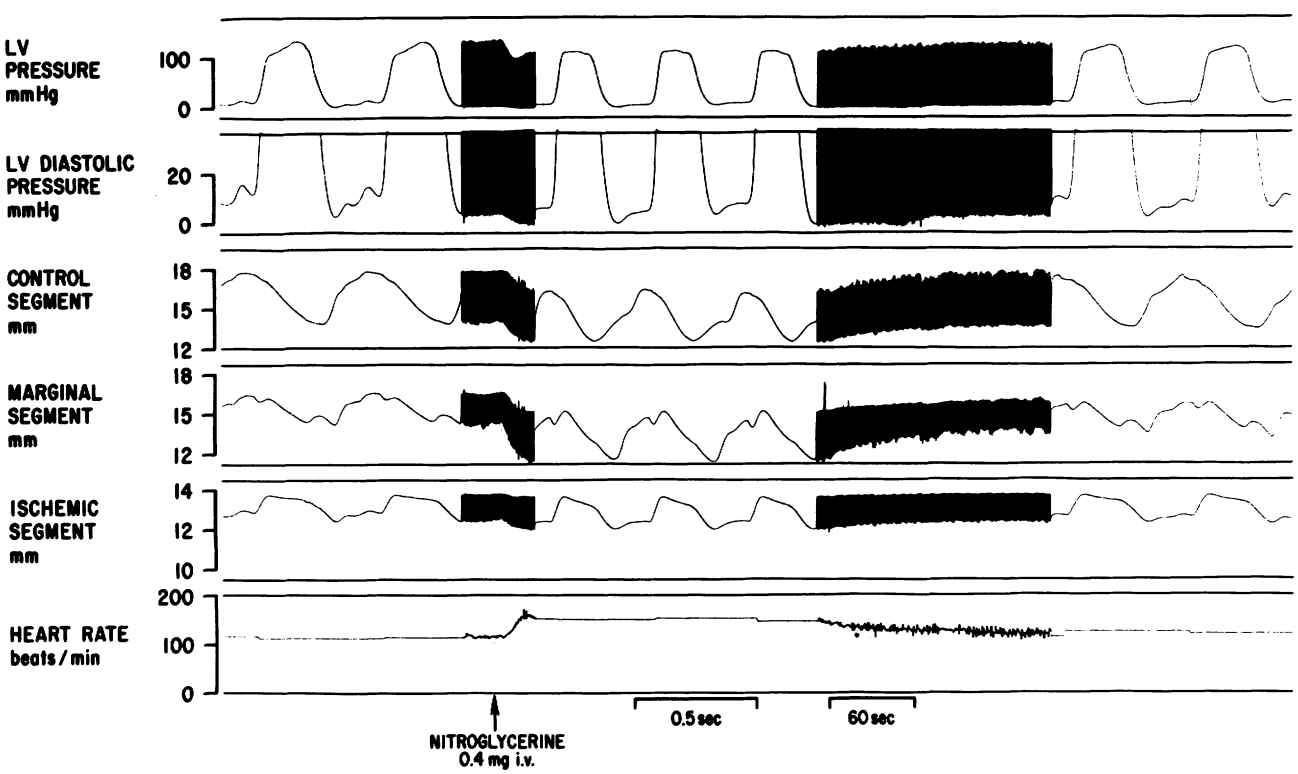

FIGURE 6 *Effects of nitroglycerin injected in the conscious dog during an acute coronary occlusion performed approximately 2 min prior to the onset of recording. Following nitroglycerin, left ventricular pressure is decreased and the dimensions of all three segments are reduced. In the control segment, the end-diastolic dimension falls and the extent of shortening is little altered. The extent of shortening is markedly improved in the marginal segment and the late systolic expansion is abolished. In the ischemic segment, despite a slight increase in shortening during the ejection phase, marked paradoxical expansion persists. Notice that the segment changes appear to closely follow the changes in left ventricular pressure. Time marks indicate slow and fast paper speeds.*

reduction in the effective net afterload on the normal myocardium, thereby leading to enhanced and more prolonged shortening in the control segment. This phenomenon was transitory and was associated with a transient decrease in negative dP/dt. Although a local, reflex increase in contractility could have been involved in this response, this seems less likely because of its occurrence very early, five or six beats after the onset of coronary occlusion (fig. 1). Others have noted reduced time to peak tension and early relaxation in hypoxic[15] and ischemic[16] cardiac muscle, and recently a concomitant late systolic shortening of normal myocardium has also been noted by Lewartowski and Sedek in the open-chest dog.[17] Following these initial changes, the control segment then exhibited an increase in end-diastolic length along with an increase in the extent of shortening compared to that prior to the coronary occlusion. However, in contrast to the studies in the anesthetized dog,[2] for a similar increase in end-diastolic length there was less increase in the extent of shortening, only a slight increase in the velocity of shortening, and no significant increase in the control segment work. Thus, while the Frank-Starling mechanism appeared to be operative in the control, nonischemic myocardium during coronary occlusion, the response was less marked in the unanesthetized dog. Factors that might account for this difference include higher heart rate, less Frank-Starling reserve in the control state due to the higher left ventricular end-diastolic pressures, increased systolic wall force in the control segment,[18] unfavorable effects of enhanced early systolic shortening,[17] or mild depression of myocardial contractility in the control segment of uncertain cause. Some support for the latter is provided by the observation that at two minutes after release of the occlusion, shortening and velocity of shortening in the control segment were significantly below control (table 1).

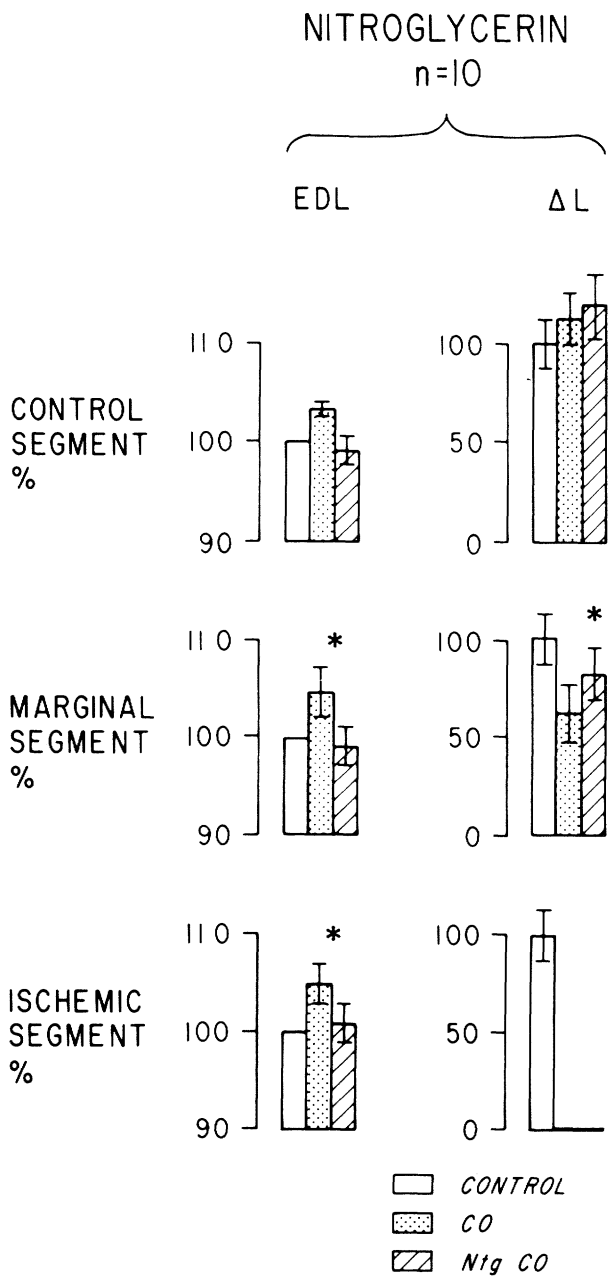

FIGURE 7 *Graphical representation of the regional myocardial effects of nitroglycerin on end-diastolic length (EDL) and systolic shortening (ΔL) during coronary occlusion (see table 2). A bolus of nitroglycerin (Ntg) was injected intravenously 2 min after occlusion of the coronary artery. The effects of the occlusion and the subsequent changes caused by Ntg are shown. * indicates a significant difference between the values during occlusion without medication and the values during occlusion with medication.*

In the marginal segment, an increase in the end-diastolic length with a concomitant decrease in all measures of active function indicated that this segment was working on a depressed function curve. Thus, a zone that appears to be partially ischemic has been identified. It seems likely that this response represents the net effect of inclusion between the crystals of some cells that are partially ischemic, some that are normal and others that are fully nonfunctional. Nevertheless, the fact that this region responded differently from the control and ischemic segments to therapeutic interventions indicates that, from a functional standpoint, it is truly a marginal region where therapeutic interventions can be tested for their effects on mechanical performance, as well as on other measures such as the epicardial ECG.[19]

A description of the effects of reperfusion following a brief coronary occlusion was not a specific goal of this study. Nevertheless, verification that regional myocardial function had returned to control levels following such short periods of coronary occlusion was an essential element in the experimental protocol, and the time course of the recovery deserves comment. Study of the phase of ventricular isovolumetric relaxation showed late shortening in the marginal and ischemic segments during ischemia, while a concomitant lengthening in the control segment occurred. These changes were present after peak negative dP/dt had returned to control (fig. 2). Following release of the occlusion the initial recovery to near control levels occurred in a few minutes, very nearly equal to the time required for full response to the initial occlusion. However, the isovolumetric relaxation phase of contraction in the ischemic segments remained significantly different from control levels for as long as 45 minutes, indicating that full recovery from even a brief occlusion required a considerably longer time than had been anticipated. These observations could relate to the tension prolongation described following hypoxia in

isolated papillary muscles,[15] and to those during recovery from ischemia in the open-chest, anesthetized dog instrumented with an isometric strain gauge.[20] Decreases in the rate of ventricular relaxation, evidenced by reduction of negative dP/dt, have been reported in anesthetized animals after five hours of coronary occlusion,[13] as well as during atrial pacing in patients with ischemic heart disease.[21, 22] During angina pectoris induced by pacing, ventricular diastolic stiffness also has been reported to increase.[23]

The effects of morphine in the unanesthetized dog were of particular interest since this drug is frequently administered after acute myocardial infarction in man, and its effects on ventricular function in the latter setting are unknown. The actions of morphine were first examined in the basal state prior to coronary occlusion, shortly after drug administration, when the animals usually had passed into a light sleep from which they could be easily aroused. Heart rate slowed slightly but significantly, and dP/dt was decreased by 9%. Left ventricular end-diastolic pressure was not significantly increased, and there were no obvious modifications in segment dimensions or shortening characteristics. It is possible that the slight effect on dP/dt can be explained in part by the cardiac slowing,[24] which in turn could relate to the sedative effect.[25] Thus, in the unanesthetized dog the effects of morphine on the heart appeared minimal. During the coronary occlusion the effects of morphine were more striking. The early (presumably reflex) increase in heart rate was greatly reduced, and the increases in end-diastolic dimensions in the marginal and ischemic segments and in the left ventricular end-diastolic pressure were significantly less than with control occlusions. Moreover, the reduced function in the marginal segment during the control coronary occlusion was markedly improved after morphine, suggesting a more favorable balance of oxygen supply and demand. The effects of morphine at 2 min of occlusion, prior to the agitation, could be due primarily to prevention of reflex tachycardia and perhaps also to peripheral vasodilatation.[25] Thus, when compared to propranolol, whereas the effects on heart rate were nearly identical, during the occlusions after propranolol average left ventricular end-diastolic pressure rose and end-diastolic dimensions increased in all three segments; although these changes were not significantly different from the control occlusions, they were opposite in direction from those occurring after morphine. Finally, when the occlusion was maintained longer than two minutes, the effects of the agitation reaction were abolished. The characteristics of this reaction (fig. 4) suggest that it was a pain-induced sympathetic discharge. Since catecholamines previously have been shown to expand the size of a zone of ischemic injury,[2, 19] this salutary effect of morphine probably resulted from its analgesic effect in preventing this sympathetic reaction. The findings suggest that morphine may have diminished the extent of ischemic injury.

Propranolol administered prior to coronary occlusion produced more bradycardia than did morphine administered before the occlusion, but the heart rates during coronary occlusion were closely similar (table 2). However, during coronary occlusion after propranolol ventricular end-diastolic pressure and the end-diastolic length of the control segment were significantly higher and shortening was less than with morphine. As with morphine, there was a relative improvement in the shortening of the marginal segment. This beneficial effect of propranolol may be due to a more favorable balance between oxygen supply and demand in the marginal zone, related to the slower heart rate and to reduced contractility, but the depressed inotropic state produced by propranolol resulted in some impairment of over-all cardiac function. Previous studies in the open-chest dog have shown a beneficial effect of beta blockade on segmental function[2] and on myocardial infarct size.[19, 26, 27] It is of interest that similar results on marginal segment function were obtained with morphine, despite its lack of a cardiac depressant effect.

Nitroglycerin during coronary occlusion resulted in increased shortening in the marginal segment, and in the ischemic segment a slight amount of shortening was restored during the ejection phase; however, in the latter segment the end-systolic length was still longer than the end-diastolic length, and whether this slightly increased shortening reflected recovery of active contraction or simply a passive response to the lowered left ventricular systolic pressure and wall force remains to be determined. However, unpublished observations in our laboratory of segments studied during the late stages of myocardial infarction, when the segment consists of transmural scar, have shown similar slight increases in shortening during ejection (without net shortening during systole), suggesting that these changes may represent a passive mechanical effect. Our findings further suggest that nitroglycerin, by unloading the left ventricle, may be useful for unmasking active function in marginal zones. However, caution in interpreting these results is required by the finding that net shortening in ischemic zones was not restored by nitroglycerin, despite the fact that function could be fully restored by reperfusion. Similar effects on regional wall motion after nitroglycerin have been observed in patients with previous myocardial infarction, studied by noninvasive techniques,[28] and there had been clinical interest in the use of nitroglycerin for detecting myocardial regions in which malfunction may be reversible.[29]

Lidocaine in this study, as in others,[30] mildly depressed over-all indices of left ventricular performance during coronary occlusion. As with propranolol, heart size was larger, but the heart rate was faster after lidocaine and, unlike the effect of propranolol, the extent of shortening was reduced in the marginal segment. Thus, intravenous lidocaine has a transient detrimental effect on regional myocardial function during coronary occlusion.

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