The relative role of subendocardium and subepicardium in left ventricular mechanics

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Although numerous studies have focused on the characterization of global performance of the left ventricle (26) and on regional changes that may occur within the myocardium between the epicardial and deep crystals, a small tract was created with an 18 gauge needle. The epicardial crystals were sutured in direct alignment above the subendocardial and midwall crystals. Both pairs of ultrasonic crystals were placed within 1 cm of each other. Autopsy showed that the subendocardial crystal was not lodged in the anterior papillary muscle in any of the dogs.

Method

Ventricular wall thickening and segment-length changes. Wall thickening and changes of segment length in both the deep and superficial layers of the wall of the left ventricle were measured in seven mongrel dogs. The dogs weighed 15–24 kg and were anesthetized with 30 mg/kg iv pentobarbital sodium. In all dogs, a left thoracotomy was performed and the pericardium was opened.

Left ventricular wall thickness was measured with ultrasonic-dimension gauges (Schenk, Cardiff by the Sea, CA) placed at two depths within the free wall of the left ventricle. One pair of ultrasonic crystals was placed across the entire free wall of the left ventricle. One crystal was sutured to the surface of the epicardium, and the other was inserted as near as possible to the endocardium without perforating the left ventricular cavity. Another pair of crystals measured the thickness of the external portion of the free wall, which was approximately one-half of the thickness of the wall. This was accomplished by suturing one crystal to the epicardial surface and by inserting the other crystal approximately midway into the wall. The epicardial crystals were 1.5 mm thick and 4 mm diam. and the subendocardial and midwall crystals were 1 mm thick and 2 mm diam. In each case, the location of the crystals was confirmed at autopsy. The crystals at the midwall and in the subendocardium were introduced at an angle of 45° relative to the epicardial surface to avoid injury of the myocardium between the epicardial and deep crystals (Fig. 1). In implanting the midwall and subendocardial crystals, a small tract was created with an 18-gauge needle. The epicardial crystals were sutured in direct alignment above the subendocardial and midwall crystals. Both pairs of ultrasonic crystals were placed within 1 cm of each other. Autopsy showed that the subendocardial crystal was not lodged in the anterior papillary muscle in any of the dogs.

Changes of the length of the subendocardial and subepicardial segments of the free wall of the left ventricle were measured simultaneously with the wall thick-
ness. Two pairs of ultrasonic crystals were used. The crystals that were used for the measurement of changes of the subendocardial segment length were placed approximately 10 mm deep within the free wall of the ventricle. They were separated by a distance of 1.3–1.6 cm. The crystals used for the measurement of changes of the subepicardial segment length were inserted approximately 3–4 mm into the ventricular wall and were also separated by a distance of 1.3–1.6 mm. The subendocardial crystals were placed perpendicular to the long axis of the ventricle and, therefore, parallel to the direction of the circumferential hoop fibers (13, 21) (Fig. 1). The subepicardial crystals were oriented in the direction of the epicardial fibers, which, according to Streeter et al. (21) and LeWinter et al. (13), run obliquely across the surface of the ventricle at an angle of approximately 20° to the long axis (Fig. 1). All of the crystals used for the measurement of changes of segment length were 1 mm thick and 2 mm diam.

Aortic and left ventricular pressure were measured with catheter-tip micromanometers (Millar Instruments, Houston, TX). Simultaneous recordings of pressure, wall thickness, and changes of segment length and lead two of the electrocardiogram were made on a VR-12 photographic recorder (Electronics for Medicine, White Plains, NY) at paper speeds of 250 mm/s as well as at slower speeds.

Measurements of wall thickness and segment length were made at the moment of left ventricular end-diastolic pressure and at the moment of the incisura of central aortic pressure. Changes of subendocardial wall thickness were calculated as the difference between the total wall thickness and the thickness of the epicardial portion of the wall. The maximal rate of change of wall thickness during systole and diastole were calculated as the tangent of the steepest portion of the analog signal. The rate of shortening and rate of lengthening of the subepicardial and subendocardial segments were measured in the same way. This method was shown to be accurate to within 5% of values calculated by means of an electronic digitizer on-line with a computer.

Measurements of left ventricular internal and external diameters. The left ventricular internal and external diameters, approximately at the minor axis of the left ventricle, were measured simultaneously with ultrasonic-dimension gauges in five additional dogs.

The method for insertion of the endocardial ultrasonic gauges was similar to that described by Horwitz et al. (11). Two no. 00 control stitches were placed just below and perpendicular to the first diagonal branch of the left anterior descending coronary artery. The wires of one of the ultrasonic gauges was threaded through a 4-mm 13-gauge stainless steel needle from which the hub had been removed. A stab incision was made through the anterior wall. The tube was then removed. A gentle pull on the wires positioned the ultrasonic crystal against the endocardial surface of the posterior wall (Fig. 1). The control stitches, previously inserted, were then pulled toward each other to prevent bleeding. The wires of the second crystal were passed through the lumen of a 4-cm-long rigid plastic tube with an internal diameter of 1.5 mm. The plastic tube was used to push the crystal through the incision in the anterior wall. The tube was then removed. A gentle pull on the wires positioned the ultrasonic crystal against the anterior endocardial surface of the left ventricle (Fig. 1). The crystals were anchored in position by purse-string sutures. We did not find it necessary to occlude the inferior or superior vena cava during the procedure as had been done by others to reduce bleeding during the procedure (11). The crystals that were used for the measurement of the internal diameter were hemispheric with a diameter of 5 mm and a maximal thickness of 1.5 mm. Both crystals were placed on the endocardial surface with the convex surfaces of the crystals pointing toward each other (Fig. 1). The location of the crystals on the endocardial surface was confirmed at autopsy.

The external diameter of the left ventricle (from the anterior epicardial surface to the posterior epicardial surface) was measured with a pair of ultrasonic crystals simultaneously with measurements of the internal ventricular diameter. A pair of ultrasonic crystals was secured to the epicardial surfaces of the left ventricle in proximity to the wires of the endocardial crystals. The diameter of the crystals used for measuring the external
diameter was 4 mm. The crystals were mounted on a cloth and were sutured with their convex surfaces facing each other (Fig. 1).

Aortic, left ventricular, and left atrial pressures were measured simultaneously with the internal and external diameters using catheter-tip micromanometers. The micromanometer used to measure left atrial pressure was introduced directly into the left atrium through an incision in the left atrial appendage. Bleeding was controlled by tying the tip of the left atrial appendage around the catheter. Atrial fibrillation was not induced in any of the dogs. The hematocrits in these dogs, after complete instrumentation, ranged from 35 to 46 ml/100 ml.

The anesthetic agent used in the five dogs in which the left ventricular internal and external diameters were measured differed from the anesthetic agent used in the series of dogs in which wall thickness and segment length changes were measured. In the dogs in which diameters were measured, we used 1.2 mm/kg droperidol and 0.24 mg/kg fentanyl (0.6 ml/kg Innovar-Vet). These dogs weighed 20-28 kg. The depth of anesthesia was maintained throughout the procedure with a continuous intravenous infusion of 0.7 mg/min droperidol, 0.01 mg/min fentanyl, and 0.17 mg/min pentobarbitol.

Cineroentgenographic measurements of endocardial and epicardial dimensions. Epicardial and endocardial dimensions during systole and diastole were measured by cineroentgenography in five mongrel dogs. The dogs weighed 14-28 kg and were anesthetized with 30 mg/kg iv pentobarbital sodium. Eight to 10 radiopaque markers were sewn on the epicardial surface of the left ventricle approximately 1.5 cm apart from each other. The markers were sewn along the epicardial border of the plane described by the major and minor axes of the heart as visualized anteriorly from the external surface (Fig. 1). After the radiopaque markers were sewn in place, the pericardium was closed loosely. Then the chest was closed, and the dog was positioned on its left side. Under fluoroscopy, the dog was rotated until the radiopaque markers appeared to define the outer border of the free wall of the left ventricle.

A pig-tail catheter was introduced through the carotid artery and passed retrograde across the aortic valve into the left ventricle. Ventriculograms were recorded on 35-mm cine at 60 frames/s during the injection of 20 ml sodium and meglumine diatrizoates (Renografin, 76%). Magnification was determined by utilization of a two-dimensional scale placed at the level of the heart. Only the first four beats of each injection were analyzed to avoid possible alterations of contractility due to contrast material passing through the coronary circulation. Care was taken to exclude from the analysis any premature ventricular contractions and postextrasystolic beats. The areas of the projected image of the cavity and the external area of the left ventricle, as outlined by the radiopaque markers, were calculated by integration with the aid of an electronic digitizer on-line with a computer.

The volume of the left ventricular cavity and the external volume of the left ventricle were calculated by the single-plane area-length method (9). Throughout the entire study, statistical analyses were based on the paired t test.

RESULTS

Changes of ventricular wall thickness. Wall thickness increased from 8.9 ± 0.4 (SE) mm at end diastole to 10.6 ± 0.4 mm at end systole. The subepicardial portion of the ventricular wall increased only from 5.6 ± 0.3 mm at end diastole to 5.9 ± 0.3 mm at end systole (Fig. 2). The subendocardial portion of the ventricular wall represented the difference between total wall thickness and the thickness of the subepicardial portion. The subendocardial portion of the left ventricular wall increased from 3.3 ± 0.4 mm at end diastole to 4.7 ± 0.4 mm at end
VENTRICULAR MECHANICS

ments of the subendocardium shortened from 9.2 ± 0.5 mm at end diastole to 7.6 ± 0.5 mm at end systole. Segments of the subepicardium shortened from 8.5 ± 0.5 mm at end diastole to 7.6 ± 0.5 mm at end systole (Fig. 2). Therefore, the subendocardial segment showed 18 ± 2% shortening, whereas the subepicardial segment showed 10 ± 1% shortening (P < 0.01) (Fig. 3).

The maximal rate of systolic shortening of the total ventricular wall, 13 ± 2 mm/s, was higher than the maximal rate of systolic thickening of the epicardial portion 3 ± 0.6 mm/s (P < 0.01) (Fig. 4). Similarly, the maximal rate of thinning of the total wall during diastole, 25 ± 2 mm/s, was significantly greater than that of the epicardial portion, 5 ± 1 mm/s (P < 0.001) (Fig. 5). These observations suggest that the maximal rate of systolic thickening and of diastolic thinning of the subendocardial portion of the ventricular wall exceeded that of the subepicardial portion.

Changes of left ventricular segment length. The segments of the subendocardium shortened from 9.2 ± 0.5 mm at end diastole to 7.6 ± 0.5 mm at end systole. Segments of the subepicardium shortened from 8.5 ± 0.5 mm at end diastole to 7.6 ± 0.5 mm at end systole (Fig. 2). Therefore, the subendocardial segment showed 18 ± 2% shortening, whereas the subepicardial segment showed 10 ± 1% shortening (P < 0.01) (Fig. 3).

The maximal rate of systolic shortening of the segment of the subendocardium, 16 ± 3 mm/s, was significantly higher than that of the subepicardial segment, 8 ± 1 mm/s (P < 0.02) (Fig. 4). The maximal rate of systolic thickening of the segment of the subendocardium, 21 ± 3 mm/s, also exceeded that of the subepicardial segment, 11 ± 1 mm/s (P < 0.01) (Fig. 5).

Changes of the internal and external diameter of left ventricle. The internal dimensions, approximating the

![Diagram](http://ajpheart.physiology.org/)

**FIG. 3.** Left: contribution of subendocardium (Endo) and subepicardium (Epi) to total change of wall thickness. Center: change of segment length in subendocardium (Endo) and subepicardium (Epi). In each dog, changes of length of subendocardial segment exceeded changes of subepicardial segment. Right: changes of left ventricular internal (Int) and external (Ext) diameter.

![Diagram](http://ajpheart.physiology.org/)

**FIG. 4.** Left: maximal rate of wall thickening during systole measured across entire left ventricular wall (Total) and across outer half of wall (Epi). Center: maximal rate of shortening of segments of subendocardium (Endo) and subepicardium (Epi) during systole. In each dog, maximal rate of shortening in subendocardium exceeded rate of shortening in subepicardium. Right: maximal rate of systolic reduction of left ventricular internal (Int) and external (Ext) diameter.
minor axis, decreased from 37 ± 3 mm at end diastole to 30 ± 3 mm at end systole. The external dimensions, approximating the external minor axis, decreased from 55 ± 1 mm at end diastole to 51 ± 1 mm at end systole (Fig. 6). Therefore, the percent reduction of the internal dimension, 22 ± 1%, exceeded the percent reduction of the external dimension 6 ± 1% ($P < 0.001$) (Fig. 3). The maximal rate of reduction of the internal dimension during systole was 86 ± 7 mm/s. This was higher than the maximal rate of reduction of the external dimension, which was 45 ± 6 mm/s ($P < 0.02$) (Fig. 4). The maximal rate of increase of the internal dimension during diastole was 96 ± 8 mm/s. This was greater than the maximal rate of increase of the external diameter during diastole, which was 57 ± 5 mm/s ($P < 0.01$) (Fig. 5).

Cinerentgenographic measurement of changes of left ventricular dimensions. During systole, the internal minor axis of the left ventricle decreased from 4.7 ± 0.5 to 3.5 ± 0.4 cm, whereas the external minor axis decreased only from 6.6 ± 0.3 to 6.3 ± 0.3 cm. The percent reduction of the internal minor axis, 26%, was higher than the percent reduction of the external minor axis, 5%.

During systole, the projected area of the ventricular cavity diminished from 23 ± 2 to 15 ± 2 cm$^2$. The projected area of the external surface of the ventricle during systole diminished from 38 ± 3 to 33 ± 3 cm$^2$ (Fig. 7). Consequently, the internal area decreased 34 ± 5% during systole, whereas the external projected area decreased 13 ± 2%. With the assumption of a prolate ellipsoid and application of the area-length method, the internal volume of the left ventricle during systole diminished from 65 ± 2 to 37 ± 9 ml, which represented a 45% reduction of internal volume. The external volume of the left ventricle, on the other hand, decreased during systole from 168 ± 18 to 144 ± 20 ml, which represented a 14% reduction of the external volume during systole. Assessment of the volume of the left ventricular wall from these measurements indicates that it remained essentially constant during systole.

DISCUSSION

A prominent difference of the magnitude and velocity of thickening of the wall and shortening of the myocardial segments was shown between the superficial and deep layers of the canine left ventricular wall during systole. The subendocardial layers underwent greater changes than the subepicardial layers. It appears that the left ventricle expels its contents during systole by a reduction of the endocardial dimensions, while at the same time the epicardial dimensions change only a small amount. The observed difference between the internal and external dimensions during ejection appear to be the consequence of greater wall thickening and segment shortening in the subendocardium. Since the subendocardium accounted for approximately 83% of the total change of wall thickness during ejection, it is apparent that the subendocardium contributes prominently to wall thickening during systole and, therefore, contributes significantly to the overall pump function of the left ventricle.

The greater dimensional changes observed in the subendocardium during systole appear to be consistent with predictions based on geometric constraints. Because the myocardium is essentially incompressible, changes of the internal radius of the left ventricle can be predicted based on observed changes of the external radius. The volume
of the myocardium \( V_m \), assuming the configuration of a thick wall spherical shell, can be calculated during diastole as

\[
V_m = \frac{4}{3}\pi (R_1^3 - r_1^3)
\]

where \( r_1 \) is the initial (diastolic) internal radius and \( R_1 \) is the initial (diastolic) external radius. If a force is applied externally to such a thick wall shell, causing the external dimensions to diminish, the volume of the wall of the shell (myocardium) being incompressible would remain unchanged. It can be calculated as

\[
V_m = \frac{4}{3}\pi (R_2^3 - r_2^3)
\]

where \( R_2 \) is the external radius of the shell after the application of an external force and \( r_2 \) is the internal radius of the shell after the application of an external force. Therefore

\[
r_2^3 = r_1^3 - R_1^3 + R_2^3
\]

When numerical values of \( r_1, R_1, \) and \( R_2 \) are substituted into the above equation, the calculated value of \( r_2 \) is comparable with the measured value of the internal radius of the left ventricle at end systole. The predicted value of the internal diameter of the left ventricle at the end of ejection was 25 ± 7 mm, which was comparable to the measured value of 30 ± 3 mm. Calculations based on the geometric constraints also indicate that the percent change of the internal diameter would exceed the percent change of the external diameter. This prediction is also compatible with experimental observations made in this study.

Our observations of the differences of dimensional changes between the subendocardium and the subepicardium can be interpreted to reflect the imposed geometric constraints. This interpretation appears consistent with results obtained from mathematic modeling of ventricular contraction (2). When the ventricular wall was simulated with a series of concentric cylinders (assuming anisotropy of the myocardial material and taking into consideration myocardial fiber orientation), it was shown that active fiber shortening was nearly the same in all layers of the myocardial wall despite a greater circumferential shortening within the subendocardium than in the subepicardium (2). This seemingly paradoxical behavior
was explained on the basis of torsion resulting from apical twisting during systole (2). The latter was suggested to cause equalization of the amount of sarcomere shortening in the subendocardial and subepicardial layers made possible by the presence of an appropriate transmural course of fiber orientation (2).

Although our observations are predictable on the basis of geometric constraints, the possibility of the existence of different levels of performance across the left ventricular wall cannot be discounted without further experimental evidence. It is possible that the subendocardium actively thickens and shortens with a greater magnitude and at a higher rate than in the subepicardium, perhaps to comply with imposed geometric constraints.

The assessment of global ventricular dimensions in systole and diastole largely has been limited to measurements of left ventricular internal dimensions (3, 4, 11, 24). Ventricular dimensions were measured at the epicardial surface in only a few studies (8, 10, 16, 18). Our measurements of changes of the internal ventricular diameter and changes of the external diameter were within the range reported by others (11, 15, 18). Our observations of a greater reduction of the endocardial thickness and volume than the epicardial dimensions during systole are also consistent with previous observations (17). It was shown that metal markers on the subendocardial surface of the left ventricle were displaced greater distances during systole than were markers on the epicardial surface (17).

Measurements of left ventricular wall thickening have been limited to measurements across the entire wall (6, 7, 19, 22). The changes of total wall thickening that we observed were comparable to the measurements made by these investigators. The percent change of segment length that we measured was also within the range described by others in the subepicardium (13) and the subendocardium (14) of the normal canine left ventricle. Differences of segmental shortening between the subepicardium and midwall have been observed at the apex, midportion of the free wall, and base of the canine left ventricle (13).

In conclusion, our observations indicate that a non-uniformity of thickening and shortening exists across the left ventricular wall during systole. Greater changes occur within subendocardium.

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