End-systolic measures of regional ventricular performance

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ABSTRACT Dimension change measures of regional ventricular function, such as absolute or percent wall thickening (ΔT or %ΔT) or segmental shortening (ΔL or %ΔL), are highly load dependent. In 16 anesthetized mongrel dogs we assessed use of the end-systolic pressure-thickness and end-systolic pressure-length relationships (ESPTR,ESPLR) as more load-independent measures of regional function. We found that the ESPTR and ESPLR could be measured without detectable baroreceptor-mediated reflex changes in cardiac contractile state. Systemic administration of dobutamine shifted the ESPTR to the right and the ESPLR to the left of control, mainly due to a change in the slope (Ees) of the relationships. Both ΔT,%ΔT and ΔL,%ΔL failed to detect the positive inotropic effect of dobutamine because of an associated reduction in preload. With systemic administration of propranolol, ESPTR, ESPLR, ΔT,%ΔT, and ΔL,%ΔL detected the negative inotropic effect. Thus systemic propranolol shifted the ESPTR to the left and the ESPLR to the right of control, mainly due to a change in Ees. Regional administration of dobutamine shifted the ESPTR and the ESPLR in the direction of positive contractility in the region receiving the drug, whereas simple dimension change measures of regional function failed to detect the inotropic effect because preload fell and the timing of regional end-systole was altered. With regional propranolol both the ESPTR,ESPLR and simple dimension change measures detected the negative inotropic effect. Thus the ESPTR,ESPLR is a reliable measure of regional ventricular function and may be better than simple dimension change measures of regional function, particularly when loading conditions or the timing of regional systole is altered by an intervention.
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DETERMINATION of regional myocardial contractile state is of interest in many experimental and clinical settings. Currently available methods for estimation of regional performance typically involve measurement of dimension changes, either absolute or percent wall thickening (ΔT or %ΔT) or segment length shortening (ΔL or %ΔL). Change in the value of these quantities is usually taken as indicating a change in regional contractile state or performance. However, dimension change measures of regional myocardial performance are highly load dependent. That is, their value is determined not only by the intrinsic contractile state of the myocardium but also by ventricular loading conditions. For example, wall thickening may increase as a result of a rise in preload, a fall in afterload, or a change in contractile state. It is clear from these considerations that simple dimension change measures can be unreliable estimates of regional myocardial contractile state.

Just as load dependence is a problem with dimension change measures of regional contractile state, most measures of global ventricular function have suffered from the same limitation. The end-systolic pressure-volume relationship (ESPVR) has been suggested as a relatively load-independent measure of global ventricular function.[1–3] The variables used to define the ESPVR, the slope Ees, and volume-axis intercept V0 have been shown to be functions of cardiac contractile state,[2] to be relatively independent of preload and afterload,[3] and to be altered by ischemia.[4]

Osakada et al.[5] were the first to suggest that end-systolic measures of ventricular performance could be applied regionally. In their preliminary study, the end-systolic pressure-thickness relationship (ESPTR) was constructed by changing ventricular loading conditions pharmacologically. The ESPTR was shown to reflect

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changes in contractile state after systemic administration of inotropic agents, a shift to the right of control indicating positive and to the left of control negative contractility.[5] Similarly, Millar et al.[6] using a rapid volume loading technique to change ventricular loading conditions showed that the end-systolic pressure-length relationship (ESPLR) shifts to the left with positive inotropic agents and to the right with negative inotropic agents (although with negative inotropic agents the shift from control was not significant). In neither of these studies was the potential confounding influence of baroreceptor-mediated reflex changes in cardiac contractile state examined. Furthermore, the effect of regionally (as opposed to systemically) applied inotropic agents was not studied.

This study was undertaken to examine the use of the ESPTR and the ESPLR as an index of regional myocardial contractile state in the intact, open-chest dog. Since measurement of ESPTR,ESPLR requires changing ventricular loading conditions, which in turn alters systemic pressure, the potential influence of baroreceptor-mediated reflex changes in cardiac contractile state on ESPTR,ESPLR was studied. Changes in ESPTR,ESPLR were also observed during systemic and regional administration of positive and negative inotropic agents. ESPTR and ESPLR were compared with standard dimension change indexes of regional performance under these varying inotropic states.

Methods

General preparation. Sixteen mongrel dogs of either sex weighing 18 to 30 kg were anesthetized with intravenous sodium thiamylal (12.5 mg/kg) and intramuscular chloralose (100 mg/kg in urethane), intubated, and ventilated with a piston respirator on supplemental oxygen. A thoracotomy was performed in the left fifth intercostal space, exposing the heart and great vessels. The pericardium was incised near the base, the incision being of sufficient size that the heart could be removed and replaced in the pericardial sac as desired. A miniature, solid-state pressure transducer (Millar MikroTip Model PC-350, Millar Instruments, Inc.) was placed in the left ventricle through a left atrial introducer for measurement of left ventricular pressure and its first derivative with respect to time, left ventricular dP/dt. Aortic pressure was measured with a fluid-filled catheter placed in the descending thoracic aorta via the femoral artery. A catheter inserted into the right femoral vein served for infusion of drugs and fluids. A catheter fitted with a 40 to 50 ml inflatable latex balloon was inserted into the left femoral vein and advanced so that the balloon was just below the right atrium.

Miniature piezoelectric crystals (Vernitron, Inc.) were placed in the anterior and posterior left ventricular wall in the region of the left anterior descending (LAD) and left circumflex (LCx) coronary arteries, respectively, for measurement of wall thickness and, in most animals, segment length. For measurement of wall thickness, one crystal of each pair was advanced tangentially to the endocardial surface and the other placed epicardially and aligned so that the distance between the crystals was minimized. For measurement of segment length, two crystals separated by 1 to 2 cm were placed in the midwall left ventricular myocardium and aligned so that the intercrystal axis was parallel to the expected direction of myocardial fiber shortening.[7] Wall thickness and segment lengths were measured with a pulse transit sonomicrometer (Model Sono-1-XB, James Davis Consultants).

Aortic pressure was measured with a Statham P23-ID transducer (Gould Statham, Inc.). Data were recorded in analog fashion on an eight-channel Brush recorder (Model 200, Gould Statham, Inc.), as well as digitally on a NorthStar Horizon Computer (NorthStar Computers, Torrance, CA) with a 12-bit analog-to-digital converter (Tecmar, Inc.) at a sample frequency of 150 Hz.

Additional instrumentation was different in two groups of animals:

Preparation I animals. In seven animals, bilateral cervical vagotomy was performed. The common carotid arteries were dissected, cannulated, and perfused via an external perfusion circuit. Blood was pumped from the left subclavian artery into a pressurized reservoir that was kept warmed to 37° C with a water jacket. Pressure in the reservoir, and therefore in the carotid arteries, was controlled by adjustment of a release valve. Carotid pressure distal to the cannula tip was monitored with a Statham P23-ID transducer (Gould Statham, Inc.) via a fluid-filled catheter advanced through a side-arm in the cannula.

Preparation II animals. In the other nine animals, the carotid arteries were not cannulated and the vagi were left intact. The proximal LCx was dissected, cannulated, and perfused via a short length of stiff tubing from the subclavian artery. In six animals LCx pressure distal to the cannula tip was measured and averaged 9 ± 3 mm Hg lower than systemic aortic pressure. A 22-gauge needle inserted into the plastic cannulation tubing served for selective infusion of drugs into the LCx.

Data collection for ESPTR. Representative data from which the ESPTR was constructed are illustrated in figure 1. For collection of such data, the inferior vena cava (IVC) was gradually occluded by inflation of the IVC balloon. As a result, left ventricular end-diastolic pressure and peak systolic pressure fell. Left ventricular pressure and wall thickness data were collected over a 7 sec period just before and during the fall in left ventricular pressure. Typically, peak left ventricular pressure fell 30 mm Hg over a range of 120 to 70 mm Hg.

For construction of the ESPTR, pressure and thickness data recorded from several cardiac cycles obtained as left ventricular pressure fell during IVC occlusion were used. For each cardiac cycle, instantaneous left ventricular pressure and thickness data were used to calculate Ees and T0, the slope and thickness-axis intercept, respectively, of the ESPTR as defined by:

$$Ees = Pes/(Tes - T0)$$

where Ees = slope of the ESPTR, Pes = left ventricular pressure at end-systole, Tes = wall thickness at end-systole, and T0 = thickness-axis intercept of the ESPTR. Since T0 is not known a priori, its value was assumed to be 2 mm greater than the maximum left ventricular wall thickness recorded. For each cardiac cycle, the left ventricular pressure–thickness point that maximized the value of Ees was taken as the end-systolic pressure-thickness point. End-systolic pressure-thickness points from each beat were then linearized by least-squares linear regression to calculate the parameters Ees and T0, defining the ESPTR. The new, calculated value of T0 was then used in a second iteration of the data. Iterations were repeated until both Ees and T0 were constant (usually two to three iterations).

A similar procedure was used to construct the ESPLR except that the initial length-axis intercept of the ESPLR (L0) was taken as zero.

Although Ees and T0 completely define the ESPTR, it should be noted that T0 is calculated from data collected over a relatively narrow range of high left ventricular pressures. Thus, to estimate T0, an extrapolation of at least 70 mm Hg is required. Since the ESPTR can also be defined by a slope and thickness at any pressure, we will also present the calculated end-systolic thickness at a left ventricular pressure of 70 mm Hg (T70), the lower end of the actual data collection range. Similarly, the calculated end-systolic segment length at a left ventricular pressure of 70 mm Hg is reported as L70.

Standard sonomicrometry. Absolute thickening was calculated as end-systolic thickness (EST) minus end-diastolic thickness (EDT); and absolute segmental shortening was calculated as end-diastolic length (EDL) minus end-systolic length (ESL). Percent thickening and shortening (%ΔT and %ΔL) were calculated as their respective absolute dimension changes divided by the end-diastolic dimension and multiplied by 100. For standard sonomicrometry, EST and ESL were defined as those dimensions occurring 20 msec before peak negative left ventricular dP/dt[8]; EDT and EDL were defined as occurring just before the upstroke of left ventricular dP/dt.

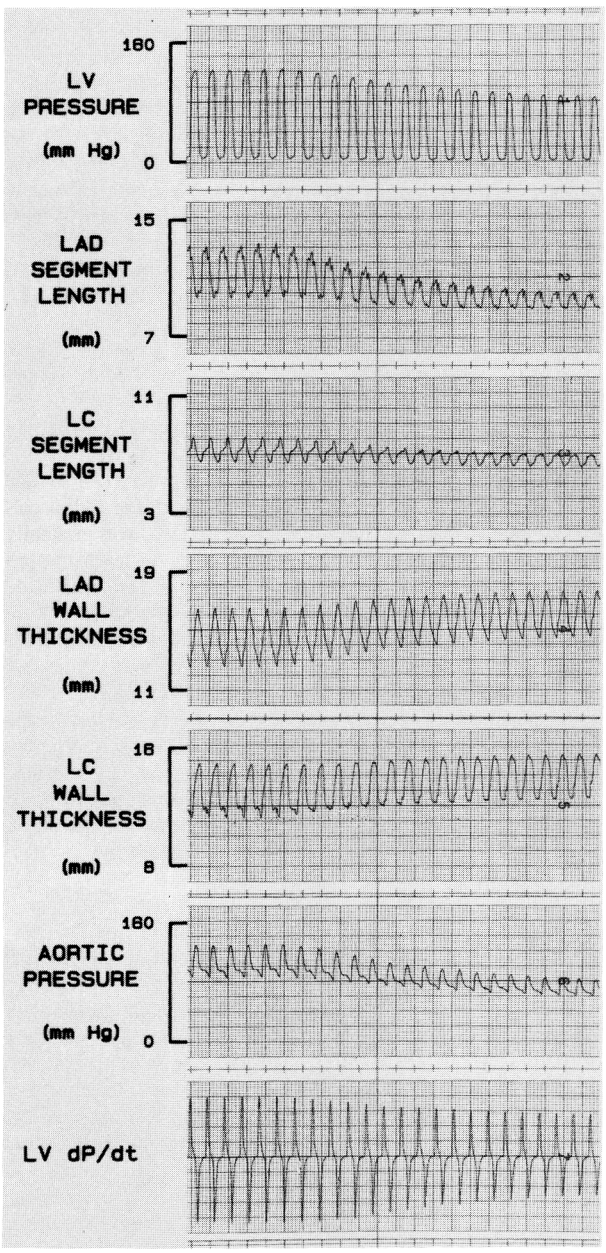

FIGURE 1. Data obtained from one animal during a single occlusion of the IVC. See text for details. LV = left ventricular; LC = left circumflex coronary artery (LCx).

Protocols. Three different protocols were performed:

(1) Reflex changes. To assess the potential influence of baroreceptor reflex–mediated changes in contractility that might occur during measurement of the ESPTR, preparation I animals were studied with three different types of carotid pressure manipulations. In control runs, carotid pressure was adjusted to approximate mean aortic pressure and was held constant during IVC occlusion and the 7 sec ESPTR,ESPLR data collection period. In a second type of run, the carotid perfusion tubing was clamped at the beginning of IVC occlusion, rapidly dropping carotid pressure from mean aortic pressure to 30 to 40 mm Hg. The tubing remained clamped during the 7 sec ESPTR,ESPLR data collection period and was reopened immediately thereafter. In a third type of run, carotid pressure was gradually decreased during ESPTR,ESPLR data collection to simulate the gradual fall in aortic pressure that would occur during this period if carotid pressure were uncontrolled.

(2) Systemic inotropic stimulation. In six preparation I animals, with carotid pressure fixed at mean aortic pressure, and in two preparation II animals, the influence of systemically administered positive and negative inotropic agents on the ESPTR/ESPLR was studied. Data for both standard sonomicrometer measurements and for the ESPTR/ESPLR were collected during control (no drug) periods and during drug administration. After control measurements, seven animals received dobutamine (9.82 ± 1.55 μg/kg/min) intravenously and one animal received norepinephrine (0.17 μg/kg/min). Measurements were made during positive inotropic stimulation. After infusion of the positive inotropic agent, at least 20 min was allowed to elapse before control measurements were again made. Propranolol was then given as an intravenous bolus (0.13 ± 0.09 mg/kg) and measurements were repeated. In two animals, data from one of two crystal pairs for measurement of wall thickness were eliminated because of artifact (one LCx and one LAD crystal pair). Similarly, of the six animals instrumented with crystals for measurement of segment length, data from one of two crystal pairs in two animals were eliminated because of artifact (both LAD region crystal pairs).

(3) Regional inotropic stimulation. In seven preparation II animals and in one preparation I animal (in which an intracoronary catheter was placed), measurement of standard sonomicrometry and the ESPTR/ESPLR were obtained during control conditions and during intracoronary administration of dobutamine and propranolol. As in protocol 2 above, control measurements were made before administration of any drug. Intracoronary infusion of dobutamine at 9.77 ± 3.10 μg/min was then begun into the LCx and measurements at this low dose were made. The infusion was then increased to 21.0 ± 5.56 μg/min and measurements were repeated. Infusion of dobutamine was then terminated and at least 20 min was allowed to elapse before control measurements were repeated. Once control observations had been recorded, low-dose intracoronary propranolol (0.92 ±0.18 mg) was administered and measurements were again made. Finally, additional intracoronary propranolol was administered (2.17 ± 0.37 mg, total dose) and measurements were repeated.

Eight animals with both LCx and LAD crystals for measurement of wall thickness received intracoronary dobutamine (one preparation I, seven preparation II). In six animals two dosage levels of dobutamine were studied. ESPTR and standard sonomicrometer data from these six animals are presented below.

Results in the other two animals that received a single dosage level of dobutamine were identical but could not be included in the analysis of variance. In six animals LCx region segment length data were obtained at a single dosage level of dobutamine. In only five animals could LAD (control) region segment length crystals be placed.

In seven of eight animals instrumented with both LCx and LAD wall thickness crystals, two dosage levels of propranolol were studied; results presented below are from all seven of these animals. In six animals LCx region (region receiving negative inotropic agent) segment length crystals were placed; in five of these animals LAD region (control region) segment length crystals could be placed.

Statistical analysis between two treatment groups was made by paired t test. When three means were compared (protocol 3), a repeated measures analysis of variance was performed and significant differences between any two treatments were determined by a Newman-Keuls test.[9] All data are reported as mean ± SEM unless otherwise noted.

Results

ESPTR/ESPLR variability. In the seven preparation I dogs multiple predrug control measurements were made before, between, and after the various carotid pressure manipulations described in protocol 1. To express the variability in the measurement of ESPTR, ESPLR parameters in control runs (runs in which carotid pressure was kept constant), the coefficient of variation for each of these parameters was calculated for each animal. For an average of two to three preintervention control runs in each of seven animals, the average coefficient of variation for LAD region ESPTR parameters was greater for Ees than for T0 or T70: Ees, 18%; T70, 2%; and T0, 3%. Similar variability in these parameters was found for the LCx region ESPTR and the ESPLRs.

Reflexes. Reflex changes were studied in seven preparation I animals. Figure 2 shows a representative ESPTR with constant carotid pressure controlled at mean aortic pressure during data acquisition. For the LCx region, Ees for the ESPTR was −81 ± 15 mm Hg/mm, T70 was 13.2 ± 0.7 mm, and T0 was 14.3 ± 0.8 mm. Similarly, control ESPTRs in the LAD region had an Ees of −122 ± 25 mm Hg/mm, a T70 of 14.2 ± 1.0 mm, and a T70 of 15.1 ± 1.2 mm. With both gradually declining carotid pressure and perfusion circuit clamping, the ESPTR did not change from control as illustrated in figure 3.

A typical ESPLR is shown in figure 4. The ESPLR did not change in either the LAD or LCx regions during the various carotid pressure manipulations, as shown in figure 3.

Thus, both the ESPTR and the ESPLR can be measured in the intact, open-chest dog during a 7 sec IVC occlusion without detectable baroreceptor-mediated reflex effects on cardiac contractile state.

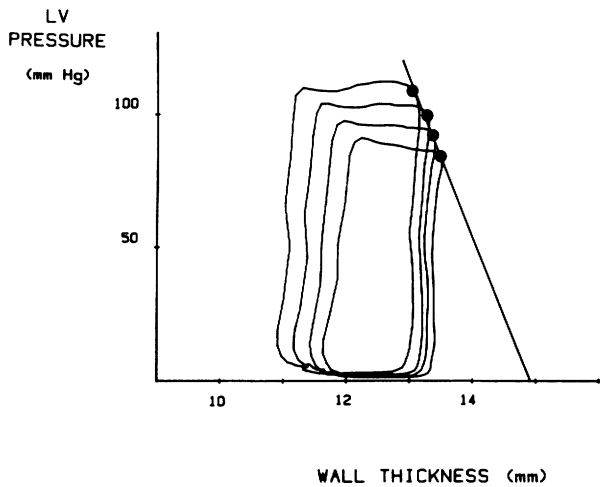

FIGURE 2. Four representative pressure-thickness loops obtained from one animal during a single occlusion of the IVC. Solid circles represent the end-systolic pressure-thickness points on each loop; the solid line represents the end-systolic pressure-thickness relationship. See text for details.

Systemic inotropic stimulation. Data obtained during systemic inotropic stimulation are summarized in table 1.

ESPTR/ESPLR. Hemodynamic data for all animals are shown in table 2. After systemic administration of dobutamine there was no significant change in aortic or end-diastolic left ventricular pressures, whereas heart rate increased significantly by 24 beats/min.

As illustrated in figure 5 for one animal and summarized in table 1 for all animals, with intravenous dobutamine the ESPTR in both the LCx and LAD regions shifted to the right of control because of an increase in T70 and increasing negativity of Ees. The extrapolated thickness-axis intercept, T0, did not change significantly in either region.

The ESPLRs in both the LAD and LCx regions shifted to the left of control with administration of positive inotropic agents. As with the ESPTR, this shift was caused by an increase in Ees and a reduction of L70, with no significant change in L0.

With dobutamine there was a decrease in the time to Ees (the number of milliseconds after the onset of systole that the maximum slope of the ESPTR,ESPLR occurs). Time to Ees expressed as a percentage of the RR interval, however, did not change (44% vs 42%), since heart rate increased significantly.

ESPTRs obtained at least 20 min after administration of positive inotropic drugs suggested slight residual positive contractility. After systemic propranolol, neither aortic nor left ventricular end-diastolic pressures changed significantly, but heart rate decreased significantly.

Systemic administration of propranolol resulted in a

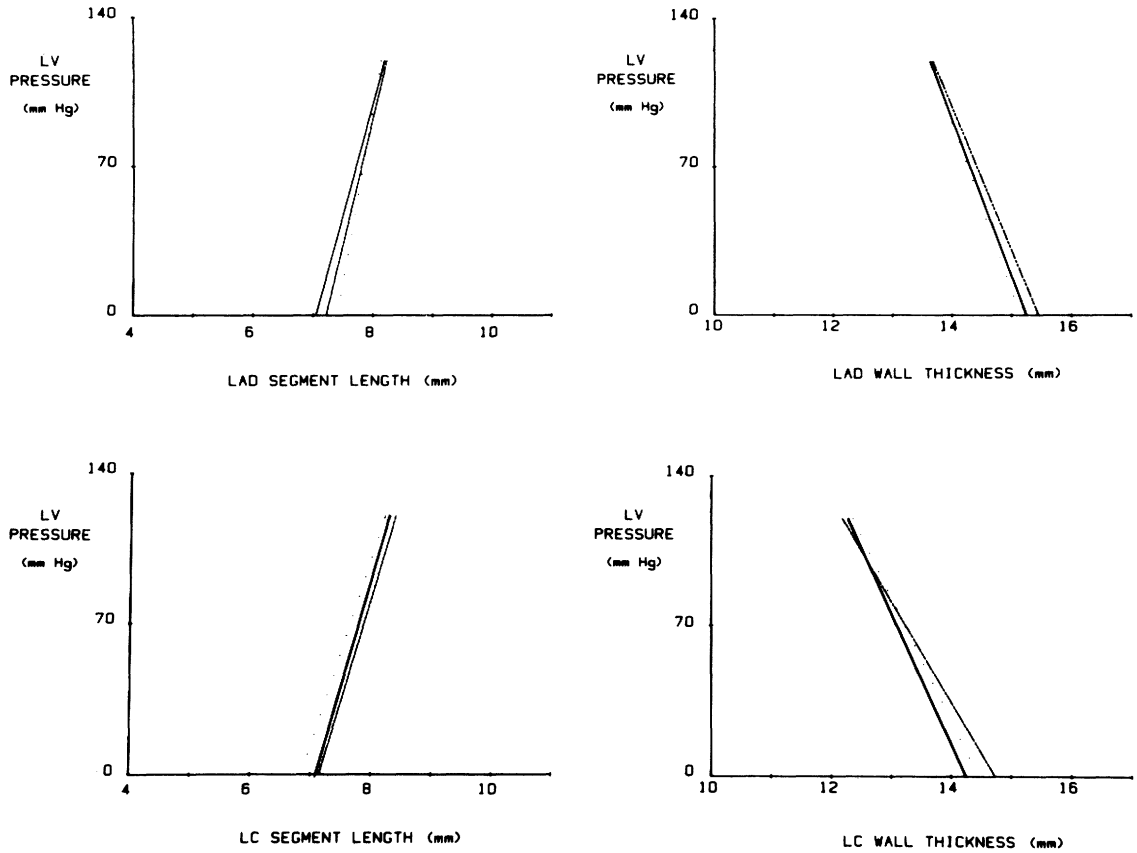

FIGURE 3. End-systolic pressure-thickness and pressure-length relationships in the LAD and LCx regions with various carotid pressure manipulations: control (solid line), sudden reduction of carotid pressure (dashed line), and gradual reduction of carotid pressure (dotted line). See text for details. Abbreviations as in figure 1.

leftward shift of the ESPTR, as illustrated for one animal in figure 6. This shift was caused by a reduction of both Ees and T70 of the ESPTR, with no significant change in T0.

After systemic administration of propranolol, the ESPLR in both the LCx and LAD regions shifted to the right, defined by a reduction of Ees and an increase of L70, with no significant change in L0.

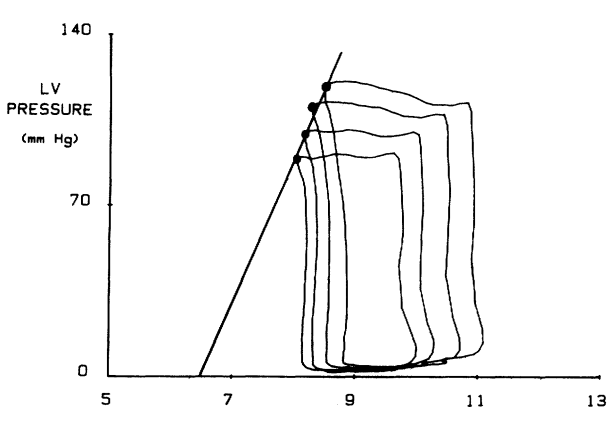

FIGURE 4. Four representative pressure-length loops obtained from one animal during a single occlusion of the IVC. Solid circles represent the end-systolic pressure-length points on each loop; the solid line represents the end-systolic pressure-length relationshp. See text for details.

Propranolol increased the time to Ees. Since heart rate fell, however, time to Ees expressed as a percentage of the RR interval did not increase significantly (44% to 47%).

Dimension change measures. Systemic administration of dobutamine resulted in a significant increase in both EDT and EST. Analogously, EDL and ESL both decreased. As a result, standard sonomicrometer measurements of absolute and percent wall thickening and segment length shortening failed to show any changes with positive inotropic stimulation.

Systemic administration of propranolol resulted in a significant decrease in EDT and EST in both the LCx and LAD regions. The relatively large fall in EDT in the LAD region was associated with a change in neither ΔT nor $\%\Delta T$ after propranolol. The somewhat smaller reduction of EDT in the LCx region was associated with significant reductions of both ΔT and $\%\Delta T$. Analogously, EDL and ESL increased in both the LCx and LAD regions; this was associated with

TABLE 1
Wall thickness, segment length, ESPTR, and ESPLR data during systemic administration of inotropic agents

	LAD: Wall thickness							LCx: Wall thickness						
	n	EDT (mm)	EST (mm)	%ΔT	T0 (mm)	T70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)	n	EDT (mm)	EST (mm)	%ΔT	T0 (mm)	T70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
CD		13.4 ±0.9	15.5 ±1.3	14.9 ±2.1	17.4 ±1.1	16.1 ±1.2	−67 ±14	241 ±21		11.2 ±0.8	12.6 ±0.8	13.5 ±3.9	14.8 ±0.7	13.1 ±0.9	−53 ±7	247 ±23
	7								7							
D		14.3[B] ±1.1	16.5[B] ±1.4	14.8 ±1.8	17.7 ±1.0	17.0[B] ±1.2	−231[A] ±59	191[A] ±36		11.9[B] ±0.8	13.6[B] ±0.8	16.8 ±5.9	14.9 ±0.8	14.0[A] ±0.7	−158[A] ±41	210[A] ±33
CP		13.9 ±0.9	15.8 ±1.1	13.5 ±1.2	17.3 ±1.3	16.4 ±1.2	−139 ±36	213 ±11		11.8 ±0.9	13.2 ±0.9	12.7 ±4.5	14.8 ±0.8	13.7 ±0.8	−89 ±16	229 ±11
	8								8							
P		13.3[B] ±0.9	14.8[B] ±1.2	11.3 ±2.6	17.3 ±1.1	15.4[B] ±1.1	−42[A] ±5	261[B] ±18		11.4[B] ±0.9	12.1[B] ±0.8	7.3[B] ±3.4	14.9 ±0.7	12.7[A] ±0.8	−41[A] ±7	270[B] ±20

	LAD: Segment length							LCx: Segment length						
	n	EDL (mm)	ESL (mm)	%ΔL	L0 (mm)	L70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)	n	EDL (mm)	ESL (mm)	%ΔL	L0 (mm)	L70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
CD		10.3 ±0.9	8.8 ±0.5	13.9 ±3.6	7.9 ±0.4	8.5 ±0.5	125 ±26	273 ±55		9.6 ±0.7	8.3 ±0.8	13.8 ±3.5	7.6 ±0.8	8.1 ±0.8	158 ±24	250 ±39
	4								6							
D		10.1 ±0.8	8.5 ±0.5	15.6 ±3.8	7.9 ±0.5	8.2 ±0.5	277 ±84	244 ±69		9.1 ±0.7	8.0[B] ±0.9	13.1 ±3.1	7.4 ±0.7	7.8[B] ±0.9	263[A] ±44	195[A] ±51
CP		10.7 ±0.9	8.8 ±0.6	16.7 ±3.6	7.8 ±0.4	8.5 ±0.5	122 ±20	236 ±10		10.2 ±0.5	8.8 ±0.5	13.1 ±3.4	8.2 ±0.4	8.6 ±0.5	274 ±108	224 ±16
	6								6							
P		11.4 ±1.1	10.0[A] ±0.9	11.9[A] ±3.0	7.7 ±0.6	9.3[A] ±0.8	45[B] ±7	275[A] ±24		10.5 ±0.5	9.8[B] ±0.5	7.2[B] ±2.4	7.7[B] ±0.5	9.2[B] ±0.4	49 ±4	268[A] ±28

CD = predobutamine control; D = dobutamine; CP = prepropranolol control; P = propranolol; TIMEes = time to Ees. Other abbreviations as in text.

[A]$p < .05$; [B]$p < .01$.

See text for details.

significant reductions of both ΔL and %ΔL after propranolol.

Regional inotropic stimulation. Data obtained during regional inotropic stimulation are summarized in tables 3 and 4.

ESPTR/ESPLR. Hemodynamic data for all animals are summarized in table 5. After regional administration of dobutamine and propranolol there were no significant hemodynamic changes.

Figure 7 shows a representative example of the effect of intracoronary dobutamine (administered into the LCx) on the LCx ESPTR in one animal. Table 3 summarizes results in all animals. With low-dose dobutamine, the LCx region ESPTR shifted to the right, while there was no change in the LAD region ESPTR. Although both Ees and T70 increased, only the increase in T70 was statistically significant. T0 was unchanged. With high-dose intracoronary dobutamine, the LCx region ESPTRs shifted further to the right. The LAD region also shifted to the right at the high dose of dobutamine. This shift was caused by an increase in both Ees and T70 in the LCx region. In the LAD region, Ees did not change but T70 increased significantly.

For ESPLRs, only control and high-dose intracoronary dobutamine were compared. With high-dose dobutamine, LCx region ESPLR shifted slightly to the left. The increase in LCx region Ees was not quite statistically significant ($p = .0579$). Furthermore, the decrease in L70 was not significant and L0 actually

TABLE 2
Hemodynamic data during systemic administration of inotropic agents

	n	PAO (mm Hg) SYS	PAO (mm Hg) DIA	LVEDP (mm Hg)	HR (bpm)
C		103 ±7	73 ±7	6 ±1	109 ±9
	8				
D		117 ±9	82 ±13	5 ±1	133[A] ±11
C		114 ±6	77 ±6	7 ±2	114 ±8
	8				
P		97 ±4	66 ±5	12 ±3	92[A] ±5

PAO = aortic pressure; SYS = systolic; DIA = diastolic; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; other abbreviations as in table 1.

[A]$p < .05$.

increased. Although only five animals were studied, LAD region ESPLR parameters did not change significantly, although there was a tendency for Ees to increase and L70 to decrease with high-dose dobutamine.

With increasing doses of dobutamine, time to Ees progressively decreased in the LCx region. In the LAD region, however, time to Ees decreased only modestly even with the highest dose of dobutamine.

As summarized in table 4 and illustrated in figure 8, intracoronary propranolol shifted the ESPTR to the left, due mainly to a reduction of T70. Although there was a marked reduction of the LCx region Ees after propranolol, the change in slope did not quite reach statistical significance. The LAD region ESPTR showed no change after low-dose propranolol. After high-dose propranolol, however, a significant decrease in T70 occurred in the LAD region. Although Ees also fell in the LAD region, this did not reach statistical significance.

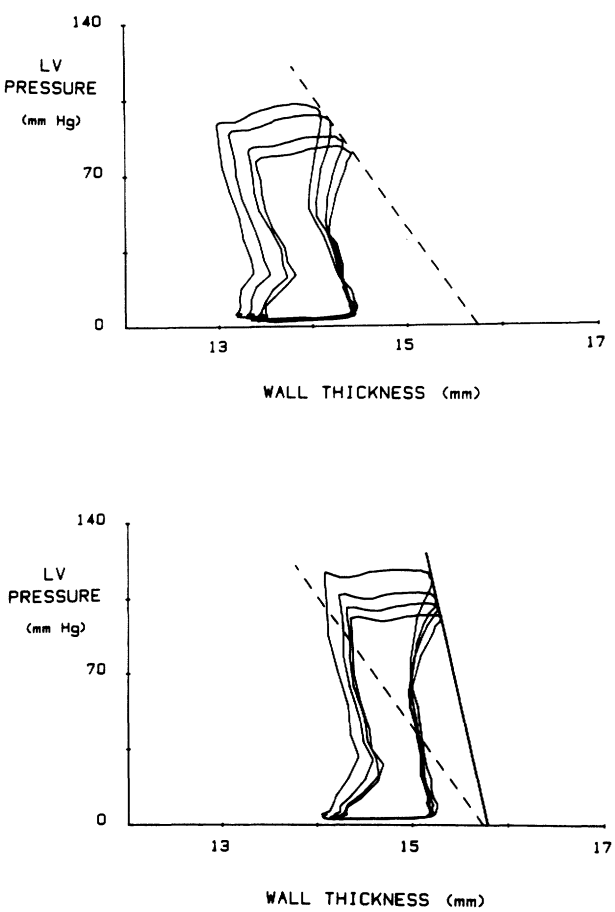

FIGURE 5. Pressure-thickness loops and end-systolic pressure-thickness relationships before *(top panel)* and after *(bottom panel)* systemic administration of dobutamine. Dashed line, control ESPTR; solid line, ESPTR after dobutamine.

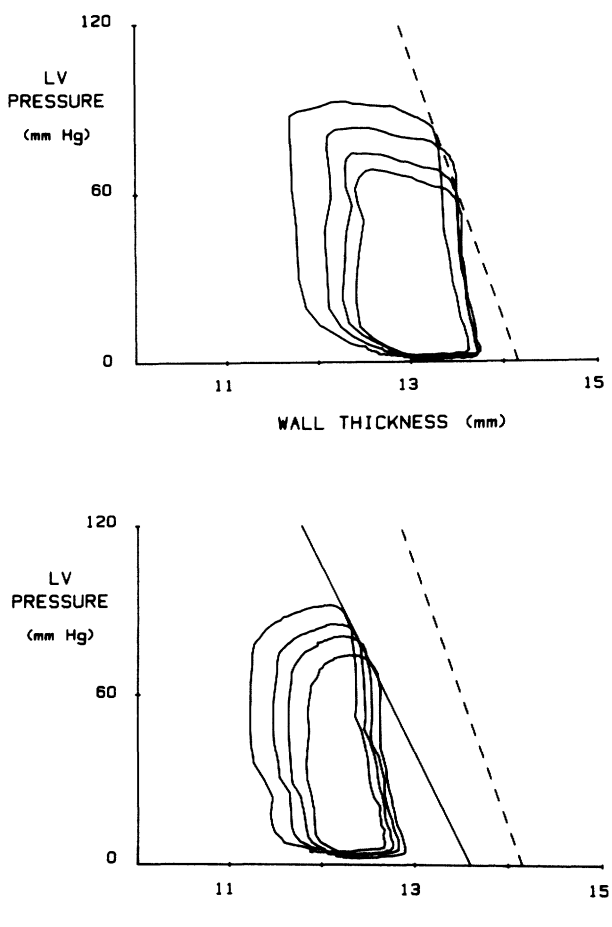

FIGURE 6. Pressure-thickness loops and end-systolic pressure-thickness relationships before *(top panel)* and after *(bottom panel)* systemic administration of propranolol. Dashed line, control ESPTR; solid line, ESPTR after propranolol.

As shown in table 4, analogous shifts in the ESPLR in both the LAD and LCx regions occurred. Thus the LCx region ESPLR shifted to the right with both low- and high-dose propranolol. This rightward shift was caused by both a significant decrease in Ees and an increase in L70. LAD region ESPLR was unchanged with low-dose propranolol but shifted leftward with high-dose propranolol because of a decrease in L70 with no change in Ees.

Dimension change measures. EDT and EST both increased after intracoronary infusion of dobutamine as shown in table 3. By the standard definition of EST

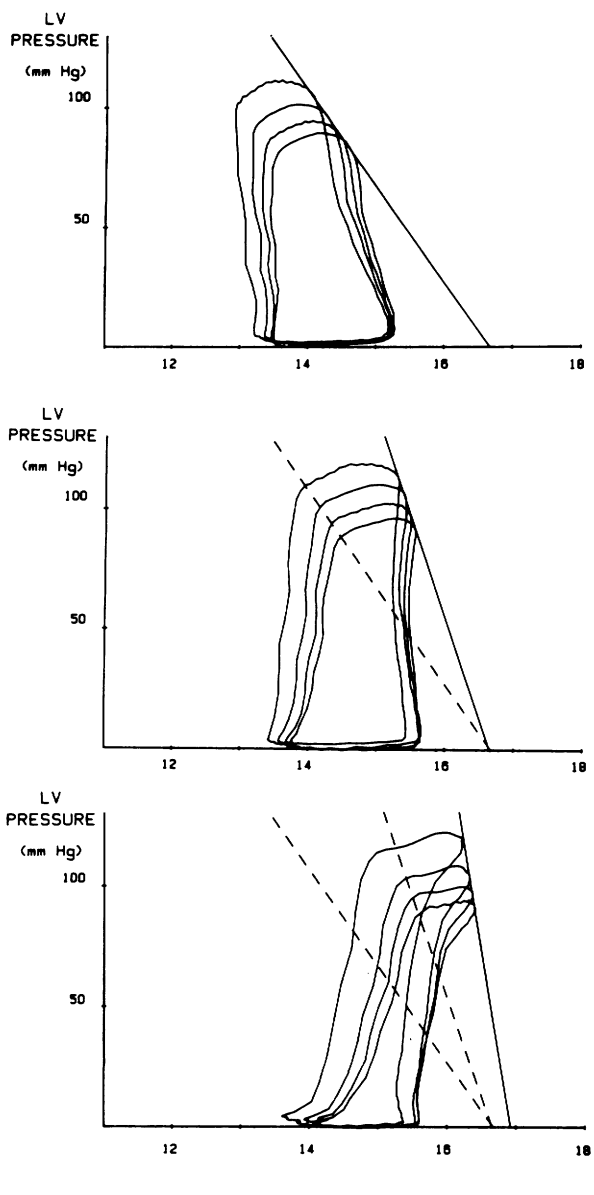

FIGURE 7. LCx region pressure-thickness loops and end-systolic pressure-thickness relationships before *(top panel)* and after *(middle* and *bottom panels)* administration of dobutamine into the LCx. *Top,* Control; *middle,* low-dose dobutamine; *bottom,* high-dose dobutamine. Dashed lines are ESPTRs of panel above.

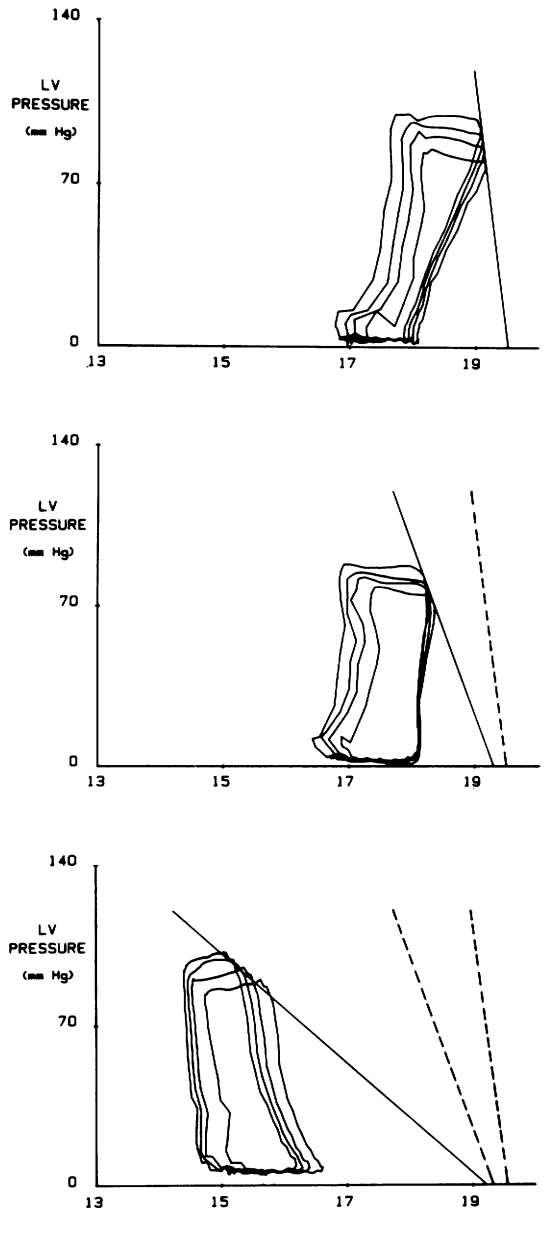

FIGURE 8. LCx region pressure-thickness loops and end-systolic pressure-thickness relationships before *(top panel)* and after *(middle* and *bottom panels*) administration of propranolol into the LCx. *Top,* Control; *middle,* low-dose propranolol; *bottom,* high-dose propranolol. Dashed lines are ESPTRs of panel above.

(wall thickness occurring 20 msec before peak negative left ventricular dP/dt), neither ΔT nor %ΔT increased significantly after LCx infusion of dobutamine in either the LCx or LAD region. By an alternative definition of end-systole, in which EST was defined as maximum wall thickness occurring any time before peak negative left ventricular dP/dt, both ΔT and %ΔT in the LCx region increased significantly whereas LAD region ΔT and %ΔT did not change. The region receiving dobutamine reached maximum end-systolic

TABLE 3
Wall thickness, segment length, ESPTR, and ESPLR data during regional infusion of dobutamine into the LCx

	LCx: Wall thickness											
			EST (mm)		%ΔT		TIME (msec)				Ees (mm Hg/	
	n	EDT (mm)	STD	MAX	STD	MAX	STD	MAX	T0 (mm)	T70 (mm)	mm)	TIMEes (msec)
CD	6	11.6 ±1.2	12.9 ±1.4	12.9 ±1.4	10.8 ±1.4	10.8 ±1.4	223 ±10	223 ±10	14.9 ±1.4	13.5 ±1.3	−55 ±6	195 ±8
DL		12.0 ±1.3	13.7[A] ±1.5	13.9[A] ±1.5	14.0 ±2.4	15.4[A] ±2.3	204 ±7	188[A] ±12	15.2 ±1.4	14.3[A] ±1.5	−121 ±38	172 ±10
DH		12.5[B] ±1.3	14.1[B] ±1.6	14.8[B] ±1.5	11.9 ±2.5	17.9[B] ±1.0	191[A] ±5	147[B] ±4	15.6 ±1.3	15.0[B] ±1.4	−183[A] ±36	137[B] ±4
	LCx: Segment length											
			ESL (mm)		%ΔL		TIME (msec)				Ees (mm Hg/	
	n	EDL (mm)	STD	MAX	STD	MAX	STD	MAX	L0 (mm)	L70 (mm)	mm)	TIMEes (msec)
CD	6	10.1 ±1.1	8.5 ±1.0	8.5 ±1.0	15.4 ±2.1	15.5 ±2.1	225 ±7	221 ±7	6.9 ±1.0	8.0 ±1.0	104 ±27	196 ±5
DH		9.6 ±1.0	7.9[A] ±1.0	7.8[A] ±1.0	17.9 ±8.6	19.0 ±8.6	191[A] ±9	166[A] ±11	7.4[A] ±1.0	7.7 ±1.0	367[C] ±100	150[A] ±11

CD = predobutamine control; DL = low-dose dobutamine; DH = high-dose dobutamine; STD = value when estimated from the standard definition of end-systole (20 msec before peak negative left ventricular dP/dt); MAX = value when estimated from alternative definition of end-systole (point at which dimension is greatest any time before peak negative left ventricular dP/dt); TIME = msec after onset of systole that end-systole occurs with either the MAX or STD definitions of end-systole; other abbreviations as in table 1 and text.

[A] $p < .05$ compared with control; [B] $p < .05$ compared with control and with low-dose dobutamine value; [C] $p = .057$ compared with control. See text for details.

thickening earlier than the region not receiving positive inotropic stimulation. This alternative "end-systolic time" agreed well with the time to reach Ees in the LCx region. In the LAD region, EST defined by either method was the same.

ESL decreased significantly in both the LCx and LAD regions after intracoronary dobutamine. EDL also decreased in both regions, although this decrease did not quite reach statistical significance in the LCx region. Although the alternative definition of end-systole did increase the calculated ΔL and %ΔL in the LCx region, the increase in segment shortening did not reach statistical significance. No change in ΔL or %ΔL in the LAD region was observed.

Intracoronary propranolol caused a significant decrease in EDT and EST at both dosage levels in the LAD and LCx regions. Furthermore, LCx region ΔT and %ΔT fell significantly with both low- and high-dose intracoronary propranolol. However, LAD region ΔT and %ΔT did not change significantly from control, as shown in table 4. Changes in segment length after propranolol in the LAD and LCx regions were analogous to changes in wall thickness.

Discussion

The major findings of this study are: (1) the ESPTR, ESPLR can be measured in the intact, open-chest dog during a 7 sec IVC occlusion without detectable baroreceptor reflex–mediated effects on cardiac contractile state; (2) the ESPTR,ESPLR serves as a sensitive, relatively load-independent index of changes in regional contractile state, particularly in settings in which simple dimension change measures of regional function (ΔT, %ΔT, etc.) are unreliable because of changes in loading conditions; (3) unlike dimension change measures of regional function, which depend upon left ventricular dP/dt to define end-systolic dimensions, the ESPTR,ESPLR do not depend on timing regional end-systole with this parameter; therefore, the ESPTR,ESPLR may be a more sensitive index of regional function when "regional end-systole" occurs at different times in different regions of the ventricle

TABLE 3
(Continued)

n	EDT (mm)	%ΔT	T0 (mm)	T70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
LAD: Wall thickness						
6	13.6 ± 1.0	9.7 ± 1.6	16.6 ± 1.4	15.5 ± 1.2	−75 ± 14	194 ± 8
	13.6 ± 0.7	11.8 ± 2.8	17.1 ± 1.4	15.7 ± 1.1	−62 ± 9	185 ± 7
	14.1 ± 1.0	11.7 ± 1.8	17.0 ± 1.2	16.1[B] ± 1.3	−72 ± 3	174[B] ± 6
LAD: Segment length						
n	EDL (mm)	%ΔL	L0 (mm)	L70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
5	10.6 ± 1.6	15.5 ± 4.0	6.6 ± 0.9	7.7 ± 1.2	148 ± 50	203 ± 7
	9.9 ± 1.4	14.0 ± 2.9	5.6 ± 0.5	7.2 ± 0.9	160 ± 73	171[A] ± 16

(due to, for example, a nonhomogeneous inotropic state).

Experimental limitations. The current experiments were conducted in open-chest, anesthetized animals. Therefore the absence of detectable baroreceptor reflex–mediated changes in cardiac contractile state during measurement of the ESPTR,ESPLR may reflect our inability to observe such changes in the setting of the already high level of sympathetic tone associated with the open-chest, anesthetized state. It is possible that such reflex effects are more important in the awake animal.

Because measurement of the ESPTR,ESPLR requires lowering systemic and therefore coronary pressure, it is possible that the myocardium becomes transiently ischemic during the measurement period, particularly when the inotropic state of the heart is augmented. In earlier experiments in the isolated heart, Sunagawa et al.[10] showed that the end-systolic pressure-volume relationship did not change until coronary perfusion pressure fell below approximately 65 mm Hg. In our study, we used data collected above a peak systolic pressure of 70 mm Hg for construction of the ESPTR,ESPLR so that this problem could be avoided. In addition, ischemia is expected to shift the ESPTR to the left[12]; increasing inotropic state, however, shifted the ESPTR to the right, making it unlikely that ischemia occurred even in the setting of increased myocardial oxygen demand. The brief (7 sec) data collection period also makes significant ischemia unlikely. Nonetheless, the potential influence of ischemia on the measured ESPTR,ESPLR cannot be completely ruled out in these experiments.

Actual data points for the ESPTR,ESPLR are gathered over an approximately 30 mm Hg range of left ventricular end-systolic pressures, typically between 120 and 70 mm Hg. Because data are collected over such a narrow pressure range, the relatively high variability of the slope of the ESPTR,ESPLR is not surprising; small changes in position of data points can change the slope of such a line greatly. The variability of Ees and the lengthy extrapolation required to estimate T0 and L0 suggested that EST or segment length at a left ventricular pressure nearer the actual data collection pressure range might be more suitable as the "intercept" used to define the ESPTR and ESPLR, respectively. Because of this and because the true shape of the ESPTR,ESPLR was not defined at lower pressures (since no end-systolic data were collected below 70 mm Hg), the calculated end-systolic dimension at a left ventricular pressure of 70 mm Hg (T70 and L70) was used in combination with Ees to express the ESPTR,ESPLR.

Although used in a manner analogous to ventricular volume elastance, the slope of the ESPTR,ESPLR must be interpreted with caution. For the relationships expressed in this article, both T70 and Ees are parameters that define the position of end-systolic points in pressure-thickness loops obtained by varying preload in a given inotropic state. The position of these points in the pressure-dimension plane changes with inotropic state. Ees, T0, and T70 (and their ESPLR counterparts) are parameters that conveniently allow us to express such changes in position. However, statements about changes in regional elastance (which would relate stress to strain), although clearly tempting, are not justified since neither regional stress nor strain were measured.

Measurement of regional elastance would require measurement of the tension-length or stress-strain relationship. Since left ventricular wall tension and stress in the intact heart cannot be measured with confidence currently, these parameters can only be calculated with left ventricular pressure in one of a number of geometric models of varying complexity. These models make simplifying assumptions about left ventricular geometry and material properties to make such calculations possible. Rather than calculating regional wall tension or stress on the basis of a particular model of the

TABLE 4
Wall thickness, segment length, ESPTR, and ESPLR data during regional administration of propranolol into the LCx

	LAD: Wall thickness								LCx: Wall thickness							
	n	EDT (mm)	EST (mm)	%ΔT	T0 (mm)	T70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)	n	EDT (mm)	EST (mm)	%ΔT	T0 (mm)	T70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
C	6	12.4 ±1.0	13.5 ±1.2	9.2 ±1.6	14.6 ±1.1	13.9 ±1.2	−138 ±39	191 ±10	6	14.5 ±1.2	16.2 ±1.4	11.6 ±1.3	17.3 ±1.3	16.6 ±1.4	−138 ±41	186 ±7
PL		12.0 ±1.0	12.1[A] ±1.3	0.5[A] ±3.2	13.9 ±1.3	12.6[A] ±1.3	−59 ±7	191 ±7		14.4 ±1.2	15.8 ±1.3	11.3 ±1.9	17.2 ±1.4	16.3 ±1.4	−101 ±20	194 ±7
PH		11.6[A] ±0.8	11.3[B] ±1.9	−3.1[A] ±2.3	13.2[A] ±1.2	11.8[B] ±1.0	−57 ±9	199 ±8		13.9[B] ±1.2	15.3[B] ±1.3	10.5 ±1.9	17.0 ±1.5	15.9[A] ±1.4	−83 ±18	197 ±4
	LCx: Segment length								LAD: Segment length							
	n	EDL (mm)	ESL (mm)	%ΔL	L0 (mm)	L70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)	n	EDL (mm)	ESL (mm)	%ΔL	L0 (mm)	L70 (mm)	Ees (mm Hg/mm)	TIMEes (msec)
C	6	10.2 ±1.1	8.8 ±1.2	14.5 ±3.7	8.0 ±1.2	8.5 ±1.2	149 ±33	193 ±8	4	10.1 ±1.2	8.1 ±1.4	19.1 ±1.0	7.0 ±1.0	7.9 ±1.3	165 ±64	189 ±11
PL		10.4 ±1.1	9.7[A] ±1.2	7.8[A] ±3.4	8.0 ±1.5	9.2[A] ±1.4	70[A] ±13	197 ±7		10.3 ±1.7	8.2 ±1.3	19.7 ±1.3	6.6 ±0.5	7.9 ±1.1	130 ±66	192 ±15
PH		11.0[B] ±1.3	10.5[B] ±1.3	4.5[B] ±2.2	8.1 ±1.4	9.8[B] ±1.4	48[A] ±15	208[A] ±5		11.0 ±1.8	9.0[B] ±1.4	18.1 ±1.6	7.2 ±1.3	8.4[B] ±1.3	102 ±46	198 ±9

CP = prepropranolol control; PL = low-dose propranolol; PH = high-dose propranolol; other abbreviations as in table 1 and text.
[A]$p < .05$ compared with control; [B]$p < .05$ compared with control and low-dose propranolol.
See text for details.

ventricle, we have chosen to use an easily measured index of ventricular load, left ventricular pressure. An underlying assumption in our study is that some relationship between regional load and left ventricular pressure does exist and, further, that this relationship does not change with interventions studied. This latter statement is probably approximately true as long as large changes in ventricular geometry or material properties do not occur with the intervention.

Measurement of the ESPTR,ESPLR requires changing ventricular loading conditions. This procedure alters ventricular volume and potentially alters the dynamic geometric changes occurring during the cardiac cycle. Administration of inotropic agents may also alter ventricular volumes and dynamic geometry. Rankin et al.[11] have pointed out that left ventricular volume importantly influences the way in which the ventricle reduces its volume during systole. Thus, at high left ventricular volumes the ventricle appears to eject blood by reducing short-axis diameter, whereas at low left ventricular volumes the relative importance of long-axis shortening increases.[11] This observation has potentially important implications for measurement of end-systolic pressure-dimension relationships, particularly the ESPLR. Short-axis shortening is related to segment length shortening in the left ventricular circumference. If an intervention reduces left ventricular volume, short-axis shortening decreases and long-axis shortening increases in relative importance in systole, particularly in the acute, open-chest animal. As a result, there may be relatively less shortening (and conceivably even lengthening) in the left ventricular circumferential direction.

Measurement of the ESPLR by means of IVC occlusion requires reduction of left ventricular volume. Thus it is possible that if the dynamic geometric changes that occur during systole importantly involve long-axis shortening, then the ESPLR could record either an extremely steep Ees or even a negative Ees. That is, the reductions in ventricular volume during measurement of the ESPLR may not be reflected in reduction of circumferential segment lengths. There-

TABLE 5
Hemodynamic data during regional administration of inotropic agents

	n	PAO (mm Hg) SYS	PAO (mm Hg) DIA	LVEDP (mm Hg)	HR (bpm)
CD		122	82	5	132
		±14	±6	±1	±6
	8				
DL		107	75	6	130
		±7	±7	±1	±6
DH		112	79	5	135
		±4	±5	±1	±5
CP		105	75	5	130
		±4	±4	±1	±5
PL		102	75	5	128
		±4	±4	±1	±5
PH		102	74	7	125
		±3	±3	±1	±4

CD = predobutamine control; DL = low-dose dobutamine; DH = high-dose dobutamine; CP = prepropranolol control; PL = low-dose propranolol; PH = high-dose propranolol; other abbreviations as in table 2.

fore end-systolic segment length may shorten little or potentially even lengthen when end-systolic pressure (and therefore volume) is reduced. This may explain, in part, the relatively steep slopes of the ESPLRs compared with the ESPTRs. It may also explain why the change in the LCx region ESPLR after intracoronary dobutamine was not quite statistically significant. Because wall thickness changes both when short-axis and long-axis shortening occurs, the ESPTR may be less sensitive to changes in left ventricular volume than the ESPLR and may be more generally applicable.

Finally, an underlying assumption in measurement of wall thickness or segment length by crystals is that crystal alignment does not change in the course of the experiment. Poor initial alignment or alteration of alignment with an intervention may importantly influence the measured myocardial dimension. Malalignment of crystals may not be apparent even when crystal position is examined postmortem. Unfortunately, the problem of alteration of the relationship between measuring device and measured myocardium exists with any method applied to determine regional myocardial dimensions.

Other studies. In a preliminary report, the ESPTR was first suggested by Osakada et al.[5] as a potentially useful measure of regional ventricular function. In this study, the ESPTR was constructed by changing ventricular loading conditions with drugs (phenylephrine, nitroprusside) in chronically instrumented dogs. The values for slope of the ESPTR generally are somewhat lower than those in our study (−30 vs −70 mm Hg/mm), which may reflect the relatively lower sympathetic tone and therefore lower contractile state of the ventricle of the awake animal. As in our study, these authors observed that the ESPTR shifted to the right of control with positive inotropic stimulation and to the left with negative inotropic stimulation.[5] However, the shift was due only to a change in T0, not in slope (Ees). Differences in methods may explain, in part, the relatively minor differences in results between this study and ours. Perhaps most important is that loading conditions were changed relatively slowly with drugs, making the potential contribution of reflex changes in cardic contractile state more likely than in our study.

In another study, Osakada et al[12] studied the effect of ischemia on end-systolic measures of regional function. In these experiments, however, only a single end-systolic pressure-thickness point was obtained for each intervention in most dogs (end-systole was defined as the maximum wall thickening in the control region occurring at or before 20 msec before peak negative left ventricular dP/dt). Thus the ESPTR was not actually obtained but only a single point in this relationship. Unless loading conditions remain unchanged, this method is, of course, not generally useful to estimate changes in regional function. If loading conditions are changed by the intervention, changes in the end-systolic pressure-thickness point could represent a change to another position on the same ESPTR (indicating no change in contractile state) or movement to another ESPTR (representing a true change in contractile state). The authors did illustrate, and suggest, however, use of an IVC balloon occlusion to change loading conditions for construction of the entire ESPTR.[12] Their results show that the ESPTR shifts leftward with ischemia due to a shift in thickness-axis intercept (T0) without a change in slope.

Miller et. al.[6] used a rapid left ventricular volume loading technique to change loading during construction of the ESPLR in the intact open-chest pig. These investigators found an increase in the slope of the ESPLR with no change in L0 after systemic dobutamine, which is in agreement with the findings of the present study. Unlike us, however, they detected no change in the ESPLR after systemic administration of propranolol. Comparison of propranolol dosage levels is made difficult because bolus doses were used in our study, whereas these authors used constant infusion. In addition, they found relatively poor agreement between changes in regional contractile state (estimated

from the ESPLR) and global contractile state (estimated from the end-systolic pressure-diameter relationship). For this reason, the authors concluded that the slope of the ESPLR, which they refer to as elastance, may not reflect specific changes in contractility. As noted above, the slope of the ESPLR is not truly elastance because it is dimensionally incorrect. Furthermore, their measure of global elastance uses the short axis-diameter end-systolic pressure-diameter relationship. As discussed above, the unknown and potentially changing contribution of changes in long-axis diameter to both global and regional elastance, particularly when the latter is estimated by the ESPLR, is complex and may vary with left ventricular volume. It is not surprising, then, that regional and global "elastance" as used by these authors do not always change directionally in the same manner.

Implications. Dimension change measures of both global and regional ventricular performance all have the disadvantage of being highly dependent on ventricular loading conditions. In this study, the usefulness of the ESPTR and the ESPLR as measures of contractile state in settings in which preload is changed by an intervention is clear, as is the limitation of simple dimension change measures of regional function. These experiments also reveal that when fixed to a global timer of end-systole, differences in timing of regional end-systole due to changes in regional contractile state can be missed. Neither the ESPTR nor the ESPLR depend on left ventricular dP/dt to time end-systole regionally. They are therefore capable of estimating changes in regional contractile state even when end-systole occurs at different times in the nonhomogeneous ventricle. Finally, although both the ESPTR and ESPLR appear useful, the ESPTR may be more generally applicable because measurement of wall thickness is less dependent on ventricular dynamic geometry than measurement of segment length, particularly when left ventricular volume is small.

Although the ESPTR,ESPLR has been shown to be useful in detecting and defining changes in contractile performance, it has not been normalized, making comparisons of absolute values between animals difficult to interpret. Any normalization scheme presumes that the same quantity is measured in each animal, e.g., full left ventricular wall thickness. The ventricle is trabeculated and has papillary muscles, so that full thickness is highly variable even in the same ventricle. Furthermore, even if the ventricle had uniform thickness, it is likely that sonomicrometer crystals are not always placed perfectly on the endocardium and epicardium, so that full thickness is not really measured all the time. If one is concerned with *changes* in left ventricular wall thickness, these anatomic and technical problems are of less importance. However, in a normalization scheme, where absolute wall thickness is one parameter of interest, they are critical. At the present time, these factors limit our ability to define normalized parameters for the ESPTR and ESPLR. Finally, any normalization scheme would need to account for left ventricular mass, since both Ees and T0 vary greatly depending on the size of the left ventricle.

References

1. Suga H, Sagawa K: Instantaneous pressure-volume relationships and their ratio in the excised, supported canini left ventricle. Circ Res **35:** 117, 1974
2. Suga H, Sagawa K, Kostiuk DP: Controls of ventricular contractility assessed by pressure-volume ratio, Emax. Cardiovasc Res **10:** 582, 1976
3. Suga H, Sagawa K, Shoukas AA: Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res **32:** 314, 1973
4. Sunagawa K, Maughan WL, Sagawa K: Effect of regional ischemia on the left ventricular end-systolic pressure-volume relationship of isolated canine hearts. Circ Res **52:** 170, 1983
5. Osakada G, Hess OM, Gallagher KP, Lavelle JF, Kemper WS, Ross J Jr: End-systolic wall thickness-pressure, and wall thickness-stress relations for assessing myocardial contractility. Circulation **60**(suppl III): III-203, 1980 (abst)
6. Miller WP, Liedtke AJ, Nellis SH: Regional end-systolic pressure-length relationships using a volume-loading technique in the intact pig heart. Circ Res **55:** 326, 1984
7. Streeter DD, Spotnitz HM, Patel DP, Ross J Jr, Sonnenblick EH: Fiber orientation in the canine left ventricle during diastole and systole. Circ Res **24:** 339, 1969
8. Theroux P, Ross J Jr, Franklin D, Covell JW, Bloor CM, Sasayama S: Regional myocardial function and dimensions early and late after myocardial infarction in the unanesthetized dog. Circ Res **40:** 158, 1977
9. Snedecor GW, Cochran WG: One-way classification: analysis of variance. *In* Statistical methods, ed 7. Ames, IA, The Iowa State University Press, pp 215–237
10. Sunagawa K, Maughan WL, Friesinger G, Guzman P, Chang M-S, Sagawa K: Effects of coronary arterial pressure on left ventricular end-systolic pressure-volume relation of isolated canine heart. Circ Res **50:** 727, 1982
11. Rankin JS, McHale PA, Arentzen CE, Ling DM, Greenfield JC, Anderson RW: The three-dimensional dynamic geometry of the left ventricle in the conscious dog. Circ Res **39:** 304, 1976
12. Osakada G, Hess OM, Gallagher KP, Kemper WS, Ross J Jr: End-systolic dimension-wall thickness relations during myocardial ischemia in conscious dogs: a new approach for defining regional function. Am J Cardiol **51:** 1750, 1983