Regional End-Systolic Pressure-Length Relationships Using a Volume-Loading Technique in the Intact Pig Heart

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SUMMARY. The purpose of this study was to characterize left ventricular systolic elastances as derived from pressure-segment length and pressure-diameter relationships, and to compare the resulting regional and global elastances to known changes in inotropy. Left ventricular pressure-segment length and pressure-diameter were varied in a series of consecutive beats by means of a volume-loading technique, and both regional and global relationships at 20-msec intervals throughout systole were found to be nonlinear and to exhibit hysteresis. In eight animals, regional hysteresis was present after vagotomy, propranolol (1.0 mg/kg), and atropine (0.1 mg/kg), and was present no matter whether hearts were loaded by volume (45–60 ml/sec) or by pressure (partial aortic occlusion) over a similar range of left ventricular systolic pressures. Elastance was linearly approximated by the slope of the major axis of the hysteresis loops. In each instance, elastance increased to a maximum and then decreased, thus defining end-systole. In seven animals, maximum elastance-length and -diameter were compared before and after treatments with dobutamine (5–13 μg/kg per min) and propranolol (6–51 μg/kg per min), or after induction of global ischemia. Dobutamine increased maximum elastance-diameter by 37% (P < 0.01) and maximum elastance-length by 159% (P < 0.05). Propranolol decreased maximum elastance-diameter by 27% (P < 0.05) and maximum elastance-length by 6% (P = NS). Global ischemia (50% reduction in coronary flow) did not significantly change either maximum elastance-diameter or -length. However, with ischemia, the diameter intercept of maximum elastance-diameter increased by 24% (P < 0.025), and the time to maximum elastance-length decreased by 33% (P < 0.01). Comparing all interventions, the percent changes in maximum elastance-length and -diameter related directly but with a low correlation coefficient (r = 0.49). These differences in regional and global elastance suggest a complex relationship between regional and global myocardial mechanics, and may not necessarily reflect specific changes in contractility. (Circ Res 55: 326–335, 1984)

RECENT efforts to quantify myocardial contractility have utilized the end-systolic pressure (force)-volume (length) relationships as described by Sagawa (1978, 1981). The experimental work which established this relationship, though elegant, was obtained largely from surgically isolated heart prepa-

rations (Suga and Sagawa, 1974; Weber et al., 1976) which were areflexic and required both pacing and perfusion support. Instantaneous ventricular vol-

umes from these models could be measured only by fixing predefined ventricular filling and ejecting pressures in a manner different from those control mechanisms which operate in the normally ejecting heart. Further, measurements were obtained only at steady state conditions following loading changes by minutes, and more transient changes in myocardial mechanics were not evaluated.

Given the early success of this end-systolic relationship in describing contractility in the isolated heart preparation, this relationship was soon applied clinically and in intact hearts. In intact hearts, how-

ever, it was not easy to change afterload and obtain multiple pressure (force)-volume (length) data points without evoking interdependent changes in the contractile state of the heart (Sagawa, 1981). Certain investigators attempted to minimize these changes by pharmacological denervation (Mehmel et al., 1981). Others manipulated afterload by time-

consuming interventions with drugs such as phen-

ylephrine, nitroprusside, nitroglycerin, and meth-

oxamine (Mahler et al., 1975; Grossman et al., 1977; Borow et al., 1982a). Still other workers attempted to circumvent loading considerations entirely by mathematical modeling (Schoff et al., 1983). Further, end-ejection relationships were usually substi-

tuted for end-systolic relationships, which Sagawa (1981) cautioned might be significantly different in magnitude and meaning.

Despite these variations in approach, the global end-systolic or end-ejection pressure (force)-volume
(length) relationships have provided an empirically useful means to describe global left ventricular function. However, the application of this concept has not as yet been extended to estimate regional performance. Although it is intuitively attractive to hypothesize that function in a region of myocardium is but a subset of overall ventricular function, this has not been substantiated. In fact, Elzinga and Westerhof (1981) showed that the time-varying compliance of the intact ventricle was not seen in isolated heart muscle, suggesting that time-varying compliance represents a property of the intact ventricle, not of the heart muscle, itself.

In this study, we proposed to test whether the left ventricular end-systolic pressure-segment length relationship could be applied as a marker in describing contractility in a region of myocardium. Relationships were developed in the intact, working, whole blood-perfused pig heart, using an acute volume-loading technique. The study was divided into two parts. First, we determined the characteristics and limitations of the volume-loading method, tested the influence of autonomic reflexes on the derived pressure-dimension relationships, and compared any differences in the relationships as obtained by volume loading with acute and steady state pressure-loading techniques. Second, we assessed whether regional contractility, as indexed by the end-systolic left ventricular pressure-segment length relationship, followed global contractility as measured by the end-systolic left ventricular pressure-diameter relationship. Global contractility was altered by intervention treatments with known inotropic drugs and with global ischemia.

Methods

Fifteen pigs of either sex, weighing 39–56 kg (average 46 kg), were studied following anesthesia with pentobarbital (35 mg/kg, iv) and the establishment of controlled positive pressure ventilation with 100% oxygen. Additional pentobarbital was given as needed to ensure adequate anesthesia throughout the study. Frequent determinations of the animals' arterial pH, PO2, and PCO2 were obtained during each study to ensure adequacy of ventilation and acid-base balance (pH = 7.40 ± 0.01, PO2 = 265.1 ± 13.6, PCO2 = 37.2 ± 1.8).

Preparation and Data Acquisition

Studies were performed in an intact working heart preparation in open-chest domestic pigs, which has been described previously (Liedtke et al., 1978). In brief, after bilateral thoracotomy with transsternotomy and treatment with heparin (20,000 U, iv), two separate extracorporeal perfusion circuits were constructed connecting the cannulated left femoral artery to the left main and right coronary arteries (Fig. 1). The left main coronary artery was perfused via a Gregg cannula inserted retrogradely through the left subclavian artery, and the right coronary artery was perfused by a cannula positioned near its origin. Individual flows to these arteries were controlled by separate low-flow Sarnes perfusion pumps, model 6050. Control flows were set in each of these circulations by adjusting the respective mean perfusion pressures to average aortic pressure corrected for perfusion line resistances. The resulting coronary blood flow is approximately 175% of that required under basal conditions (Liedtke et al., 1978).

Two catheters were placed in the left ventricle (Fig. 1). A 7F high-fidelity micromanometer-tipped pressure device (Millar Mikro-Tip catheter) was advanced retrogradely from the right internal mammary artery into the left ventricle to measure left ventricular pressure. The micromanometer was calibrated against mercury at the body temperature of the animal before and after each experiment. A 10F 100-cm NIH catheter was advanced retrogradely from the right internal carotid artery into the left ventricle. The NIH catheter was connected to a power injector (Medrad Mark III) and was used to infuse volume injections of whole blood obtained from the animal. Injections were timed to begin at the same time in late diastole and were triggered by the R wave of the electrocardiogram. Injection continued at the set rate until the entire volume was delivered, which was generally over three to four cardiac cycles. We chose to adopt this volume-loading technique to minimize the influence of autonomic reflexes on cardiac contractility.

Ultrasound crystals were used to measure a mid-myocardial circumferential segment length and a left ventricular internal diameter (Fig. 1). Segment length in all 15 animals was measured in myocardium contained within the left anterior descending perfusion bed with a pair of ultrasonic crystals (2–3 mm in diameter) and an ultrasonic dimension system (Schuessler and Associates). The specif-
ics of the ultrasonic technique have been described previously (Theroux et al., 1974). The crystals were implanted approximately 1 cm apart in the mid-myocardium in a circumferential direction midway between apex and base. This placement was chosen because the majority of muscle fibers in the mid-myocardium are oriented in the circumferential direction (Streeeter et al., 1966, 1969), and these fibers have been used previously to represent myocardial fiber length (Weber et al., 1976). In seven animals, an additional pair of ultrasonic crystals (4–6 mm in diameter) was implanted on the left ventricular endocardium midway between apex and base by a modification of the technique described by Stinson et al. (1974). The rationale here was that shortening of this internal minor axis diameter accounts for the majority of stroke volume during ejection (Rankin et al., 1976). The above placements were confirmed in every instance by direct visualization at the completion of each experiment.

Right and left main coronary artery pressures, segment length and internal diameter, left ventricular pressure and its first derivative (dP/dt), and the electrocardiogram were displayed and recorded on an eight-channel recorder (Gould Brush 200). In addition, the above data were collected on-line by a PDP 11/10 computer at selected intervals, digitized at 500 samples/sec, and stored on floppy discs for later analysis. All data were acquired during held expiration.

**Experimental Protocol and Data Analysis**

The experiments were divided into two parts. In the first part, eight animals were studied to determine the limitations of obtaining left ventricular systolic pressure-segment length relationships from the volume-loading technique. Data were collected sequentially from one to three control beats, and four to 12 variably volume-loaded beats, during a power injection of 50–80 ml of blood at 45–60 ml/sec. Ventricular ectopy sometimes occurred with the early power injections, but could be virtually eliminated by a combination of repositioning the catheter, injecting the blood at slower injection rates, and treating the animals with lidocaine (0.5–1.0 mg/kg, iv). Once injections were performed successfully without ectopy, the volume and rate of injection were kept constant in that animal for the remainder of the study. If ectopy occurred during an injection, the data were discarded and the injection repeated.

Multiple injections were performed in each of the eight animals prior to any intervention. Injections were also performed after vagotomy in two animals, after vagotomy and propranolol (0.5 mg/kg) in one animal, and after propranolol (0.5–1.0 mg/kg) and atropine (0.01 mg/kg) in five animals. The effects of transient and steady state pressure loading by partial occlusion of the descending aorta with a Satinsky clamp was compared with volume loading by the power injection technique in five animals. Four of these five animals received propranolol (1.0 mg/kg) and atropine (0.01 mg/kg) to prevent reflex changes in contractility evoked by aortic occlusions. Data collection during pressure loading from partial aortic occlusions was recorded as previously described for the volume-loading technique. Data from beats taken during the transients of pressure loading between steady state levels were sampled in three animals. During steady state pressure-loading studies, step changes in left ventricular pressure ranged from 5 to 37 mm Hg, and the time between steps was the minimum necessary to obtain steady state (5–90 sec).

Three to nine beats at each steady state pressure were analyzed in four animals.

In the second part of the study, seven animals were studied to assess the response of the end-systolic pressure-segment length relationship to known global inotropic interventions and ischemia. In each experiment, the heart rate was held constant by right atrial pacing. The left ventricular internal diameter and left ventricular dP/dt were measured as previously described. In all seven animals, the protocol consisted of a series of two to three power injections at 5-minute intervals, followed by the infusion of dobutamine (5–13 μg/kg per min, iv) until LVmax dP/dt increased. A series of two to three injections were again performed, after which the animal was allowed to return to a baseline hemodynamic state (approximately 30 min), and control injections repeated. This was followed by the infusion of propranolol (6–51 μg/kg per min, iv) until LVmax dP/dt decreased and the volume injections were repeated. In five of the seven animals, global coronary blood flow was then decreased by 50% and injections were again performed.

The data recorded during the studies were later analyzed off-line with a PDP 11/10 computer and a graphics terminal (Tektronix 4051). These data included heart rate, peak left ventricular pressure (LVP), left ventricular end-diastolic pressure (LVEDP), and the maximum first derivative of isovolumic left ventricular pressure development (LVdP/dtmax), all of which provided estimates of global left ventricular pump function. Regional segment length data and an index of regional work defined as [LVP(dl/dt)dt] were also obtained (Liedtke and Nellis, 1979).

Left ventricular pressure-segment length and left ventricular pressure-internal diameter curves were constructed for an average preinjection beat. Pressure-length and pressure-diameter data from each sequential variably loaded beat were then generated at 2-msec intervals from the R wave of the ECG for each beat. These data then were reviewed on the graphics terminal at 20-msec intervals from the onset of shortening to the onset of lengthening. Because the data showed hysteresis, the following technique was selected. Utilizing an interactive program, we placed a line through the pressure-length and pressure-diameter data at each 20-msec time interval. This was accomplished by selecting a point on each end of the hysteresis loop that visually best defined the major axis of the loop (Fig. 2). We defined time-varying elastance as the slope of this line. The elastance values and the segment length or diameter intercepts were calculated by the computer at each time interval. Selected data were also plotted on a digital plotter (Tektronix 4662), as shown in the figures.

Paired Student’s t-tests were used in all studies in which statistical significance is estimated. The statistical analysis of the end-systolic elastance data as described by slopes were expressed in degrees from the length/diameter axis (slope angle, Fig. 2), rather than mm Hg/mm. This was more appropriate for statistical comparison of the large absolute slope values obtained, especially regionally, because the slope angle is a monotonically increasing function, whereas the slope itself becomes discontinuous (i.e., as the slope angle approaches 90°, the slope approaches infinity). Linear regression analysis was used to compare regional and global data. Significance was defined for probability values less than 5%. Distribution of data, where listed, appears as the standard error of the mean.
FIGURE 2. A typical set of left ventricular pressure-segment length curves resulting from volume loading in one animal are shown in the left panel. The same pressure-segment length data from sequential cardiac contractions at 0.100, 0.240, and 0.300 second after the R wave of the ECG for each beat are shown by the solid dots in both panels. The beat-to-beat relationship of these data points is indicated by the dashed lines in the right panel. The relationship shows hysteresis in the early part of the ejection phase of contraction (0.100 sec) and with falling left ventricular pressure (0.300 sec), but is nearly linear at end-shortening (0.240 sec). The direction of hysteresis reversed from clockwise to counterclockwise between the 0.100- and 0.300-second time intervals. Time-varying regional elastance (E) was defined by the slope of the major axis of the hysteresis loops, as is shown at 0.100 second by the solid line in the right panel. The slope of this line (slope angle) and its length intercept L0 are also shown.

Results

Part I

The volume-loading technique resulted in a maximum increase in left ventricular peak pressure of 17-49 mm Hg (average 32 ± 1 mm Hg). There was no significant change in the R-R interval or coronary artery perfusion pressures during or after injections. Global coronary perfusion was kept constant throughout each study, as previously described.

The time-varying left ventricular systolic pressure-segment length relationship with volume loading was nonlinear and exhibited hysteresis, as shown in Figure 2. Hysteresis was most marked in the early part of the ejection phase of contraction, but became nearly linear after shortening ceased. Hysteresis was again noted as pressure declined, and its direction was generally in the opposite direction (counterclockwise) from that exhibited during shortening (Fig. 2).

Withdrawal of parasympathetic and sympathetic tone did not qualitatively influence the occurrence of hysteresis with the volume injection technique. This was demonstrated after vagotomy alone in three animals, after vagotomy and propranolol (0.5 mg/kg, iv) in one animal, and after propranolol (0.5-1.0 mg/kg, iv) alone or in combination with atropine (≥0.1 mg/kg, iv) in five animals.

In the four animals that received propranolol (1.0 mg/kg, iv) and atropine (≥0.1 mg/kg, iv), left ventricular systolic pressure-segment length relationships were also assessed during left ventricular pressure loading by partial aortic occlusions. As with the volume-loading technique, transient left ventricular pressure loadings were nonlinear and exhibited hysteresis. A typical example of such nonlinearity is shown in Figure 3.

A comparison of acute volume and steady state pressure loadings in one of the four animals pretreated with propranolol and atropine is shown in Figure 4. At the same time interval from the R wave of the ECG, an elastance curve obtained by the volume-loading technique is compared with that obtained by steady state partial aortic occlusion. Over a similar physiological range of left ventricular systolic pressures, the slopes of the major axis of the hysteresis loops were similar to the slopes of the steady state pressure-loading data.

To quantify the instantaneous left ventricular systolic pressure-segment length relationship, we defined regional elastance (E) as the slope of a line drawn through the major axis of the hysteresis loop (Fig. 2). The slope of the line and its length intercept were determined by the computer. With both volume and pressure loadings, E at 20-msec intervals increased until reaching a maximum, and then decreased. End-systole was defined as the time of maximum E (E_max), as suggested by Suga and Sagawa (1974). Thus, the nonlinear elastance curve obtained by volume loading could be redefined lin-
Early and quantified at a maximum value to estimate regional contractility. $E_{\text{imax}}$ measured in volume-loaded ventricles was similar to $E_{\text{imax}}$ values obtained from steady state pressure loadings over a similar range of left ventricular pressures.

Part II

The second part of the study was designed to study and compare $E_{\text{imax}}$ as a regional index of myocardial contractility with that of its global analogue ($E_{\text{dmax}}$). The sensitivities of both $E_{\text{max}}$ estimates in describing the changes effected by global inotropic interventions were also compared. Interestingly, the left ventricular systolic pressure-internal diameter relationship as developed by volume loading also proved nonlinear and exhibited hysteresis similar to that demonstrated regionally. Because of this, time-varying global elastance ($E_g$) was again defined as the slope of the major axis of the hysteresis loop. The computer determined the slope and diameter intercept. $E_{\text{dmax}}$ was defined as the maximum value of this slope, and was used to identify end-systole.

Global hemodynamic data and the segment length data for the seven animals studied are shown in Table 1. In the five animals that were additionally rendered globally ischemic, the propranolol data served as controls for statistical comparison. With the exception of the dobutamine treatment, where two animals exceeded the paced rate, there was no significant change in heart rate between interventions. Peak left ventricular pressure (+20%, P < 0.005) and left ventricular $dP/dt_{\text{max}}$ (+81%, P < 0.005) increased significantly with dobutamine. Propranolol resulted in a significant decrease in peak left ventricular pressure (−26%, P < 0.005) and in left ventricular $dP/dt_{\text{max}}$ (−41%, P < 0.005). Global ischemia from a 50% reduction in coronary blood flow effected no significant change in peak left ventricular pressure (−16%; P = NS), but did decrease left ventricular $dP/dt_{\text{max}}$ (−22%, P < 0.05). Other findings in the baseline data included an increase in end-systolic segment length (+4%, P < 0.025) noted with global ischemia and a decline in regional work (−56%, P < 0.01) with propranolol. Other shifts in the data were not statistically significant.

Volume loading resulted in a maximum increase in left ventricular peak pressure of 16–55 mm Hg (average 35 ± 1 mm Hg). Time-varying elastance data at 20-msec intervals in a typical experiment are shown in Table 2. In all animals, both regional and global time-varying elastance increased to a maximum and then decreased. The effect of known global inotropic interventions and of ischemia on the regional and global elastance data for all of the animals are shown in Table 3. Regional elastance as described by $E_{\text{imax}}$ increased significantly with dobutamine (+159%, P < 0.05). The time to $E_{\text{imax}}$ tended to be shorter (−13%, P = NS). There was no significant change in $E_{\text{imax}}$ after treatment with propranolol (−6%, P = NS), but the time to $E_{\text{imax}}$ was delayed (+10%, P < 0.025). Global ischemia tended to decrease $E_{\text{imax}}$ (−53%, P = NS) which occurred earlier in the cardiac cycle (−33%, P < 0.01). There was no change in $L_0$, the segment length intercept of $E_{\text{imax}}$, with any intervention.

Globally, elastance defined by $E_{\text{dmax}}$ increased significantly with dobutamine (+37%, P < 0.01) and the time to $E_{\text{dmax}}$ occurred significantly earlier (−13%, P < 0.05). Propranolol resulted in a significant decrease in $E_{\text{dmax}}$ (−27%, P < 0.05) and occurred later (+12%, P < 0.01). With ischemia, there was no change in $E_{\text{dmax}}$, or its time to occurrence (−8%, P = NS). However, ischemia did result in a significant increase in $D_0$, the diameter intercept of $E_{\text{dmax}}$ (+24%, P < 0.025). No significant shifts in $D_0$ were observed with dobutamine or propranolol.

To compare how regional myocardial function defined by $E_{\text{imax}}$ related to global myocardial func-
tion defined by $E_{\text{edmax}}$, we correlated the two parameters. The percent change in $E_{\text{emax}}$ and $E_{\text{max}}$ for the several states (including subsequent controls) were related to initial control values before treatment in all seven animals. A linear regression of the percent change in $E_{\text{max}}$ with respect to the percent change in $E_{\text{edmax}}$ was defined by the equation: % change $E_{\text{max}}$ = (1.5 × % change $E_{\text{edmax}}$) -1.3%. The R value was +0.49 ($P < 0.025$). Though positively correlated, the relationship between regional and global elastance changes suggested an insensitivity of $E_{\text{edmax}}$ in perceiving global shifts.

Moreover, in individual animals, there was considerable variability in the regional and global responses to global interventions (e.g., dobutamine in Table 2). In fact, in some experiments, regional function was at variance with global function. One example is illustrated in Figure 5. During global ischemia, the preinjection left ventricular pressure-segment length curve, indicated by the solid line, is clockwise, suggesting that work is being done on the region in the direction of the segment length (Tyberg et al., 1974). The left ventricle was at the same time performing positive work, as is evidenced by the development of left ventricular pressure and the maintenance of forward cardiac output, and is suggested by the counterclockwise preinjection left ventricular pressure-diameter curve (not shown). This discordance of regional and global function during global ischemia was also evident in the time

**Table 1**

<table>
<thead>
<tr>
<th>Global Hemodynamics and Segment Length Data</th>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>HR</strong> (beats/min)</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Dobutamine (n = 7)</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Propranolol (n = 7)</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Propranolol</td>
</tr>
<tr>
<td>Propranolol</td>
</tr>
<tr>
<td>Global ischemia (n = 5)</td>
</tr>
</tbody>
</table>

**Abbreviations:** HR = heart rate; LVP = peak left ventricular pressure; LVEDP = left ventricular end-diastolic pressure; LVdP/dt_{max} = maximum first derivative of isovolumic left ventricular pressure development; ED = end-diastolic segment length; ES = end-systolic segment length at end-ejection.

**Figure 4.** Comparison of the volume method of loading (left panel) with the steady state partial aortic occlusion-loading technique (right panel) shown in one animal previously denervated pharmacologically. Beats prior to loading are again illustrated by solid lines, sequentially loaded beats by points and dashed lines (left panel), and steady state beats by points (right panel). In both panels, points were sampled at a common time after the R wave (0.240 sec). The slope of the major axis of the hysteresis loop in the left panel corresponds to the slope of the steady state data shown in the right panel.
to maximum elastance (t-E\textsubscript{\text{max}} and t-E\textsubscript{d\text{max}}) and in the dimension intercepts (L\textsubscript{0} and D\textsubscript{0}), as previously noted.

**Discussion**

The volume-loading technique as described here is similar to that used in contrast ventriculography and provides a simplified approach to varying loading conditions in the intact ventricle. The technique rapidly provides a number of variability volume-loaded beats, making it possible to define systolic left ventricular pressure-length and diameter relationships without the protracted intervals required by pharmacological afterload manipulation. The effect of the injection technique on the contractile state of the heart appears to be minimal. This is supported by the minimal change in the R-R interval during injections performed prior to any autonomic blockade (0.532 ± 0.014 vs. 0.538 ± 0.014). Also, the rapid return of the ventricular pressure-dimension relationships to their baseline suggests that the technique does not significantly interfere with the animal’s baseline hemodynamic state. Furthermore, the results from volume loading appear to correspond closely with those obtained by steady state pressure loading. This approach appears well suited for studies in the intact experimental animal, as has been shown here, and may have potential for clinical application in the cardiac catheterization laboratory.

Others have used volume loading or withdrawal techniques to study ventricular myocardial mechanics (Templeton et al., 1974; Schierack and Boom, 1978; Hunter et al., 1983). Their approaches, however, have been to use small volumes (0.5–3 ml).

**TABLE 2**

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Control Dobutamine</th>
<th>Control Dobutamine</th>
<th>Propranolol Ischemia</th>
<th>Control Dobutamine</th>
<th>Control Dobutamine</th>
<th>Propranolol Ischemia</th>
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<tr>
<td>0.140</td>
<td>171 116 112</td>
<td>17 21 21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.160</td>
<td>198 122 131</td>
<td>18 22 22</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0.180</td>
<td>233 150 179</td>
<td>19 23 22</td>
<td>0.140 60</td>
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<td>22 28 25</td>
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<tr>
<td>0.220</td>
<td>462 288 498</td>
<td>22 28 25</td>
<td>26 43 26</td>
<td>18 17</td>
<td></td>
<td></td>
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<tr>
<td>0.240</td>
<td>774 343 674</td>
<td>29 65 31</td>
<td>69.87 ± 2.24</td>
<td>66.0 ± 2.0</td>
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<tr>
<td>0.260</td>
<td>1042* 503* 1178*</td>
<td>35 101* 42</td>
<td>70.95 ± 1.12</td>
<td>19 20*</td>
<td></td>
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<tr>
<td>0.280</td>
<td>707 315 521</td>
<td>48 54 46* 23*</td>
<td>75.91 ± 1.95</td>
<td>19 20*</td>
<td></td>
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<tr>
<td>0.300</td>
<td>424 190 358</td>
<td>51* 47 31</td>
<td>76.60 ± 2.25</td>
<td>19 20*</td>
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<tr>
<td>0.320</td>
<td>310 136 100</td>
<td>25 23 19</td>
<td>80.16 ± 2.29</td>
<td>19 20*</td>
<td></td>
<td></td>
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<tr>
<td>0.340</td>
<td>122 100 132</td>
<td>13 9 12</td>
<td>89.29 ± 0.26</td>
<td>19 20*</td>
<td></td>
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<tr>
<td>0.360</td>
<td>58 81 67</td>
<td>8 11</td>
<td>9.26 ± 0.64</td>
<td>19 20*</td>
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* Maximum elastance.

**TABLE 3**

**Regional and Global Elastance Data**

<table>
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<th>Regional</th>
<th>Global</th>
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<tbody>
<tr>
<td>E\textsubscript{\text{max}} (mm Hg/ (sec))</td>
<td>E\textsubscript{\text{max}} (mm Hg/ (sec))</td>
</tr>
<tr>
<td>L\textsubscript{0} (mm)</td>
<td>L\textsubscript{0} (mm)</td>
</tr>
<tr>
<td>Angle\textsuperscript{o}</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>88.17 ± 0.55</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>312</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>89.29 ± 0.26</td>
</tr>
<tr>
<td>Propranolol</td>
<td>87.65 ± 0.56</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>243</td>
</tr>
<tr>
<td>Propranolol</td>
<td>87.50 ± 0.70</td>
</tr>
<tr>
<td>Ischemia</td>
<td>88.33 ± 0.09</td>
</tr>
<tr>
<td>(n = 5)</td>
<td>342</td>
</tr>
</tbody>
</table>

Abbreviations: E\textsubscript{\text{max}} = maximum regional elastance; t-E\textsubscript{\text{max}} = time from the R wave to E\textsubscript{\text{max}} in seconds; L\textsubscript{0} = segment length intercept of the E\textsubscript{\text{max}} slope line; E\textsubscript{\text{dmax}} = maximum diameter elastance; t-E\textsubscript{\text{dmax}} = time from the R wave to E\textsubscript{\text{dmax}} in seconds; D\textsubscript{0} = diameter intercept of the E\textsubscript{\text{dmax}} slope line.

* Slope angle in degrees from the respective x-axis. See text and Figure 2.
The nonlinear nature of the pressure-dimension relation ally with ischemia. It was because of the clearly direction and degree of the hysteresis depended on the state of the myocardium, as was shown regionally with ischemia where there was a rightward shift in \( D_0 \) but no change in \( E_{d_{\text{max}}} \). This was particularly evident with ischemia where the work was being done on the region. Ei, max occurred at 0.160 second, in this case. Hysteresis was clockwise prior to Ei\(_{\text{max}}\) and counterclockwise after Ei\(_{\text{max}}\). During systolic bulging, the hysteresis loops became large and almost circular.

The preinjection pressure-length curve (solid line) is clockwise, suggesting that work is being done on the region. Ei\(_{\text{max}}\) occurred at 0.160 second, in this case. Hysteresis was clockwise prior to Ei\(_{\text{max}}\) and counterclockwise after Ei\(_{\text{max}}\). During systolic bulging, the hysteresis loops became large and almost circular.

The relationship of regional and global myocardial contractility as indexed by the elastance parameters Ei\(_{\text{max}}\) and Ei\(_{\text{d_{\text{max}}}}\) was evaluated in the second part of the study. Global interventions were chosen to determine whether changes in regional function followed global inotropic changes. The global parameter, Ei\(_{\text{d_{\text{max}}}}\), proved to be an acceptable measurement of the global inotropic state, in that it appropriately followed the known global inotropic interventions resulting from dobutamine and propranolol. It was a quantitatively better marker for sensing positive inotropic shifts than negative ones, but did not appear to be as sensitive as left ventricular \( dP/dt_{\text{max}} \). This was particularly evident with ischemia where there was a rightward shift in \( D_0 \) but no change in Ei\(_{\text{d_{\text{max}}}}\). Thus, our data differ from those obtained in
isolated dog hearts where global ischemia resulted in a decrease in the slope of the end-systolic pressure-volume relationships with no change in $V_o$ (Sunagawa et al., 1982). It is of interest that in the same isolated preparation, Sunagawa et al. (1983) obtained results similar to our own with regional ischemia effected by coronary ligations. This may reflect a difference in animal preparations (intact pig vs. isolated dog), techniques of affecting ischemia, or that our ischemia resulted in more "regional" than "global" effects.

The use of the left ventricular pressure-internal diameter relationship as an index of left ventricular function has been previously developed. The diameter at end-ejection was shown to be linearly related to systolic pressure in the intact conscious dog (Mahler et al., 1975). In that study, treatments with isoproterenol caused a leftward shift in the diameter intercept but no change in the slope of the line. In another report, Sagawa et al. (1977) showed in a small series of four conscious intact dogs a change in intercept and a change in slope with calcium infusions. Clinically, a number of investigators have shown that the slope of the end-ejection left ventricular pressure-internal diameter relationship is linear and sensitive to changes in the inotropic state (Marsh et al., 1979, Reichek et al., 1981, Borow et al., 1982a, 1982b). In none of these studies, however, were time-varying systolic left ventricular pressure-diameter relationships obtained to determine $E_{imax}$ as originally defined (Suga and Sagawa, 1974). This study shows that such an analysis is possible in the intact heart by means of the volume-loading technique.

Shifts in the regional elastance parameter, $E_{imax}$, were not as evident as with $E_{imax}$. In fact, only changes reflecting an enhanced inotropic state were sensed. Theoretically, one might have expected the regional index to follow global function closely. This is particularly true, since the left ventricular pressure (force)-mid-myocardial circumferential length relationship has previously been shown to be a valid index of myocardial contractility in the isolated dog heart preparation (Weber et al., 1976). However, in that study, circumferential length was a derived rather than measured value, and was calculated from left ventricular volumes.

It is unclear from these data why the changes in mid-myocardial shortening do not more closely follow global changes in dimension. The present data showed that the region has a much higher elastance than the ventricle. This is at least in part because of the smaller absolute differences in length being measured, and this may make it difficult to effect demonstrable changes in regional elastance. That this was not an artifact of the acute volume-loading technique was evidenced by its presence also with steady state pressure loading. Also, others have found similar values for regional elastance in intact dog hearts (Piene and Covell, 1981). A more likely explanation for the different responses in regional and global elastance parameters probably relates again to the complexity of the intact ventricle and includes its geometry, anisotropy, inhomogeneity, regional differences in electrical and mechanical onset of contraction and relaxation, and no doubt other factors yet to be defined. It will be of interest to explore further the complex interactions between regional and global elastance in the intact heart in future studies.

We gratefully acknowledge the assistance of Mary Ann Wood in the performance of these studies, and the secretarial assistance of Susan Landucci, Teri Light, and Sandy Yost in the preparation of this manuscript.

Supported in part by a Fellowship from the American Heart Association, South Central Pennsylvania Chapter (Dr. Miller), by U.S. Public Health Service Grant HH-21209-05 (Dr. Liedtke), and the Rennebohm Foundation of Wisconsin.

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Received April 18, 1983; accepted for publication June 14, 1984.

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INDEX TERMS: Regional myocardial function • Maximal elastance • End-systolic pressure-length relationships • Myocardial mechanics
Regional end-systolic pressure-length relationships using a volume-loading technique in the intact pig heart.
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doi: 10.1161/01.RES.55.3.326

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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