A comparison of pressure-volume relations of the fetal, newborn, and adult heart

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A comparison of pressure-volume relations of the fetal, newborn, and adult heart. Am. J. Physiol. 222(5): 1285–1290. 1972.—A marked paucity of information exists concerning the physiological characteristics of the developing heart. The purpose of the present investigation was to analyze and compare the compliance of the right and left ventricles in hearts obtained from 8 fetal and 9 newborn lambs and 10 adult sheep. Moreover, to assess the influence of filling of the contralateral chamber on distensibility, the distensibility of each ventricle was determined both with the opposite ventricle empty and at various fixed pressures. Using various models of left and right ventricular geometry, the pressure-volume data were converted to units of wall tension and percentage change in internal radius, allowing a direct comparison of all of the age groups studied. In addition, the concentrations of ventricular hydroxyproline were determined to evaluate the contribution of connective tissue to compliance at each age level. The major findings of the present study indicate that the pressure-volume and wall tension-radius relations of both the left and right ventricles are comparable in the fetal lamb close to term. In the newborn period, the right ventricle has compliance characteristics similar to the right ventricle of the fetus. The adult right ventricle is significantly more compliant than both the fetus and newborn. In the early postnatal period, the left ventricle alters its pressure-volume and stress-strain characteristics and assumes an intermediate position between fetus and adult. At all ages the right ventricle is more compliant than the left ventricle. When one evaluates the influence of filling one ventricle on reducing the distensibility of the opposite ventricle, the most profound effect is observed in the fetus, followed by the newborn, and then the adult.

MATERIAL AND METHODS

Whole hearts were excised rapidly from 14 adult sheep (1–3 years old) and 14 newborn lambs (12 ± 4 SE days old) after pentobarbital anesthesia (15 mg/kg iv). The group of newborns ranged in age from 1 to 25 days and included 7 lambs less than 10 days of age. Adult and newborn animals were ventilated artificially with a Harvard positive-pressure respirator. Pregnancies were confirmed radiographically in ewes with known breeding dates. The hearts of 19 fetal lambs (138 ± 3 days gestational age, term = 147 days) were removed rapidly after hysterotomy under spinal anesthesia (4 ml of 1% lidocaine).

All hearts were rinsed and suspended in saline at a constant temperature of 32°C. The coronary arteries were ligated immediately beyond the coronary ostia, and each A-V groove was clamped to prevent ventriculoatrial regurgitation. Grooved steel plugs incorporating three metallic cannulas were tied into the aortic and into the pulmonary annulus. One cannula was connected to a pressure transducer (Statham model P23 Db), another to a spring-loaded manual syringe, and the third cannula was connected to a vertical tubing utilized to regulate intracavitary pressure.

Pressure-volume determinations were begun within 15 min of cardiectomy. The pressure signals and volume increments were inscribed on a Clevite-Brush recorder, model 260. During continuous monitoring of intraventricular pressure, intracavitary ventricular volume changes
were accomplished by infusing or withdrawing preset incre-
ments of saline at 32 °C at fixed intervals: 2 ml for the adult
heart and 0.2 ml for the newborn and fetal hearts. The
initial pressure-volume relationship for each ventricle was
determined with the opposite ventricle empty. Zero pressure
was defined arbitrarily as the intracavitary pressure existing
at zero volume, and the absence of a leak in the system was
verified by measured withdrawal of the total amount of
infused fluid after each experimental run. To avoid over-
distension of the ventricles, the volume infusion was stopped
arbitrarily at an intracavitary pressure of 30 mm Hg.

Following the inscription of pressure-volume relations
with the opposite ventricle empty, each ventricular chamber
was kept at a constant pressure of 5 or 15 mm Hg by saline
infusions and adjustment of the height of the vertical siphon
tube in order to study the influence of different ventricular
filling pressures (5 and 15 mm Hg) on the pressure-volume
relations of the opposite ventricle. A final pressure-volume
relation was determined for each ventricle with the contra-
lateral chamber empty. All final measurements were within
10% of those obtained at the beginning of the experiment.

Cardiac dimensions were determined with the heart at
the zero-pressure point. The wall thickness was measured
at the anterolateral aspect of the wall in both ventricles, 3 cm below the A-V groove in the adult, 1 cm in the new-
born and fetus. These values were not used to calculate
ventricular wall tension (vide infra). The RV and LV long
axes were the longest distances measured between the apex
and base.

The RV and LV circumferences were measured at the
level of the tricuspid and mitral orifices, respectively. Cir-
cumference/axis ratios were employed as indicators of
ventricular shape.

Connective Tissue Comparison

Hearts were removed from a separate group of eight fetal
lambs and eight adult sheep whose ages matched those
employed in the pressure volume experiments. Samples of
interventricular septum were dissected free of epicardium
and endocardium, minced, blotted, and weighed. Water
content was determined by drying to constant weight (24
hr at 100 °C in vacuo over P2O5). Dry samples, weighing
between 5 and 10 mg, were assayed for hydroxyproline by
the method of Prockop and Udenfriend (16), and the con-
centration of hydroxyproline was expressed in micro-
grams per milligram of either dry or wet weight.

Stress-Strain Calculations

A) Left ventricle. Left ventricular wall tension was calcu-
lated using two different spherical and one ellipsoidal
geometrical model (1, 3, 7, 8, 20, 22, 23). For all calcula-
tions, left ventricular mass corresponded to the left ventricu-
lar free wall and septum, and its homogeneous distribution
was assumed. Wall thickness was calculated by subtracting
the internal radius (Ri) derived at any given volume from
the external radius (R0).

The following equations for tension (g/cm²) were em-
ployed:

\[ \text{Sphere 1:} \quad \frac{\text{PR} \cdot R_i^2}{2h} \quad (1) \]

where PR = pressure (g/cm²), \( R_i \) = internal radius (cm),
\( R_0 \) = external radius (cm), \( h \) = wall thickness (cm), \( L \) = lon-
gitudinal axis (cm).

The relationships between the tension-radius curves of
the fetal, newborn, and adult groups were not dependent
on the geometrical model utilized for calculating left ven-
tricular wall tension. Thus, only data derived from em-
ploying equation 1 (\( \text{PR} \cdot R_i^2/2h \)) will be presented in
this report.

B) Right ventricle. Right ventricular wall tension was
calculated employing equation 3 above. \( R_1 \) was calculated by
assuming that right ventricular internal volume was
represented by a hemiellipsoid, and right ventricular free
wall mass was distributed homogeneously about the curved
surface. Right ventricular wall thickness was calculated in
the manner described above for the left ventricle.

Methods of Comparison

In order to compare directly the distensibility of the
fetal, newborn, and adult right and left ventricles, all of
different sizes and weights, the changes in wall tension were
analyzed as a function of the percentage change in \( R_i \). The
control value for \( R_i \) corresponded to the calculated \( R_i \) at a
wall tension of 5 g/cm².

In order to calculate ventricular compliance, the pressure-
volume and tension-radius data of each chamber, with zero
volume and pressure in the opposite ventricle, were fitted
to an exponential relationship in every experiment by the
method of least squares approximation (21). The pressure
volume and tension-radius relations were defined as
\( P = a + b \cdot e^{-y} \) and \( T = a + b \cdot e^{-b \cdot t} \), respectively, when \( P = \) pressure (mm Hg), \( T = \) tension (g/cm²), \( V = \) volume
(ml), \( R_i = \) internal radius, and \( a, b, c \) are constants.

It is apparent from these equations that the slope of
either the pressure-volume or tension-radius curves at any
level of pressure or tension depends primarily on the
magnitude of the constant \( c \).

RESULTS

Anatomic Findings

Cardiac chamber weights and dimensions are summarized
in Table 1 and related to body weight in Fig. 1. There were
no significant differences between the weights of the free
walls of either ventricle in the fetus or between the thickness
of the fetal and the newborn right ventricles. Figure 1
demonstrates that relative to body weight there is a disprop-
ortionate growth of the left ventricle in the postnatal
period. Moreover, total heart weight constituted a signifi-
cantly greater percentage of body weight in both the fetus
(0.60%) and newborn (0.73%) when compared to the
adult (0.49%, \( P < 0.001 \)). Although the absolute weights
of both ventricles increased postnatally, the newborn right
ventricle was only 29.7% heavier than the fetal right
ventricle, whereas the left ventricular free wall almost
TABLE 1. Cardiac chamber weights and dimensions

<table>
<thead>
<tr>
<th></th>
<th>Fetus (8)</th>
<th>Newborn (9)</th>
<th>Adult (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>138 ± 3 days</td>
<td>11.9 ± 4 days</td>
<td>1.7 ± 0.5 years</td>
</tr>
<tr>
<td>Body wt, kg</td>
<td>3.9 ± 0.2*</td>
<td>5.27 ± 0.5*</td>
<td>50.4 ± 3.3*</td>
</tr>
<tr>
<td>Heart wt, g</td>
<td>23.3 ± 1.4</td>
<td>38.1 ± 3.4</td>
<td>251.1 ± 16.7</td>
</tr>
<tr>
<td>LV wt + septum, g</td>
<td>12.6 ± 0.3</td>
<td>21.8 ± 2.8</td>
<td>146.9 ± 9.7</td>
</tr>
<tr>
<td>LV wt free wall, g</td>
<td>8.0 ± 0.6</td>
<td>14.7 ± 1.9</td>
<td>100.3 ± 5.4</td>
</tr>
<tr>
<td>RV wt free wall, g</td>
<td>NS</td>
<td>9.6 ± 0.7</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>LV wall thickness, mm</td>
<td>P &lt; 0.05</td>
<td>8.0 ± 0.4</td>
<td>55.2 ± 3.5</td>
</tr>
<tr>
<td>RV wall thickness, mm</td>
<td>NS</td>
<td>P &lt; 0.001</td>
<td>15.9 ± 0.7</td>
</tr>
<tr>
<td>RV long axis, cm</td>
<td>7.4 ± 0.4</td>
<td>P &lt; 0.01</td>
<td>6.95 ± 0.6</td>
</tr>
<tr>
<td>LV long axis, cm</td>
<td>3.8 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>8.19 ± 0.3</td>
</tr>
<tr>
<td>RV long axis, cm</td>
<td>NS</td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>LV circumf, cm</td>
<td>3.7 ± 0.3</td>
<td>3.6 ± 0.1</td>
<td>7.16 ± 0.2</td>
</tr>
<tr>
<td>RV circumf, cm</td>
<td>4.86 ± 0.26</td>
<td>3.9/0 ± 0.17</td>
<td>10.55 ± 0.44</td>
</tr>
<tr>
<td>LV circumf</td>
<td>NS</td>
<td>P &lt; 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>LV long axis</td>
<td>1.27 ± 0.07</td>
<td>1.31 ± 0.10</td>
<td>1.31 ± 0.06</td>
</tr>
<tr>
<td>RV long axis</td>
<td>4.14 ± 0.26</td>
<td>4.23 ± 0.18</td>
<td>10.36 ± 0.47</td>
</tr>
<tr>
<td>RV circumf</td>
<td>1.09 ± 0.06</td>
<td>NS</td>
<td>1.19 ± 0.08</td>
</tr>
<tr>
<td>LV wall thickness, mm</td>
<td>P &lt; 0.05</td>
<td>1.9 ± 0.2</td>
<td>1.46 ± 0.09</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate number of observations. * Values are averages ± SE.

Pressures-Volme Relations of Developing Heart

The average pressure-volume curve for each ventricle at each age is shown in Fig. 2. No significant differences existed in the pressure-volume relations of either ventricle in the fetus, whereas the relatively greater stiffness of the left ventricle compared to the right becomes apparent in the newborn period and is quite striking in the adult.

The influence of filling of either ventricle on the pressure-volume relationships of the opposite ventricle is illustrated in Fig. 3. Both right and left ventricular pressure-volume relationships were comparable with either 0 or 5 mm Hg pressure in the opposite ventricle. However, at any age, pressures of 15 mm Hg in either ventricle significantly decreased the volume necessary to achieve an intracavitary pressure of 5 mm Hg in the contralateral chamber. This


doubled in weight (+03.8%). The weight gain of the ventricular septum more closely paralleled that of the left ventricle (+54.3%). The wall thickness of both ventricles was comparable in the fetus. However, the postnatal changes in left ventricular wall thickness are considerable (+42.9%), while the thickness of the newborn right ventricle is little changed from that of the fetus (+9.1%).

Hydroxyproline is found only in collagen and forms a constant concentration of collagen (9). In order to evaluate the influence of collagen on ventricular distensibility, the concentration of hydroxyproline in fetal and adult ventricles was determined (Table 2). When compared to the adult, the fetal ventricle has a lower hydroxyproline concentration per gram of wet weight, but since the fetal myocardium contained a significantly higher water content (79 ± 0.9 vs. 74.3 ± 0.5yo, respectively, P < 0.001), there were similar hydroxyproline concentrations when the data were expressed in terms of dry weight.

TABLE 2. Hydroxyproline concentrations and water content

<table>
<thead>
<tr>
<th></th>
<th>Water Content (%)</th>
<th>HOFO, µg/g wet wt</th>
<th>HOFO, µg/g dry wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetus (8)</td>
<td>79.7 ± 0.9*</td>
<td>0.427 ± 0.03</td>
<td>1.8 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.01</td>
<td>P = NS</td>
</tr>
<tr>
<td>Adult (8)</td>
<td>74.3 ± 0.5</td>
<td>0.791 ± 0.09</td>
<td>2.5 ± 0.41</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate number of observations. * Values are averages ± SE.

pressure-volume relationships of the opposite ventricle is illustrated in Fig. 3. Both right and left ventricular pressure-volume relationships were comparable with either 0 or 5 mm Hg pressure in the opposite ventricle. However, at any age, pressures of 15 mm Hg in either ventricle significantly decreased the volume necessary to achieve an intracavitary pressure of 5 mm Hg in the contralateral chamber. This
The absolute left ventricular pressure-volume data for each group were pooled and fitted exponentially as described under Methods (Table 3). It was evident that the constant $c$, the major determinant of the slope of the curves, was significantly higher for the fetal left ventricle when compared to either the newborn ($P < 0.05$) or adult ($P < 0.001$). In contrast, this constant for the right ventricle showed no differences between fetus and newborn, but at both young ages was substantially greater than for the adult right ventricle ($P < 0.001$) (Table 3).

### Tension-Radius Relations

Because the cardiac chambers differ in size at the various ages, it was necessary to analyze the changes in wall tension as a function of changes in internal radius in order to compare the fetus, newborn, and adult directly.

A) The left ventricular tension-radius relations with zero volume and pressure in the right ventricle are illustrated in Fig. 4.

At any increment of left ventricular internal radius, left ventricular wall tension was significantly greater in the fetus when compared to the newborn or adult ($P < 0.025$). No significant differences were demonstrated between the newborn and the adult. Moreover, the average slope of the fetal curve was significantly greater than both newborn and adult ($P < 0.001$); in the newborn the slope was significantly greater than the adult ($P < 0.01$) (Table 3).

B) Right ventricle. Comparative data for the three age groups studied are illustrated in Fig. 5. For any increment in internal radius, the development of right ventricular wall tension was significantly higher in the fetus and newborn when compared to the adult ($P < 0.01$). The fetus and newborn exhibited similar right ventricular tension-radius curves. The equations for the average slopes of these curves are noted in Table 3.

### DISCUSSION

The results of the present study indicate that the pressure-volume and wall tension-radius relations of both the left and right ventricles are comparable in the fetal lamb close to term. In the newborn period the right ventricle has compliance characteristics similar to the right ventricle of the fetus, and the adult right ventricle is significantly more compliant than either the fetal or newborn right ventricle. In the early postnatal period, the left ventricle alters its compliance characteristics and assumes an intermediate position between fetus and adult. At all ages, the right ventricle is more compliant than the left ventricle. When one evaluates the influence of filling one ventricle on reducing the distensibility of the opposite ventricle, the most profound effect is observed in the fetus, followed by the newborn and then the adult. This increased sensitivity of the fetal ventricle to filling of the contralateral chamber may explain the ease with which the prenatals and newborn human infant exhibits systemic venous congestion in the presence of lesions primarily deranging left ventricular volume or pressure (13).

A number of factors may be responsible for the distensibility differences observed between the young and old hearts. Well-known differences exist in various mammalian species in the mass relationships between the two ventricles...
### TABLE 3. Exponential fit of grouped data

<table>
<thead>
<tr>
<th></th>
<th>Left ventricle</th>
<th>Right ventricle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fetus (8)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(P = 2 + 2.4e^{0.3V})</td>
<td></td>
<td>(P = 0.93 + 1.1e^{0.4V})</td>
</tr>
<tr>
<td>(P &lt; 0.05)</td>
<td></td>
<td>(P = NS)</td>
</tr>
<tr>
<td><strong>Newborn (9)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(P = 0.01 + 1.9e^{0.4V})</td>
<td>(P = -0.18 + 1.2e^{0.6V})</td>
<td>(P &lt; 0.001)</td>
</tr>
<tr>
<td>(P &lt; 0.05)</td>
<td>(P &lt; 0.001)</td>
<td></td>
</tr>
<tr>
<td><strong>Adult (10)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(P = 3.3 + 0.2e^{-0.2V})</td>
<td></td>
<td>(P = 1.0 + 0.2e^{0.0V})</td>
</tr>
<tr>
<td>(P &lt; 0.05)</td>
<td></td>
<td>(P &lt; 0.001)</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate number of observations.

![Graph](image)

**FIG. 4.** Left ventricular tension-radius relations with right ventricle empty. Control left ventricular radius (100%) corresponds to radius at a calculated wall tension of 5 g/cm². At any radius, left ventricular wall tension was significantly greater in fetus than in newborn or adult \((P < 0.025)\). No significant differences were observed between newborn and adult.

In the perinatal period when compared to the adult \((11, 12)\), the rapidly thickening newborn left ventricle begins to approximate the adult left ventricle in its stress-strain relations, while the right ventricular wall thickness and stress-strain relations are still similar to those of the fetus.

We have found that compliance increases with advancing development in cardiac muscle isolated from the right ventricles of fetal lambs and adult sheep \((5, 17)\). These findings parallel those obtained in the present study utilizing the whole heart. However, the isolated muscle differences cannot be accounted for by the alterations in the mass relationships between the ventricles, since the curves relating resting tension to muscle length are significantly steeper in the fetus and newborn, even when the tensions generated by the isolated muscles are corrected for muscle cross-sectional area. In this regard, we have observed major ultrastructural differences between fetal and adult myocardium that may help explain a reduced compliance in the young heart \((6, 17)\). The diameter of the myofilaments is significantly less in

![Graph](image)

**FIG. 5.** Right ventricular tension-radius relations with left ventricle empty. As in Fig. 4, control right ventricular radius (100%) was defined as radius corresponding to 5 g/cm² right ventricular wall tension. At any radius right ventricular wall tension was significantly higher in both fetus and newborn than in adult \((P < 0.05)\). No significant differences existed between fetus and newborn.
the fetal than the adult heart and, furthermore, it is evident that in the young hearts the proportion of noncontractile mass (nuclei, mitochondria, and surface membranes) to the number of myofilaments is significantly higher than in the adult. Thus, relatively increased amounts of noncontractile cellular elements, including surface membranes, may contribute to the age-related differences in ventricular distensibility (6).

There are several factors that may be excluded as accounting for the apparent stiffness of the fetal and newborn hearts. Experiments demonstrating changes in pressure-volume relations following coronary perfusion with collagenase (14) indicate that passive ventricular distensibility may be influenced by interstitial connective tissue. In the present study there were no significant differences in cardiac hydroxyproline concentration when the data were corrected for dry weight. However, when corrected for wet weight, there was significantly more hydroxyproline found in the adult, since the young heart has a higher water content. Since our compliance and connective tissue findings are directionally opposite, the age-related changes in collagen concentration cannot offer an explanation for the reduced compliance found in the youngest hearts in the present study. Similarly, differences in postmortem rates of change in distensibility cannot be proposed, since there was agreement between initial and final pressure-volume curves in all hearts in the present study.

No apparent geometrical differences in left ventricular shape existed between the three groups to account for the results obtained. In this regard, the somewhat more spherical shape of the adult right ventricle may have minimized the substantial differences in right ventricular distensibility that existed at the age extremes, since the more spherical shape would increase the calculated values of wall tension (18). Moreover, because the wall thickness of either ventricle in the adult is less relative to chamber weight when compared to the fetus and newborn, even greater differences would be observed than calculated by the present methods. It is known that clamping the mitral valve may alter the slope of a pressure-volume relationship (15). In the study by Powell et al. (15) the average increase in stiffness associated with clamping the mitral valve was 0.97 cm H2O/ml of infused volume. It is unlikely that our findings were influenced significantly by A-V valve clamping, since far greater age-related differences were observed than could be accounted for in the absence of clamping.

Since the elasticity of a biological structure is a history-dependent phenomenon (7), it is possible that our results might be different if our wall tension-radius calculations were based on different initial lengths. In order to examine this question, tension-radius relations were constructed from an initial length corresponding to the internal radius at calculated ventricular wall tensions of 10 g/cm2. No alterations were produced by this technique in the age-related differences in distensibility.

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REFERENCES