Comparison of the Distribution of Intramyocardial Pressure across the Canine Left Ventricular Wall in the Beating Heart during Diastole and in the Arrested Heart

Evidence of Epicardial Muscle Tone during Diastole

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SUMMARY

Computations of compliance of the left ventricle (LV) during diastole assume passive tissue characteristics. To evaluate this assumption, we measured diastolic LV intramyocardial pressure simultaneously in the subepicardium and subendocardium in 18 open-chest dogs, using 1-mm in diameter micromanometers. Subepicardial pressure, 26 ± 1 mm Hg (mean ± SEM) exceeded subendocardial pressure, 14 ± 1 mm Hg (P < 0.001), and it exceeded left ventricular end-diastolic pressure (LVEDP) (9 ± 1 mm Hg) (P < 0.001). After an infusion of dextran-40 (10 dogs), subepicardial diastolic pressure increased to 42 ± 4 mm Hg which was higher than diastolic subendocardial pressure, 26 ± 2 mm Hg (P < 0.001) and LVEDP, 24 ± 2 mm Hg (P < 0.001). Following cardiac arrest (12 dogs) with the intramyocardial probes unchanged in position, LV intracavitary pressure, 9 ± 1 mm Hg, and subendocardial pressure, 13 ± 3 mm Hg, did not differ significantly from the pressures in the beating heart. Subepicardial pressure, 9 ± 1 mm Hg, was lower than in the beating heart (P < 0.001). Following distension of the arrested LV (12 dogs), subepicardial pressure, 31 ± 7 mm Hg, was lower than both subendocardial pressure, 58 ± 12 mm Hg (P < 0.001) and LV intracavitary pressure, 54 ± 11 mm Hg (P < 0.001). These observations indicate that tone is maintained by the subepicardium during diastole. Furthermore, the LV wall does not appear to behave as a passive shell during ventricular filling.


TRADITIONAL concepts of ventricular activity indicate that the ventricle rests during diastole and contracts during systole. The characterization of ventricular compliance is based upon the assumption that passive distension of the ventricle results from distending pressures which accompany ventricular filling (Diamond et al., 1971; Mirsky, 1969; Mirsky and Parmley, 1973; Mirsky and Rankin, 1979). If one assumes that passive distension of the ventricle occurs during filling, then one can calculate the distribution of stresses in the left ventricular wall (Gould et al., 1972; Mirsky, 1969; Panda and Natarajan, 1977). Such mathematical models have predicted that the highest stresses would occur in the subendocardial layer and the lowest in the subepicardial layer.

The availability of ultraminiature pressure transducers, with the capability of measuring localized intramyocardial pressure with minimal distortion at the site of measurement, now make it possible to measure this form of stress in the subepicardium and subendocardium (Armour and Randall, 1971; Stein et al., 1980). The purpose of this study was to measure the distribution of intramyocardial pressure to evaluate whether the distribution in the beating heart during diastole corresponds to the distribution of intramyocardial pressure stresses in the arrested heart. Such measurements permit an evaluation of the assumption, implicit in all calculations of ventricular compliance, that the ventricle distends as a passive elastic shell during diastole.

Methods

Intramyocardial pressure was measured simultaneously at two levels in the free wall of the left ventricle in 18 open-chest anesthetized dogs with the use of two MIKRO-TIP catheter pressure transducers with a hypodermic needle tip custom built by Millar Instruments, Inc., modified for this purpose. The dogs weighed 14-16 kg and were anesthetized with sodium pentobarbital, 30 mg/kg, iv, and ventilated with room air by means of a respirator attached to an endotracheal tube. The partial pressure of oxygen in arterial blood was measured with an Instrumentations Laboratory, Inc. blood gas analyzer in eight of 18 dogs and was 91 ± 4 mm Hg (mean ± SEM). A left thoracotomy was performed.
and the pericardium was opened in all dogs. The duration of surgery prior to measurements was 30-40 minutes. In 10 dogs, pressures were measured during control conditions and following an augmented preload induced by the rapid injection of 300-500 ml of dextran-40 in isotonic saline (Rheomacrodex, Pharmacia Laboratory), and in 12 dogs, intramyocardial pressure was measured following cardiac arrest.

Intramyocardial pressure was measured with an ultraminiature strain gauge transducer mounted on a stainless steel hypodermic needle 1.6 mm in diameter. The sensor was placed 5 mm from the tip of the needle. The dimensions of the sensing portion of the probe were 1 \times 1.6 \times 2 \text{ mm} (Fig. 1). The volume occupied by the sensing portion of the probe was 3.2 \text{ mm}^3. The strain gauge sensing element and its support were smaller than the diameter of the needle and were recessed in it (Fig. 1). The needle probe was inserted directly into the wall of the left ventricle and positioned at various depths in the free wall. The depth of the transducer was estimated from markings on the shaft of the transducer, and the depth of insertion was confirmed at autopsy in each dog (Fig. 1). The pressure was not affected by the orientation of the pressure probe along its longitudinal axis. The pressure also appeared to be independent of the angle of insertion of the needle probe in the range that we used (30-90° to the epicardial surface). Although we established that measurements were independent of the orientation of the transducer, it was important to maintain the position of the transducer unchanged once it had been inserted into the myocardium. The transducer remained firmly implanted in the beating ventricle throughout the study, which was usually about 1 hour. We did not observe spontaneous extrusion of the tip. Autopsy showed no hematomas or hemorrhage at the site of the sensor. The hematocrit was measured in nine dogs before the chests were opened and again following control measurements of intramyocardial pressure. Before thoracotomy Hct = 38 ± 2 ml/100 ml and after control measurements, 37 ± 1 ml/100 ml (mean ± SEM) (not significant).

Tests of the thermal stability of the micromanometers in our laboratory showed that the output did not vary by more than 3 mm Hg over a range of 26°-39°C. Overpressures of more than 4000 mm Hg did not damage the sensor, and its low mass made it insensitive to acceleration forces. The pressure sensor is a linear device with a normal output accuracy within 0.5% of any selected pressure range from −300 to +400 mm Hg. The frequency response of the sensor was flat within ±2% to 5 kHz and within ±5% to 10 kHz. The phase lag of this type of sensor was 90° at 35 kHz, which is equivalent to a time delay of approximately 7 μsec. The sensor had a baseline drift of less than 1 mm Hg in 1 hour.

A bench calibration was performed by attaching the tip of the micromanometer, by means of a saline-filled Y-connection, to a column of mercury (from a sphygmomanometer). With the air bulb, pressure in the micromanometer was increased the same amount as the pressure in the column of mercury. Calibration was made at increments of
pressure from 0 to 200 mm Hg, and the transducer was shown to be linear.

A bench calibration in a section of myocardium was accomplished as follows. A clear acrylic cylinder was constructed with a port at the bottom through which the intramyocardial pressure transducer was introduced (Fig. 2). A fresh section of the left ventricular wall of a dog was inserted through the top of the cylinder into which the transducer was inserted. Insertion of the transducer within the tissue before the addition of mercury caused a 1-3 mm Hg increase in pressure above air pressure. Incremental amounts of mercury were then added and the electrical output of the transducer in muscle was calibrated by the level of mercury above the level of the transducer (Fig. 2). The calibration was repeated on four occasions. Rotation of the transducer 180° had no effect upon the calibration. Also, insertion of the transducer vertically (from the top of the cylinder) had no effect.

In each dog, intramyocardial pressure was measured simultaneously in the subendocardium, and the subepicardium of the anterior region of the free wall of the left ventricle. The location of the sensor in the subendocardium was approximately 10 mm within the wall, and in the subepicardium it was approximately 4 mm within the wall. The thickness of the myocardium in the region of the insertion of the transducers was found at autopsy to range between 12 and 15 mm. In all instances, subendocardial and subepicardial pressures were measured in the same segment of the free wall. Care was taken to keep the position of the intramyocardial pressure probes unchanged throughout all studies in the beating and arrested heart. Subendocardial and subepicardial pressures during diastole were reported at end-diastole, as judged from the left ventricular pressure.

Aortic and left ventricular pressure were measured simultaneously with catheter-tip micromanometers (Millar Instruments, Inc.). The pressure transducers in the aorta and left ventricle had characteristics identical to those of the intramyocardial transducer. All transducers were equisensitive.

At the conclusion of measurements of intramyocardial pressure in 12 dogs (in 10 of which we studied the effects of an augmented preload), arrest of the ventricle in diastole was produced by a bolus injection of 20-30 mEq of potassium chloride. The aorta was tied around the left ventricular catheter, and the pulmonary veins also were ligated. Fluid was added or withdrawn using a rotary pump (Sarnes, model 6050) attached to a 14-gauge needle introduced into the left ventricle through the apex. Intramyocardial pressure and left ventricular pressure were measured in the arrested heart at levels of left ventricular intracavitary pressure that ranged from 0 to 130 mm Hg. Measurements in the arrested heart were made when all evidence of electrical activity on the electrocardiogram ceased. All statistical analyses, both in the beating and the arrested heart, were made on the basis of a paired t-test.

To determine the effects of a negative intracavitary pressure on diastolic intramyocardial pressure, a #22 Foley catheter was introduced directly into the left atrium of three dogs and the balloon was positioned under fluoroscopy in the region of the mitral valve. The balloon was distended with 40 ml of saline which significantly obstructed inflow to the left ventricle. Following inflow obstruction, left ventricular end-diastolic pressure decreased to an average of —2 mm Hg (range, —1 to —3 mm Hg).

To determine whether the mechanical effects of coronary perfusion are sufficient to affect intramyocardial pressure through stiffening and passive engorgement of the ventricular wall, producing increased turgor comparable to an erectile effect (Salisbury et al., 1960), we studied the immediate effects of coronary occlusion in three dogs. The left anterior descending coronary artery was dissected free from the coronary vein and surrounding tissue above the level of insertion of the intramyocardial transducers. The left anterior descending coronary artery was ligated and the effects of coronary occlusions were noted following 10 beats and again following 30 seconds of occlusion. We did not measure the effects of coronary occlusion on intramyocardial pressure for longer durations following occlusion, because any changes at later times are likely to reflect ischemia, and not the absence of mechanical distention due to engorgement of the ventricular wall by coronary flow.

Results

During control conditions (18 dogs), pressure in the subendocardium, 14 ± 1 mm Hg (mean ± SEM),
was higher than left ventricular end-diastolic pressure, 9 ± 1 mm Hg (P < 0.001) (Table 1). Subepicardial pressure, 26 ± 1 mm Hg, exceeded both left ventricular end-diastolic (P < 0.001) and subendocardial (P < 0.001) pressure (Fig. 3).

Following an infusion of dextran-40 (10 dogs) left ventricular end-diastolic pressure increased from 10 ± 1 to 24 ± 2 mm Hg (P < 0.001). Aortic pressure during the control period was 136/116 ± 7/6 mm Hg. After the administration of dextran-40, aortic pressure was 162/129 ± 10/6 mm Hg (systolic, P < 0.05; diastolic, not significant). Diastolic subendocardial pressure increased from 14 ± 1 to 26 ± 2 mm Hg (P < 0.001) (Fig. 4). The difference during increased preload between subendocardial pressure and left ventricular end-diastolic pressure was not significant. With increased preload, subepicardial diastolic pressure increased from 26 ± 2 to 42 ± 4 mm Hg (P < 0.01). During preload, subepicardial diastolic pressure exceeded left ventricular end-diastolic pressure (P < 0.001) and it also exceeded subendocardial diastolic pressure (P < 0.001).

When left ventricular diastolic pressure was caused to fall below zero by obstruction of inflow through the mitral valve (three dogs) subendocardial and subepicardial diastolic pressure remained positive. Left ventricular end-diastolic pressure decreased from 7 ± 1 to −2 ± 0.5 mm Hg. Subendocardial diastolic pressure decreased from 9 ± 4 to 6 ± 4 mm Hg, and subepicardial diastolic pressure decreased from 24 ± 3 to 13 ± 4 mm Hg.

After cardiac arrest (12 dogs), with the intramyocardial probes unchanged in position, left ventricular intracavitary pressure, 9 ± 1 mm Hg, did not differ significantly from pressures in the beating heart (14 ± 2 mm Hg). Subepicardial dia-

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### Table 1 Diastolic Intramyocardial and Ventricular Pressures in the Beating Heart

<table>
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<tr>
<th>Dog no.</th>
<th>Left ventricular end-diastolic pressure (mm Hg)</th>
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<th>Subepicardial pressure (mm Hg)</th>
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Key: C = control; PL = preload.

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**Figure 3** Subepicardial (EPI), subendocardial (ENDO), left ventricular (LV), and aortic (AO) pressure during control measurements in dog 8. During diastole, subepicardial pressure exceeded subendocardial and left ventricular pressure.
Circulatory response, 9 ± 1 mm Hg, was lower than in the beating heart, 26 ± 2 mm Hg (P < 0.001). In the arrested heart, subendocardial pressure, 13 ± 1 mm Hg, exceeded subepicardial pressure, 9 ± 1 mm Hg (P < 0.01).

Following distension of the arrested left ventricle (12 dogs), left ventricular intracavitary pressure increased from 9 ± 1 to 54 ± 11 mm Hg (P < 0.001) (Fig. 5) (Table 2). Subendocardial pressure increased from 13 ± 1 to 58 ± 12 mm Hg (P < 0.001). Subepicardial pressure increased from 9 ± 1 to 31 ± 7 mm Hg (P < 0.001). In the distended arrested heart, subendocardial pressure did not differ significantly from left ventricular intracavitary pressure. Subepicardial pressure in the distended heart (31 ± 7 mm Hg) was significantly lower than subendocardial pressure (58 ± 12 mm Hg) (P < 0.001), and it also was lower than left ventricular intracavitary pressure, 54 ± 11 mm Hg (P < 0.001) (Fig. 6). This is in contradistinction to the beating heart in which subepicardial diastolic pressure exceeded both subendocardial diastolic pressure and left ventricular end-diastolic pressure.

In the three dogs in which the mechanical effects of coronary flow upon intramyocardial pressure were evaluated, left ventricular end-diastolic pressure remained at 11 ± 2 mm Hg throughout the first 30 seconds following ligation of the left anterior descending coronary artery. Ten beats after ligation, subendocardial diastolic pressure decreased from 22 ± 7 to 14 ± 2 mm Hg and at 30 seconds following ligation it was 11 ± 1 mm Hg. Subepicardial diastolic pressure during the control period was 36 ± 9 mm Hg. It decreased to 29 ± 5 mm Hg by 10 beats after ligation and it decreased to 23 ± 4 mm Hg at 30 seconds after ligation. Even though a reduction of subendocardial and subepicardial diastolic pressure occurred, in each instance the subepicardial diastolic pressure exceeded subendocardial diastolic pressure.

**Discussion**

These observations showed that in the beating heart during diastole, subepicardial pressure exceeded both subendocardial and left ventricular end-diastolic pressure. In contradistinction, in the arrested heart, following distension, subepicardial diastolic pressure was less than subendocardial diastolic pressure and intracavitary pressure. Therefore, the distribution of stress within the myocardial wall is altered in the arrested heart.
Diastolic intramyocardial pressures have been measured infrequently, usually because of the insensitivity of the methods available in the past (Hoffman and Buckberg, 1976). Diastolic intramyocardial pressures that exceeded left ventricular end-diastolic pressure were reported by some (Baird et al., 1976; Nematzadeh et al., 1976; Peyster and Stuckey, 1976; Pifarre, 1968; Salisbury et al., 1962; Senyk et al., 1972). A diastolic intramyocardial pressure higher than left ventricular pressure has also been predicted from pressure-flow curves of the coronary circulation (Archie, 1978; Bellamy, 1978; Hoffman, 1978). Others found intramyocardial pressures in diastole that were similar to left ventricular end-diastolic pressure (Kelly and Pitt, 1973; van der Meer et al., 1970). Differences in the values reported by previous investigators may be a consequence of the depth within the myocardium at which measurements were obtained. If measurements were made at intramyocardial sites other than the subepicardium, or if the transducers were so large as to prohibit localized measurements within the subepicardium, then a prominent diastolic gradient between intramyocardial pressure and left ventricular pressure would not have been observed.

The significance of a diastolic subepicardial pressure that exceeds diastolic subendocardial pressure, in relation to diastolic compliance and cardiac function, has been stated to represent an inhomogeneity of myocardial mechanics (Nematzadeh et al., 1976). Others who showed diastolic intramyocardial pressure that exceeded intracavitary pressure did not comment on its possible relation to diastolic muscle mechanics, but did describe its significance relative to the distribution of coronary flow. The gradient in myocardial tissue pressure in diastole, when it is in a reverse direction to that present in systole, is thought to explain the preferential flow to the inner layers of the left ventricle during diastole (Baird et al., 1976; Nematzadeh et al., 1976). However, the subject may require further interpretation. It has been found that increasing preload decreases subendocardial flow if autoregulation is abolished (Kjekshus, 1973; Ellis and Klocke, 1978; Archie, 1978). Our observations showed that both subendocardial and subepicardial pressure increased with preload. Both may tend to reduce subendocardial flow. The increased subepicardial pressure may interact in this regard by increasing the resistance in the penetrating branches of the coronary vessels which supply the endocardium.

It has been shown that the turgor of the coronary vessels can influence myocardial elasticity (Salisbury et al., 1960). Subsequently, a direct relation between coronary blood flow and wall thickness was observed, which suggested a dynamic role of coronary blood flow on myocardial stiffness and diastolic wall stress (Gaasch and Bernard, 1977). To evaluate the possibility that engorgement and stiffening of the coronary vessels during diastole...
may have led to the observed pressure gradient across the left ventricle during diastole, we measured intramyocardial pressure following occlusion of the coronary artery in the region of the intramyocardial pressure probes. We limited our observations to 30 seconds following ligation to minimize the effects of ischemia upon intramyocardial pressure. Although we noted a reduction of diastolic subepicardial pressure after coronary artery ligation, subepicardial pressure remained twice the subendocardial diastolic pressure, which suggested that the observed intramyocardial diastolic pressure gradient did not result from a myocardial erectile effect.

It would be helpful to know how pressure would be expected to vary across the wall of the myocardium during diastole. Although the distribution of pressure within static fluids and the distribution in moving fluids, by use of the Navier-Stokes equations, have been derived previously, there is no existing theory for the distribution of pressure in a biological tissue which fits the characteristics of either a solid or a liquid. It is likely, however, that a true pressure can be measured within the myocardium, since the myocardium consists of 76% to 85% water by weight (Altman and Dittmer, 1971). To estimate how intramyocardial pressure would vary across the myocardium, a calculation based on mathematical modeling of the left ventricle was made (Appendix I). Such a mathematical model can be made only if the tissue is considered to be passive and noncontractile, as in the arrested heart. It appears from our mathematical model that pressure within the passively distending ventricular wall would be lower in the subepicardium than in the subendocardium (Appendix I). This supports the observations we made of intramyocardial pressure in the arrested left ventricle, and also supports the conclusion that the beating left ventricle during diastole does not behave as a passive structure.

Mechanics of the heart during diastole, based on concepts of compliance and its reciprocal, stiffness, assume that the heart is a passive elastic structure (Diamond et al., 1971; Mirsky, 1969; Mirsky and Parmley, 1973; Mirsky and Rankin, 1979). Differences of volume elastic constants reported in normal subjects and patients with hypertrophy, congestive cardiomyopathy, coronary disease, and coronary disease with congestive failure (Fester and Samet, 1974; Mirsky and Parmley, 1973), in view of the observations in our study, may not be due entirely to intrinsic differences of muscle stiffness. Our observations suggest that functional differences of muscle tone during diastole may contribute to the apparent differences of stiffness. Similarly, in view of our observations, it may be that the previously observed changes of the pressure-volume relation in humans following drugs (Alderman and Glantz, 1976; Ludbrook et al., 1977) perhaps may reflect changes of diastolic muscle tone. Calculations of the diastolic compliance and diastolic stiffness of the ventricle, which assume passive elastic mechanics of the ventricle, fail to account for diastolic muscle tension.

Under normal circumstances, the pericardium exerts minimal, if any, restrictive influence on the left ventricle (Shirato et al., 1978). However, after volume loading, the pericardium modifies the diastolic pressure-length relations of the left ventricle (Shirato et al., 1978). In view of this, one might wonder if intramyocardial pressure, with the pericardium intact, might differ markedly from that which we observed following a pericardial resection. To evaluate this possibility, we measured intramyocardial pressure in two dogs with the pericardium intact; the needle probes were inserted through the pericardium. The relative differences between intracavitary, subendocardial, and subepicardial pressure that we observed after removal of the pericardium were also observed with the pericardium intact both during control conditions and following an augmented preload. Distension of the heart following cardiac arrest with the pericardium still intact showed a reversal of the gradient similar to that which we observed in the arrested heart following pericardiectomy. Our observations therefore were consistent, irrespective of the presence of an intact pericardium.

Regarding the possibility that the pericardium may have exerted a restrictive influence, we also evaluated in two additional dogs the effects of removal of the serous layer of pericardium from the left ventricle. With careful dissection, the serous layer was removed from most of the left ventricle. In both of these dogs, with both the external fibrous layer and internal serous layer of the pericardium removed, diastolic intramyocardial pressures were comparable to those observed with only the external layer of the pericardium removed. Namely, diastolic subepicardial pressure exceeded diastolic subendocardial pressure, and both exceeded left ventricular intracavitary pressure. The apparent diastolic tone exhibited by the ventricle, therefore, does not appear to have resulted from a restrictive effect of the serous pericardium.

In conclusion, the observations of this study indicate that tone is maintained by the subepicardial muscle during diastole. Thus, the ventricle does not appear to behave as a passive shell during diastole.

**Appendix 1**

**Mathematical Prediction of the Distribution of Intramyocardial Pressure Assuming a Passive Anisotropic Tissue**

The distribution of pressure within the wall of the left ventricle during diastole, assuming that the ventricle distends as a passive, noncontracting tissue, can be estimated from the following calculations. A static fluid in a container will experience a change in pressure according to the following equation (Parker et al., 1969)

\[ \Delta P = -B \Delta V/V \] (1)
where B is the bulk modulus of elasticity of the fluid, V is the original fluid volume, and \( \Delta V \) is the change in volume of the fluid.

Since the left ventricle consists of 76–85% water by weight (Altman and Dittmer, 1971), it seems reasonable to suspect that a small cubical volume of the myocardium (containing fluid and blood interspersed within the cellular structure) will experience pressure changes similar to that described by Equation 1 for small changes in volume strain, \( \Delta V/V \).

Based on this assumption, one can compute the distribution of intramyocardial pressure with radial position by computing the values of volumetric strain (\( \Delta V/V \)) throughout the wall of the left ventricle.

For a first order approximation, assume that the left ventricle is an elastic hollow sphere with an intracavitary pressure, \( P_c \), distributed uniformly over the inner surface. The inside and outside radii are denoted by \( R_i \) and \( R_o \), respectively. The myocardium is assumed to be anisotropic, but does have transversal isotropy with respect to any radius vector drawn from the center of the sphere. The problem is analyzed by using a spherical coordinate system \( r, \theta, \phi \) with the origin at the center of the sphere (Fig. 7).

The following notation is adopted: \( \sigma_r, \sigma_\theta, \sigma_\phi, \varepsilon_r, \varepsilon_\theta, \varepsilon_\phi \) are the normal and tangential stresses and strains, respectively (\( r = \) radial, \( \phi = \) meridional, \( \theta = \) circumferential). \( E_r \) and \( E \) are the Young’s moduli for stresses and strains in the direction of the radius vector, \( r \), and in a direction perpendicular to it. \( \nu_\theta \) is the Poisson coefficient which characterizes the transverse contraction in directions perpendicular to \( r \) for tension in the direction \( r \); \( \nu \) is the Poisson coefficient which characterizes the transverse compression in the plane normal to the radius vector for tension in the same plane.

The equations of the generalized Hooke’s law are written as (Lekhnitskii, 1963)

\[
\begin{align*}
\varepsilon_r &= \frac{1}{E_r} \sigma_r - \frac{\nu_\theta}{E} (\sigma_\theta + \sigma_\phi) \\
\varepsilon_\theta &= \frac{-\nu_r}{E_r} \sigma_r + \frac{1}{E} (\sigma_\theta + \nu_\phi \sigma_r) \\
\varepsilon_\phi &= \frac{-\nu_r}{E_r} \sigma_r + \frac{1}{E} (\sigma_\phi + \nu_\theta \sigma_r)
\end{align*}
\]

Equation 2 was solved for the stresses to obtain (Lekhnitskii, 1963),

\[
\begin{align*}
\sigma_r &= A_{11} \varepsilon_r + A_{12} \varepsilon_\theta + A_{12} \varepsilon_\phi \\
\sigma_\theta &= A_{12} \varepsilon_r + A_{22} \varepsilon_\theta + A_{22} \varepsilon_\phi \\
\sigma_\phi &= A_{12} \varepsilon_r + A_{22} \varepsilon_\theta + A_{22} \varepsilon_\phi
\end{align*}
\]

where the modulii of elasticity \( A_i \) are expressed as

\[
\begin{align*}
A_{11} &= \frac{E_r(1 - \nu)}{J} \\
A_{12} &= \frac{E_r \nu}{J} \\
A_{22} &= \left( \frac{E}{1 + \nu} \right) \left( 1 - \nu \frac{r^2 E/E_r}{J} \right)
\end{align*}
\]

The stresses can be shown to be expressed as (Lekhnitskii, 1963)

\[
\begin{align*}
\sigma_r &= \frac{P_c R_i^{n+1}}{R_o^{3n} - R_i^{3n}} - \frac{P_c R_o^{3n}}{R_o^{3n} - R_i^{3n}} \cdot \frac{r^{-1.5-n}}{r^{-1.5-n}} \\
\sigma_\theta &= \frac{P_c R_i^{1.5-n}}{R_o^{2n} - R_i^{2n}} - \frac{P_c R_o^{1.5-n}}{R_o^{2n} - R_i^{2n}} \cdot \frac{r^{-1.5+n}}{r^{-1.5+n}} \\
\sigma_\phi &= \lambda_n \frac{P_c R_i^{1.5-n}}{R_o^{3n} - R_i^{3n}} - \frac{P_c R_o^{1.5-n}}{R_o^{3n} - R_i^{3n}} \cdot \frac{r^{-1.5-n}}{r^{-1.5+n}}
\end{align*}
\]

The volumetric strain, \( \Delta V/V \), can be computed by substituting Equations 2, 4, and 5 into the following equation:

\[
\frac{\Delta V}{V} = \varepsilon_r + \varepsilon_\theta + \varepsilon_\phi.
\]

After performing the substitution, we obtain the following equation

\[
\Delta V = \frac{P_c (r/R_i)^{n-1.5}}{E[(R_o/R_i)^{3n} - 1]} \left\{ \alpha - 2\nu + 2\lambda_n (1 - 2\nu) \right\}
\]
where \( \alpha = \frac{E}{E_R} = \frac{r}{r_F} \).

Once the volumetric strain in the myocardium is obtained by Equation 10, it is possible to compute the pressure change in the myocardium by using the following equation (Parker et al., 1969)

\[
\Delta P = -B \frac{A V}{V} \quad (11)
\]

where \( B \) is the bulk modulus of the fluid-cellular structure tissue.

For a given geometry and material, Equation 10 can be written as

\[
\Delta V = \frac{P_c}{E} \left[ K_1 r^{n-1.5} - K_2 r^{n+1.5} \right] (12)
\]

where \( K_1 \) and \( K_2 \) can be obtained from Equation 10.* Upon substituting Equation 12 into Equation 11, one obtains

\[
\Delta P = -\frac{B}{E} \left[ K_1 r^{n-1.5} - K_2 r^{n+1.5} \right] P_c. \quad (13)
\]

From Equation 13, it is shown that the variation of pressure within the wall of the ventricle at any depth depends on the radius at the point of measurement, \( r \), the bulk modulus, \( B \), of the myocardium, Young’s modulus of the myocardium, \( E \), and ventricular intracavitary pressure, \( P_c \). To determine how the terms vary in magnitude and, hence, how the intramyocardial pressure varies within the wall of the left ventricle, calculations were performed using a Poisson’s ratio that varied from 0.1 to 0.5, and values of the ratio of Young’s modulus in the tangential to radial direction that varied from 1 to 10. All computations, irrespective of the values of Poisson’s ratio or the ratio of Young’s moduli, showed that intramyocardial pressure was greatest near the epicardial surface and lowest near the endocardial surface.

Clearly, our mathematical model of the distribution of pressure within the myocardium of the left ventricle during diastole is an approximation containing assumptions both of spherical geometry and an unvarying Young’s modulus. Regarding the latter, there is evidence that Young’s modulus varies with stress and, therefore, is not constant (Mirskey and Rankin, 1979). Even so, the predicted distribution of intramyocardial pressure during diastole, based upon this mathematical model, which of necessity assumes a passive non-contractile left ventricle, supports our observations in the arrested heart. Conversely, the mathematical model predicts results which differ from intramyocardial pressure observed during diastole in the beating heart.

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Mechanisms for Impulse Initiation in Isolated Human Atrial Fibers

Luc Mary-Rabine, Allan J. Hordof, Peter Danilo, Jr., James R. Malm, and Michael R. Rosen

SUMMARY We used standard microelectrode techniques to study Tyrode's-superfused human atrial fibers obtained at cardiac surgery. Two types of sustained rhythmic activity occurred. One resulted from slow phase 4 depolarization and had a spontaneous rate at 20-26 beats/min. Epinephrine increased and the slow channel blockers, AHR-2666 (AHR) and verapamil decreased both phase 4 slope and spontaneous rate. Acetylcholine (ACh) and lidocaine decreased the slope of phase 4, but the slowing of rate was less than that induced by AHR and verapamil. Tetrodotoxin (TTX) also decreased the slope of phase 4 and spontaneous rate, to an extent that was intermediate between the actions of AHR-verapamil and ACh-lidocaine. A second type of sustained rhythmic activity was triggered by delayed afterdepolarizations (DAD). DAD amplitude increased as stimulus cycle length decreased and, at critical cycle lengths, DAD initiated trains of spontaneous action potentials at rates > 70 beats/min. Spontaneously occurring DAD were suppressed by AHR and were transiently diminished by ACh. This effect of ACh was accompanied by hyperpolarization of the fibers. DAD also were induced by epinephrine. These DAD were unaffected by TTX, lidocaine, or ACh and were suppressed by AHR and verapamil. In summary, the slow inward current contributes to the sustained rhythmic activity that occurs with automaticity or DAD in human atrium. A TTX-sensitive current also contributes to automaticity. DAD that occur spontaneously are largely insensitive to the effects of agents that increase K conductance (ACh, lidocaine) or TTX. Circ Res 47: 267-277, 1980

HUMAN atrial specialized fibers develop spontaneous phase 4 depolarization and automaticity (Geland et al., 1972; Trautwein et al., 1962; Mary-Rabine et al., 1978; Hordof et al., 1976) as well as delayed afterdepolarizations (Hordof et al., 1978). Phase 4 depolarization and automaticity occur in both normal and partially depolarized fibers; delayed afterdepolarizations are seen in normal fibers exposed to toxic concentrations of digitalis as well as in depolarized fibers. It may be that the phase 4 depolarization that occurs in normal human atrial specialized fibers results from a gradually diminishing \( i_{K2} \) current, the same mechanism that has been described in normal Purkinje fibers (Noble, 1975). However, other K+ currents, such as \( i_{K1} \), which appears to generate the pacemaker potential in frog atrium and in sinus node (Brown and Noble, 1969a, 1969b; Lenfant et al., 1972) have been implicated as having greater importance than \( i_{K2} \) in generation of the atrial pacemaker potential (Noble, 1975). The basis for automaticity in normal or diseased and partially depolarized human atrium has...
Comparison of the distribution of intramyocardial pressure across the canine left ventricular wall in the beating heart during diastole and in the arrested heart. Evidence of epicardial muscle tone during diastole.

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