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Epicardial deformation and left ventricular wall mechanics during ejection in the dog

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ARTS, Theo, Pieter C. Veenstra, and Robert S. Reneman. Epicardial deformation and left ventricular wall mechanics during ejection in the dog. Am. J. Physiol. 243 (Heart Circ. Physiol. 12): H379-H390, 1982.—Significant differences between epicardial and endocardial systolic stress in the wall of the left ventricle (LV) have been predicted by various models of LV mechanics. Yet a model incorporating transmural differences in fiber orientation and torsion, defined as a rotation of the apex with respect to the base around the long axis of the LV, predicts transmural equalization of stress and shortening along the fiber direction during the ejection phase. This equalization is due to an interplay between torsion and myocardial contraction. To assess the model hypothesis, predicted epicardial deformation during the ejection phase was compared with that measured experimentally. For this purpose 45 sets of measurements were performed in four open chest dogs using a triangular array of inductive gauges for the assessment of epicardial circumferential strain ($\varepsilon_c$), base-to-apex strain ($\varepsilon_z$), and shear angle ($\gamma$). Changes in shear angle are directly related to LV torsion. LV end-diastolic pressure was varied over a wide range (0–15 mmHg) by volume loading and bleeding. In the control state, the slope of the shear angle vs. volume strain curve (volume strain = $2 \varepsilon_c + \varepsilon_z$), which is related to contraction, was found to be 0.74 ± 0.10 (mean ± SD). This compares reasonably with the mathematical model prediction of a slope of 0.67. Due to an interplay between torsion and contraction, left ventricular fiber stress and fiber shortening might be uniformly distributed across the wall.

Transmural stress distribution; left ventricular torsion

Insight into left ventricular energetics is often sought through study of the relationship between left local intramyocardial mechanical loading and global ventricular pump function. The latter is usually described by hemodynamic parameters such as left ventricular and aortic pressure as well as aortic volume flow. Regional cardiac mechanics may be defined by local fiber stress, velocity of sarcomere shortening, generated mechanical power per unit of tissue volume, or intramyocardial pressure. Knowledge of fiber stress, fiber orientation, and left ventricular geometry, all of which determine intramyocardial pressure (2, 4), is important because of its relation to coronary blood supply (8, 15) and myocardial metabolic needs (19).

Overall pump function of the left ventricle can be assessed in animal experiments by measuring with conventional techniques left ventricular pressure as well as pressure and flow in the ascending aorta. In spite of several investigations using myocardial gauges (7, 11, 20), direct determination of local wall stress remains difficult and unreliable because of artifacts and tissue injury at the site of measurement (2). Hence we preferred to calculate wall stress from left ventricular pressure and dimensions using a mathematical model of left ventricular mechanics. The model that we developed differs from others (16, 21, 29) in that anisotropy of myocardial tissue as well as torsion of the left ventricle are considered. This torsion is associated with rotation of the apex with respect to the base around the long axis of the left ventricle. Furthermore, no transmural differences in mechanical properties of the myocardial tissue that were previously suggested (18) are introduced.

Analytical results obtained with this model indicate that transmural differences in local fiber stress and sarcomere length are small throughout the entire ejection phase. Further analysis showed that this essential transmural uniformity of mechanical loading is a direct consequence of consideration of anisotropy (2) and torsion (4) in the model. Because the results obtained with this model contradicted the frequently calculated higher mechanical loading of the subendocardial layers (16, 29), it was decided to test the mathematical model against left ventricular mechanical parameters measured in open-chest dogs.

In the absence of a direct and accurate measurement of transmural fiber stress distribution and intramyocardial pressure, we have chosen to study local myocardial deformations. Epicardial left ventricular free-wall deformation can be measured accurately in the open-chest dog without significantly influencing the mechanical behavior of the ventricle (3). Epicardial deformation is fully described by three parameters: i.e., circumferential natural strain, base-to-apex natural strain, and shear. The time course of these deformation parameters and their interrelation during the ejection phase were then compared with predictions by the model.

Mathematical model of left ventricular mechanics. The mathematical model relates overall left ventricular pump function to mechanical loading of local myocardial tissue. The principles of the model (1, 4) are briefly recapitulated below.

1) The left ventricle is assumed to be a thick-walled cylinder composed of eight concentric cylinder shells (Fig. 1). 2) Tangential stresses in the wall generate left ventricular pressure in accordance with Laplace’s law. In a cross section of the cylinder perpendicular to the axis,
The forces exerted by the internal pressure and by axial stresses within the cylinder wall are in equilibrium. 3) Shear stresses in the latter cross section act circumferentially and result in an equilibrium of torques. Thus the cylinder is allowed to twist, which simulates rotation of the apex with respect to the base around the long axis of the left ventricle. 4) The myocardial tissue is considered to be anisotropic and is modeled by a contractile fiber structure embedded in a soft incompressible material (2). 5) The myocardial tissue is assumed to be contractile instead of purely elastic. The contractile properties of the muscle fibers are taken to be uniform across the wall and are characterized by a stress-sarcomere length-velocity of sarcomere shortening-time relationship expressed by a first-order differential equation (APPENDIX 1). 6) The onset of muscle contraction is assumed to be synchronous. 7) Different fiber orientations (17, 26, 27), sarcomere lengths (17, 30), and stresses are used for each shell of the cylinder. 8) The afterload of the left ventricle is simulated in the model by a combination of a diode (aortic valve) in series with an inertance, a resistance (aortic characteristic impedance), and an arterial capacitance in parallel with a second (peripheral) resistance (28). The values of these parameters were determined from the relation between aortic pressure and aortic volume flow, as measured in the in vivo experiments.

Previously the fiber orientation in the left ventricular free wall was assumed to be representative for the whole circumference of the left ventricle (4), despite apparently differing fiber orientations in the right ventricular free wall and right septal layers (26). To model this asymmetry the fiber orientations of the right halves of the outer cylindrical shells were replaced by the fiber orientations of the right ventricular free wall and right septal layers (Fig. 1). For simplicity of the model the right ventricular cavity is not considered, and in the calculation of equilibrium of forces fiber stress as calculated from sarcomere length and time (APPENDIX 1) in the left and right half of the shell is assumed to be the same.

The parameter values, as substituted in the simulation, are listed in Table 1. Parameter values, related to geometry and fiber orientation, refer to the end-diastolic phase of the control state. The ratio of inner to outer radius under these circumstances is determined from the ratio of left ventricular cavity volume to wall volume, which is reported to be 0.54 in the end-diastolic phase (25). The volume of the left ventricular wall is calculated from the average weight of the left ventricle in the in vivo experiments described in this article. A flow diagram of the model calculations is presented in APPENDIX 2.

Simulation of cardiac cycles by the mathematical model. Analysis of cardiac cycles as simulated by the model is presented to allow direct comparison with results obtained in animal experiments. Thus end-diastolic left ventricular volumes of 20, 40, 60, 80, and 100 ml were used in the simulation to compute the time courses of the following variables (sampling interval 10 ms): left ventricular pressure, ascending aortic pressure, and volume flow, as well as deformation of the epicardial surface of the left ventricle. This deformation is characterized by circumferential natural strain ($\varepsilon_c$), base-to-apex natural strain ($\varepsilon_b$), and a shear angle ($\gamma$). Here natural strain is defined as the natural logarithm of the ratio of actual to reference segment length. Thus on the outer cylinder surface

$$\varepsilon_r = \ln(r/R)$$  \hspace{1cm} (1)

$$\varepsilon_b = \ln(h/H)$$  \hspace{1cm} (2)

where r is the outer radius of the cylinder, R is the reference outer radius of the cylinder, h is the height of the cylinder, and H is reference height of the cylinder.

The shear angle $\gamma$ is defined as the change of the angle between the circumferential direction and a line on the epicardium that was perpendicular to the circumference in a reference state of deformation. Shear occurs when torsion of the cylinder is present (4). This torsion, representing left ventricular torsion, is associated with rotation of the upper plane of the cylinder (Fig. 1) with respect to the lower plane around the axis of the cylinder. In the present study mainly changes in epicardial deformation parameters ($\Delta \varepsilon_c$, $\Delta \varepsilon_b$, $\Delta \gamma$) are assessed. From Eqs. 1 and 2 it follows that a change in natural strain only depends on the segment lengths before and after deformation. Therefore the actual value of the reference segment length is irrelevant to the analysis.

<table>
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<th>Fiber Angle, rad</th>
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<th>RV and septum</th>
</tr>
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<td>8 ($\varepsilon_{epi}$)</td>
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</table>

FIG. 1. Cylindrical representation of left ventricle. Subdivision into cylindrical shells, changing fiber orientation, and torsion deformation are indicated. Influence of right ventricle and septum on left ventricular function is simulated by a different fiber orientation in right half of cylinder.
Figure 2 shows theoretical results for normal contraction at an end-diastolic volume of 60 ml (i.e., control state). During ejection (indicated by forward aortic volume flow), circumferential natural strain, base-to-apex natural strain, and shear angle were predicted to decrease by 0.083, 0.095, and 0.169 rad, respectively. During aortic occlusion systolic left ventricular pressure increased by 90%, the duration of contraction was prolonged by 50 ms, and systolic changes in circumferential natural strain, base-to-apex natural strain, and shear angle were -0.01, +0.02, and 0.00 rad, respectively.

To describe the left ventricular mechanics, a basic variable had to be introduced to which all other variables could be related. Often left ventricular volume is chosen. However, its quantification throughout the cardiac cycle is difficult. Therefore natural volume strain ($\varepsilon_v$) was introduced as the basic variable, expressing the relative change of volume enclosed by the epicardial surface

$$\varepsilon_v = \ln\left(\frac{V_{lv,1} + V_w}{V_{lv,0} + V_w}\right)$$

where $V_{lv}$ is left ventricular cavity volume, $V_w$ is left ventricular wall volume, and $V_{lv,0}$ is the reference value of $V_{lv}$.

The wall volume is assumed to be constant and equal to the total volume of the left ventricular free wall and septum. Applying Eqs. 1 and 2 to Eq. 3 for a cylindrical epicardial surface

$$\varepsilon_v = 2\varepsilon_c + \varepsilon_s$$

The parameters $\varepsilon_c$ and $\varepsilon_s$ can be measured instantaneously and locally on the epicardial surface of the free wall of the left ventricle (3).

The curves in Fig. 3 represent the predicted pathway of the deformation parameters $\gamma$, $\varepsilon_c$, and $\varepsilon_s$ as a function of $\varepsilon_v$ during the ejection phase for five different beats with left ventricular end diastolic volume ($V_{lv,ed}$) in the range of 20-100 ml. The slopes of the lines connecting the beginning and end points of the control state curves (i.e., $V_{lv,ed} = 60$ ml) were 0.67, 0.32, and 0.37, respectively.

**METHODS:** In Vivo Experiments

The experiments were performed on four mongrel dogs weighing 25-34 kg. The animals were premedicated with Hyphorm (1 ml/kg im: 1 ml Hyphorm contains 10 mg fluanison and 0.2 mg fentanyl base). Anesthesia was induced by pentobarbital sodium (10 mg/kg iv) and after endotracheal intubation was maintained by oxygen and nitrous oxide. Ventilation was kept constant with a positive-pressure respirator (Pulmomat).

The electrocardiogram was derived from the limb leads. The chest was opened through the left fifth intercostal space, and the heart was suspended in a pericardial cradle. Ascending aortic pressure was measured via the carotid artery with a catheter connected to a pressure transducer (Ailtech). Left ventricular pressure was measured with a catheter-tip micromanometer (Millar) inserted through a femoral artery. The lumen of the catheter-tip micromanometer was connected to an external pressure transducer (Ailtech), which could be set at a reference level by switching a three-way cock. This reference was the center level of the left ventricular cavity. Thus end-diastolic left ventricular pressure was measured accurately by amplifying and clipping the left ventricular pressure signal measured through the lumen of the catheter-tip micromanometer (full scale: 0-2 kPa or

![FIG. 3](image-url)
0–15 mmHg). Ascending aortic volume flow was measured with an electromagnetic flowmeter (Transflow 600). The probes were calibrated in vitro prior to the experiments. The end-diastolic level of the instantaneous flow recording was used as zero flow reference. A string around the ascending aorta proximal to the electromagnetic flow probe allowed temporary occlusion of the aorta for the purpose of obtaining isovolumic left ventricular contractions.

Regional left ventricular deformation was measured with an inductive method (3) using a rotating magnetic-field–generating coil (MFGC). This coil was attached to the epicardium of the anterior free wall of the left ventricle approximately 30 mm lateral to the left anterior descending coronary artery and approximately 30 mm distal to the left circumflex coronary artery (Fig. 4). A sensor coil for detecting circumferential natural strain (SCc) was placed between the left anterior descending coronary artery and MFGC, approximately 17 mm from the latter. A sensor coil for detecting base-to-apex natural strain (SCs) was attached to the epicardium between the left circumflex coronary artery and MFGC, approximately 17 mm from the latter. Thus the three coils formed a triangle with the field-generating coil at its right angle. Natural strains were derived electronically from changes in the amplitude of the signals induced in the sensor coils. The generated magnetic field spins with a frequency of 1,500 Hz around the axis of the MFGC. Therefore, the induced voltages in SCc and SCs are out of phase with an angle equal to the angle formed by SCc-MFGC-SCs. The shear angle was determined electronically as the deviation of this phase angle from 90°.

After installation of the measuring devices the variables were recorded continuously on a 10-channel paper recorder (Schwarzer) using a paper speed of 2 mm/s. Under control conditions measurements started by recording electrical reference levels of natural strains and shear angle as well as the zero level of end-diastolic left ventricular pressure by switching of the three-way cock. All variables were registered at a paper speed of 100 mm/s for 15 s, after which an aortic occlusion was induced during diastole for at least one beat. Thereafter, paper speed was reduced to 2 mm/s for continuous monitoring.

To increase left ventricular end-diastolic volume and hence stroke volume, hypervolemia was induced by administrating physiological saline. Measurements were repeated at various levels of hypervolemia. After maximal hypervolemia (end-diastolic left ventricular pressure as high as possible but not higher than 2 kPa or 15 mmHg) blood volume was reduced by venous bleeding, and measurements were repeated at various blood volumes. When peak-systolic blood pressure decreased below 7 kPa (52 mmHg), the experiment was terminated by giving the animal a lethal dose of KCl. The heart was removed, and the ventricles were dissected from the atria just below the basal plane. Left ventricular free wall and septum were separated from the right ventricular free wall, and both parts of the cardiac muscle were weighed.

Analysis of wall shortening. To investigate whether, in the wall of the left ventricle, local wall shortening corresponded with the average value of wall shortening, in different experiments stroke volume (ΔVcalc) as calculated from changes in local natural volume strain was compared with stroke volume (ΔVme) as calculated by time integration of the instantaneous aortic volume flow. Using Eq. 3 it holds (APPENDIX 3) that

\[
\Delta V_{\text{calc}} = (V_{w} + V_{l,\text{ed}}) \left[ \exp(\epsilon_{v,\text{be}} - \epsilon_{v,\text{ed}}) - \exp(\epsilon_{v,\text{be}} - \epsilon_{v,\text{ed}}) \right]
\]

where \(V_{l,\text{ed}}\) is left ventricular cavity volume at end-diastole in the control state; \(\epsilon_{v,\text{be}}, \epsilon_{v,\text{ed}}\) and \(\epsilon_{v,\text{ed}}\) are natural volume strains at the beginning and end of ejection and at end-diastole in the control state, respectively.
and $V_w$ is measured wall volume.

In our experimental setup left ventricular cavity volume was not measured. End-diastolic left ventricular cavity volume in the control state was reported (25) to be approximately 54% of left ventricular wall volume. Thus in Eq. 5 $V_{lv,ed}$ is substituted by 0.54 $V_w$.

RESULTS

Figure 5 illustrates typical recordings of a cardiac cycle with a normal contraction followed by an isovolumic one. The ejection phase is marked by the aortic volume flow signal. During this phase epicardial deformation was generally found to occur smoothly, whereas during the isovolumic contraction and relaxation phase often abrupt deformations were measured. Table 2 presents both the epicardial deformation as measured during the ejection phase and the hemodynamic variables, as measured in four experiments during the control state, maximum hypervolemia, and maximum hypovolemia. The change in circumferential natural strain, shear angle during the ejection phase, and stroke volume ($\Delta V_{aq}$), as measured electromagnetically, increased significantly ($P < 0.001$) with increasing end-diastolic left ventricular pressure. The amplitude of the change in base-to-apex natural strain did not significantly depend ($P > 0.05$) on end-diastolic left ventricular pressure. Systolic and diastolic aortic pressure, stroke volume ($\Delta V_{aq}$), heart rate, end-diastolic left ventricular pressure, and postmortem left ventricular weight are mentioned to illustrate the hemodynamic state, whereas systolic left ventricular pressure during aortic occlusion relates to contractility of the cardiac muscle. After aortic occlusion the changes in $\varepsilon_c$, $\varepsilon_s$, and $\gamma$ during the ejection phase were less pronounced.

![FIG. 5. Results obtained from in vivo expt. A normal cardiac cycle is followed by a cardiac cycle with aortic occlusion. For explanation of symbols and vertical lines see Fig. 2. Middle tracing (Prved) is end-diastolic pressure signal](image)

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<th>$\Delta \varepsilon_s$</th>
<th>$\Delta \gamma$</th>
<th>$\Delta V_{aq}$</th>
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<th>$P_{lvd,ed}$</th>
<th>$P_{aq}$</th>
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$\Delta \varepsilon_c$. Change in epicardial circumferential strain; $\Delta \varepsilon_s$. Change in base-to-apex strain; $\gamma$, shear angle; $P_{aao}$, systolic aortic pressure; $P_{lvd,ed}$, diastolic aortic pressure; $\Delta V_{aq}$, stroke volume calculated by time integration of instantaneous aortic volume flow; HR, heart rate; $P_{lvd,ed}$, end-diastolic left ventricular pressure; $P_{aq,m}$, systolic left ventricular pressure during aortic occlusion; LV Wt, left ventricular weight. $1 \text{kPa} = 7.5 \text{mmHg}$.

For example, in Fig. 5 during the part of systole where left ventricular pressure exceeds half of its peak value, $\varepsilon_c$, $\varepsilon_s$, and $\gamma$ increased only 0.010, 0.026, and 0.023 rad, respectively. These changes are opposite and smaller compared with normal ejection. Moreover, systolic left ventricular pressure was approximately doubled, and ventricular relaxation was delayed approximately 50 ms. The peaking of the aortic volume flow seen at the onset of aortic occlusion probably represents an artifact due to a loss in contact between aorta and the electrodes of the electromagnetic flowmeter.

In Fig. 6 for 45 beats obtained from four experiments the pathway of the shear angle $\gamma$ as a function of the instantaneous natural volume strain $\varepsilon$, is plotted during the ejection phase. Each group of curves relates to one experiment. For comparison the model prediction (Fig. 3) is also plotted in this figure. For all curves the slope of the line connecting the beginning and end points of the curve was determined. Within each experiment the slope values thus obtained were plotted in another graph (not shown) as a function of midejection natural volume strain, as determined halfway between the beginning and end points of the corresponding curves. The resulting data points got a statistical weight proportional to the
change of natural volume strain during the associated ejection phase. The latter weighing procedure accounts for a greater importance of a calculated slope when the beginning and end point are further apart. The linear regression line through the data points, relating slope to midejection natural volume strain, was calculated in each experiment. The control value of the slope was calculated as the value of the linear regression line at a midejection natural volume strain, as found in the control state. Thus the slope of the relation between $\gamma$ and $\epsilon_v$ in the control state was calculated to be $0.74 \pm 0.10$ (mean $\pm$ SD). Analogously, in Fig. 7 for the same beats the base-to-apex natural strain $\epsilon_b$ is plotted as a function of $\epsilon_v$, together with the model prediction of this relation. Also analogous to the analysis of the relation between $\gamma$ and $\epsilon_v$, the slope of $\epsilon_b$ vs. $\epsilon_v$ in the control state was calculated to be $0.19 \pm 0.13$ ($n = 4$), which is significantly ($P < 0.004$) different from zero.

In Fig. 8 calculated stroke volume is plotted as a function of measured stroke volume. The slope of the relation, based on four experiments was $0.99 \pm 0.08$, which is not significantly different from unity, suggesting that local wall shortening is close to mean shortening of the wall of the left ventricle.

**DISCUSSION**

*Sensitivity of the model to parameter variations.* The model is intended to relate fiber stress and fiber shortening to left ventricular pressure and volume during the ejection phase. One of the results of the model was that during the ejection phase the mutual relation between the epicardial deformation parameters was nearly independent of variations in hemodynamic loading of the left ventricle. For instance, the relation between epicardial shear $\gamma$ and natural volume strain $\epsilon_v$ tends to coincide in one curve as shown in Fig. 3, despite wide variations in end-diastolic left ventricular volume (20–100 ml; control, 60 ml). It is interesting to note that, similarly, variation in the model situation of end-diastolic aortic pressure (range, 7–25 kPa = 52–187 mmHg; control, 11 kPa = 82
mmHg) or variation of myocardial fiber contractile force (up to 50% over control by multiplying $G_\text{m}, G_\text{n}$, and $c_\text{n}$ in APPENDIX 1 and Table 2 by a factor of 1.5) did not affect this relationship either; deviations in $\gamma$ from the curve were always less than 0.01 rad. Analogously, the relation between base-to-apex natural strain $\epsilon_\text{n}$ and natural volume strain $c_\text{n}$, also tend to coincide in one curve (Fig. 3). Deviations of $\epsilon_\text{n}$ from this curve were less than 0.002.

Because changes in hemodynamic loading (preload and afterload) and in muscle properties (contractility) did not essentially affect the mutual relationship between the epicardial deformation parameters, variation in the parameters related to aortic input impedance and muscle properties did not affect this relationship either. In summary, in the model, changes in muscle properties affect the hemodynamics without affecting the mechanism that relates muscle fiber mechanics, left ventricular hemodynamics, and epicardial deformation. Conversely, changes in hemodynamic loading affect the mechanical loading of the muscle fibers.

The parameter values related to muscle properties (APPENDIX 1) are based as much as possible on experimental measurements on isolated cardiac muscle. However, most of these measurements are performed on different species (no dogs) and at relatively low temperatures. Therefore, parameters related to the rise time, duration, and decay time of muscle contraction and those related to velocity of sarcomere shortening are chosen so that in the control situation hemodynamic variables such as duration of the ejection phase and rate of rise of left ventricular pressure were in a physiological range for the dog.

According to the model the relation between muscle fiber mechanics and left ventricular hemodynamics mainly depends on the transmural distribution of fiber orientation and sarcomere length and on the ratio of left ventricular cavity volume to wall volume. The fiber orientation is reported to be different in various parts of the wall of the left ventricle (17, 26, 27) and shows relatively large interindividual differences. A general finding in the free wall of the left ventricle is an approximately linear decrease of the fiber angle with increasing distance from the endocardium in the inner half of the wall, a plateau representing a relatively thick middle layer of circumferentially directed fibers, and a steep decrease to a more axial direction in the subepicardial layers. Using an estimate of the transmural course of fiber orientation (26) and a uniform transmural distribution of sarcomere length, fiber stress during the ejection phase in the control state was calculated. Layers with a higher stress than the average were allowed to thicken, and layers with a lower stress were allowed to thin. Thus the transmural course of fiber orientation was adjusted, and the distribution of stress across the wall was made uniform in the midsystolic phase in the control state. After setting the transmural course of fiber orientation a characteristic result unique to our model was found; namely, the transmural distribution of mechanical loading was preserved fairly well (4) when end-diastolic left ventricular volume was varied over a wide range (from 20 up to 100 ml; control, 60 ml). Figure 9 shows the calculated transmural course of systolic fiber stress, sarcomere length at the beginning of ejection, sarcomere shortening during the ejection phase, and contractile stroke work, generated per unit of muscle volume. The sensitivity of fiber stress in the different shells and the epicardial deformation parameters during the ejection phase to changes in fiber angle in the separate shells are shown in Table 3. Each row represents the increment in fiber stress in the shells and the epicardial deformation parameters as a result of a 0.1 rad increase of the fiber angle in one of the shells.

In the top row the control values of the parameters are presented. The influence of considering a different fiber orientation for the right ventricular (RV) side and septum can be estimated by comparing the ratios $\Delta \gamma/\Delta \epsilon_\text{n}$ and $\Delta \epsilon_\text{n}/\Delta \epsilon_\text{c}$ in the control beat (Fig. 2; fiber orientations RV the same as LV). With different RV fiber orientation these ratios are 0.67 and 0.37, respectively, whereas without they are 0.59 and 0.44.

In the model the ratio of left ventricular cavity to wall volume is assumed to be 0.54 (25) when calculating the slope of $\gamma$ vs. $\epsilon_\text{n}$ during ejection in the control state. A decrease of this ratio to 0.44 would change the slope of this relation from 0.67 to 0.77.

Analysis of deformation. The relation between shear angle and natural volume strain was predicted to be nonlinear (Fig. 3). So in the analysis of experimental results this relation is approximated by a quadratic function. One of the properties of such a function is that the slope of a line connecting two points on the related parabolic curve is equal to the slope of the curve where the $x$ variable equals the average of the $x$ variables belonging to the latter two points. This property is used in determining the slope of the curves and relating measured shear angle and volume strain (Fig. 6) as a function of natural volume strain.

According to the model the slope mentioned above depends on the ratio of left ventricular cavity volume to wall volume. As this ratio was not measured in our experiments, its value was obtained from data on cardiac geometry during end-diastole in the control state, as described elsewhere (25). Therefore, quantitative comparison between model and experiment was made in the control situation. In the statistical analysis the effect of
TABLE 3. Sensitivity of stress and deformation to changes in fiber orientation

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\( \Delta \gamma \), Change in shear angle; \( \Delta \epsilon_t \), change in epicardial circumferential strain; \( \Delta \epsilon_c \), change in base-to-apex strain; \( \Delta \epsilon_v \), change in natural volume strain.

Calculation of stroke volume from epicardial shortening. The assumptions made for the calculation of stroke volume (Eq. 5) were a cylindrical geometry of the left ventricle and a homogeneous distribution of epicardial shortening over the wall of the left ventricle. Furthermore, at some state of left ventricular deformation the ratio of left ventricular cavity volume to wall volume had to be known. This ratio during the end-diastolic control state was derived from data reported by Ross et al. (25). Despite these crude simplifying assumptions, stroke volume was calculated fairly accurately as indicated by the good agreement between the calculated and measured values (Fig. 8). The sensitivity of Eq. 5 to a change of the ratio of cavity to wall volume is expressed by a 7% decrease in the calculated stroke volume when changing the ratio of 0.54 to 0.44. For the measurement of natural volume strain at the epicardium various methods of segment length measurement might be used, at least when these segments are along the circumferential direction and base-to-apex direction.

Significance of epicardial deformation. The significance of epicardial deformation for the deformation of the deeper layers in the myocardial wall during contraction is mainly determined by the amount of shear between layers in the wall of the left ventricle parallel to the epicardial surface. During ejection, this shear was quantitatively determined to be 0.02 rad without preferential direction (11). The average of this shear, therefore, was approximately zero with a standard deviation in the order of 0.02 rad in all directions (APPENDIX 4). This shear is small compared to the change in strain during contraction, which is measured to be approximately 0.17 along the principal direction of the strain rate tensor. Hence in the normal heart the transmural course of deformation during ejection might be determined from the deformation of the epicardial surface with reasonable accuracy, which was also suggested by Feigl and Fry (10).

Epicardial shear was determined by Fenton and co-investigators (12). In their experiments contraction of the epicardial surface was approximately \(-0.20\) in one principal direction and zero in the perpendicular principal direction. Applying general mechanics (APPENDIX 5) to
the deformation parameters measured in our experiments ($\Delta \varepsilon_x = -0.09$, $\Delta \varepsilon_y = -0.04$, and $\Delta \gamma = -0.15$ rad), natural strains along both principal directions were calculated to be $-0.14$ and $+0.01$, respectively. The direction with maximum shortening was calculated to form an angle of $35.7^\circ$ with the circumferential direction. In the model in the control state $\Delta \varepsilon_x = -0.083$, $\Delta \varepsilon_y = -0.095$, and $\Delta \gamma = -0.169$ rad. Thus during the ejection phase natural strains along both principal directions were calculated to be $-0.174$ and $-0.004$, and the direction with maximum shortening formed an angle of $47^\circ$ with the circumferential. Fenton's measurements (12), our measurements, and the model are in good agreement with regard to the small ratio of minimum to maximum shortening along the principal directions. The differences in the amount of shortening found in the three studies are not significant, because the related biological variance is relatively large. The angles characterizing the principal direction with maximum shortening are different in the model study and in the in vivo experiments. In both experimental studies they are smaller than the angle characterizing the fiber orientation, which is in the order of $55^\circ$ at the epicardium (17, 26, 27). This finding implies that the fiber orientation does not necessarily coincide with the direction of maximum shortening as was suggested by Fenton and co-investigators (12).

Extrapolation of modeled left ventricular mechanics to the in vivo situation. The results in the present study suggest a fair agreement between the model and experiments as far as global hemodynamics and epicardial deformation during the ejection phase are concerned. Therefore, the principles of the model might be valid. The major conclusion derived from the model is the likelihood of a rather uniform distribution of mechanical loading across the wall of the left ventricle (Fig. 9). Uniformity of fiber stress across the wall could also be calculated by the use of another model based on a transmural gradient in the Young's modulus of the myocardial tissue across the wall (18). In this case, however, fiber shortening was calculated to be nonuniformly distributed across the wall. Other models (16, 21, 29) based on uniformity of mechanical characteristics across the wall calculated fiber stress and sarcomere shortening to be twice as high in the subendocardial than in the subepicardial layers. This implies an endo-epicardial ratio of four for mechanical stroke work per unit of tissue volume. Measurement of the endo-epicardial ratio of myocardial perfusion under normal circumstances revealed values close to unity (5). This finding is in agreement with results of the current model, when assuming proportionality of coronary perfusion to generated mechanical power per unit of tissue volume.

In the model quantities related to the mechanics of the wall of the left ventricle are calculated to be rather uniformly distributed across the wall. Therefore, the average of these quantities is a good representative of their local value. The average across the wall of the quantities of sarcomere length ($L_s$) and fiber stress ($\sigma_f$), which are related to local wall mechanics, can be calculated fairly accurately from the global hemodynamic parameters left ventricular volume ($V_{LV}$) and left ventricular pressure ($P_{LV}$) by a set of two equations, thus bypassing the rather complicated model of left ventricular mechanics. The first equation is empirically derived from the model (results presented in Fig. 9) and relates sarcomere length to left ventricular cavity volume and left ventricular wall volume ($V_w$) with an accuracy of $\pm 0.5\%$ in the range $0.12 < V_{LV}/V_w < 0.94$.

$$L_s/L_w = (3V_{LV}/V_w) + 1)^{1/3}$$

(6)

where $L_w$ represents the extrapolated value of sarcomere length at zero left ventricular cavity volume. Applying general laws of energetics to relation 6 (APPENDIX 6), for fiber stress it holds

$$\sigma_f = [3(V_{LV}/V_w) + 1].P.$$  

(7)

The average fiber stress thus calculated agrees with the model calculation of this stress with an accuracy of $\pm 2\%$. If the model is a good representative of the real situation, relations 6 and 7 may be applied to the left ventricle in vivo.

Conclusion. The values of epicardial deformation parameters and their interrelation during ejection as calculated by the present model of the mechanics of the left ventricle are approximately the same as the values measured in animal experiments. So the basic principles and some predictions of the model may be valid in the in vivo situation. An important prediction of the model is a quite uniform transmural distribution of fiber shortening as well as fiber stress during the ejection phase, at least when torsion of the left ventricle around the base-to-apex axis is allowed.

APPENDIX 1

Mathematical Model of Contractile Properties of Cardiac Muscle

This appendix deals with an empirically determined mathematical relation, which is used to describe the contractile properties of cardiac muscle in the model of the mechanics of the left ventricle (see also discussion on sensitivity of the model to parameter variations). The description has the following properties. 1) Maximum active muscle stress increases approximately linearly from zero at sarcomere length ($L_s$) $1.5 \mu m$ to $10^4 \text{ N/m}^2$ at $L_s = 2.1 \mu m$. For $L_s > 2.1 \mu m$ this maximum stress levels off (23). 2) An isotropic systolic stress development at $L_s = 2.1 \mu m$ is characterized by a rise time of $75 \text{ ms}$, a decay time of $75 \text{ ms}$, and a duration of $210 \text{ ms}$ between the points with $50\%$ of maximum stress. 3) The duration of the contraction decreases linearly with decreasing $L_s$ (22), and the rate is $150 \text{ ms/\mu m}$. 4) Velocity of sarcomere shortening at zero load is proportional to fiber stress during isometric contraction at that $L_s$ (23) and is $15 \text{ \mu m/s at } L_s = 2.1 \mu m$.

The mathematical formulation of this muscle contraction model is a first-order differential equation. Contraction starts at time $t = 0$ with the initialization

$$I_s = I_0.$$  

(8.1)

where $I_s$ is the instantaneous value of sarcomere length after a hypothetical quick release, and $I_0$ is the actual sarcomere length, including the series elastic element (13). The time derivative of $I_s$ is calculated by applying Hill's equation (9, 14).

$$\frac{dI_s}{dt} = \left(1 - \frac{G_{max}}{G_{max} + G_{act}(L_s - L_0)} + G_{rel}\right)$$

(8.2)

with

$$G_{max} = (x - \sqrt{x^2 + 0.01} + 1) \times G_{act} \times (1 - [I - b(L_s - L_0)]/I_{p_e})$$

(8.3)

where $x = a(L_s - L_0)$.

$G_{act}$ is associated with isosarcometric stress, which is a function of time. The value and meaning of the parameters in Eqs. 8.2 and 8.3 are listed in Table 4. Fiber stress $\sigma_f$ is calculated as the sum of an active and a passive component by
To illustrate some characteristics of the mathematical description of cardiac muscle contraction, in a computer simulation the “muscle” is loaded isotonically. Figure 10 shows the related responses of fiber stress, sarcomere length, and velocity of sarcomere shortening as a function of time for nine isotonic contractions. These responses are similar to responses reported in experiments by Brutseart et al. (6) except for the time scale. The latter responses are slower because of a relatively low temperature (26°C) in their experiments.

APPENDIX 2

Flow Diagram of Model Calculations

To elucidate the incorporation of the model of left ventricular wall mechanics as presented earlier (4) into the larger model of the heart as a pump, the related calculations are outlined below.

In a reference state, close to the end-diastolic control state, the dimensions of the cylinder, the fiber orientation, and the aortic input impedance were obtained from the input list. Then in the end-diastolic state of the cardiac cycle to be simulated, at time \( t = 0 \), initial conditions were set by passive inflation (or deflation in case of hypovolemia) of the cylinder to the end-diastolic left ventricular volume (preload), followed by setting the aortic pressure to its end-diastolic value (afterload) and the aortic volume flow to zero. As pointed out earlier (4) the torsion angle \( \gamma \) and the base-to-apex length of the cylinder \( h \) were estimated and adjusted so that the equilibria of axial force \( F_z \) and torque \( T_z \) were satisfied with sufficient accuracy. After the first output list, corresponding with \( t = 0 \), in each shell the sarcomere length of the contractile mechanism \( \sigma \) was set to the sarcomere length, as calculated for \( t = 0 \) and passive elastic muscle behavior only. Then the time derivatives of left ventricular volume and the parameters related to the aortic input impedance and to the muscle contraction in each shell (APPENDIX 1) were calculated. After increasing \( t \) by 2 ms, 

\[
\sigma_t = L_r G_{\text{net}} F_{\text{ext}}(L_r - L_s) + L_s G_{\text{pass}} \left( \exp \left[ E_0 (L_r - L_s) \right] - 1 \right) \quad (A1.3)
\]

FIG. 10. Simulation of isotonic cardiac muscle contractions. Fiber stress \( \sigma \), velocity of sarcomere shortening \( \frac{dL_s}{dt} \), and sarcomere length \( L_s \) as a function of time. The indices 1-9 indicate different contractions with increasing afterload.

FIG. 11. Flow diagram of calculations associated with model (APPENDIX 2) of mechanics of left ventricle (LV). \( t \), Time; \( \gamma \), torsion angle; \( h \), base-to-apex length of cylinder; \( F_z \), axial force; \( T_z \), axial torque; and \( k \), integer value.
APPENDIX 3

Relation Between Natural Volume Strain and Stroke Volume

After application of Eq. 3 the change in volume strain from the end-diastolic control state (subscript ed) is

\[ \epsilon = - \epsilon_{ed} = \ln[(V_B + V_w)/(V_{ned} + V_a)] \]  

(A3.1)

After taking the antilogarithm of the left and the right side of Eq. A3.1 and rearranging, the left ventricular cavity volume \((V_B)\) is expressed explicitly by

\[ V_B = (V_a + V_{ned}) \exp(\epsilon) - (V_w - \epsilon_{ed}) - V_a \]  

(A3.2)

Stroke volume \(\Delta V_{s,c,b}\) is calculated as the difference between left ventricular cavity volume at the beginning and at the end of the ejection phase (subscripts be and ee, respectively), which is expressed by Eq. 5.

APPENDIX 4

Calculation of Standard Deviation in Myocardial Shear Between Layers Parallel with Wall

Shear in the wall between layers in parallel with the wall can be represented by a vector \((x, y)\) expressing the shear components along the \(x\) and \(y\) coordinates. A two-dimensional vector that is distributed symmetrically in a Gaussian way has the following probability distribution

\[ P(x, y) = \exp\left(-\frac{(x-x_0)^2}{2\sigma^2} + \frac{(y-y_0)^2}{2\sigma^2}\right) \]  

(A4.1)

where \(\sigma^2\) is the variance, which is the same in all directions. If no preferential direction is present, it holds that \((x_0, y_0) = (0, 0)\), and the distribution can be written in polar coordinates as

\[ P(r, \phi) = \exp(-r^2/2\sigma^2) \]  

(A4.2)

After integration over \(\phi\), the one dimensional probability distribution is described as a function of \(r\) by

\[ P_r(r) = \int_0^\pi P(r, \phi) d\phi = \int_0^\pi (r/d)^2 \exp(-r^2/2\sigma^2) \]  

(A4.3)

So the expected value for the magnitude of shear is

\[ \tau = \int_0^\infty r P_r(r) dr = \sigma \sqrt{\pi/2} \]  

(A4.5)

The value of \(\tau\) is reported in the literature so the standard deviation of the shear \(\sigma\) can be calculated.

REFERENCES


APPENDIX 5

Relation Between Strain in Principal Directions and Deformation Parameters

Let us assume that \(\epsilon, \epsilon_1\), and \(\epsilon_2\) represent the circumferential natural strain, base-to-apex natural strain, and shear angle, respectively. Then a first-order approximation of the natural strain along a line, forming an angle \(\beta\) with the circumferential direction is

\[ \epsilon(\beta) = \epsilon + \cos\beta \epsilon_1 + \sin^2\beta \epsilon_2 + \gamma \cos \beta \sin \beta \]  

(A5.1)

The maximum and minimum values of \(\epsilon(\beta)\) are found by solving \(d\epsilon(\beta)/d\beta = 0\), which results in

\[ \tan(2\beta) = \gamma/(\epsilon_1 - \epsilon) \]  

(A5.2)

Substitution of the thus found values of \(\beta\) into the first equation results in the maximum \((\epsilon_{\max})\) and the minimum \((\epsilon_{\min})\) values of the natural strain, which also are the principal strains

\[ \epsilon_{\max,\min} = \epsilon + \epsilon_1 + \sqrt{(\epsilon_1 - \epsilon)^2 + \gamma^2}/2 \]  

(A5.3)

APPENDIX 6

Relation Between Fiber Stress, Sarcomere Length, Left Ventricular Volume, and Left Ventricular Pressure

A small decrease in left ventricular cavity volume \(dV_h\) is related to an amount of pumping energy

\[ dE_p = P_d dV_h \]  

(A6.1)

where \(P_d\) is left ventricular pressure. Assuming a uniform distribution of \(L_s\) and \(\sigma\) across the left ventricular wall, the energy that is generated by the fibers in the wall equals

\[ dE_f = \sigma dL dV_h \]  

(A6.2)

where \(\sigma\) is fiber stress, \(L_s\) is sarcomere length, \(dL\) is change in sarcomere length, and \(V_h\) is wall volume. Because the wall generates the pumping energy it holds

\[ dE_w = dE_f \]  

(A6.3)

After rewriting and differentiating Eq. 6, the result for \(dV_h/dL_s\) is substituted in Eq. A6.4, which finally results in Eq. 7.

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