Variation of mechanical properties along the length of the aorta in C57bl/6 mice

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Guo, Xiaomei, and Ghassan S. Kassab. Variation of mechanical properties along the length of the aorta in C57bl/6 mice. Am J Physiol Heart Circ Physiol 285: H2614–H2622, 2003; 10.1152/ajpheart.00567.2003.—The objective of the present study is to obtain a systematic set of data on the mechanical properties along the entire length of the mouse aorta. The ascending aorta of seven mice was cannulated near the aortic valve, and the aorta was preconditioned with several cyclic changes in pressure. The perfusion pressure was then increased in 30-mmHg increments from 0 to 150 mmHg. Cab-O-Sil, colloidal silica, was mixed into the perfusate to prevent flow through the microvessels and hence attain zero-flow distensions. Our results show that the residual circumferential strain leads to a uniformity of transmural strain of the aorta in the loaded state along the entire length of the aorta. This uniformity is attained in the range of 60–120 mmHg. At pressures <60 mmHg, the outer strain is greater than the inner strain, whereas at pressures >120 mmHg, the converse is true. Furthermore, we found that the circumferential and longitudinal stress-strain relationships are linear in the pressure range of 30–120 mmHg. Finally, the circumferential modulus is greatest (most rigid) near the diaphragm, and the majority of volume compliance (85%) is in the thoracic compared with the abdominal aorta. These findings are important for an understanding of the hemodynamics of the cardiovascular system of the normal mouse and will serve as a reference state for the study of various diseases in knock-in and knock-out models of this species.

stress; strain; elastic modulus; zero-stress state; strain energy function

THE AORTA acts as both a conduit and an elastic chamber. In its latter role, the elasticity of the aorta serves to convert the heart’s pulsatile flow to a steady flow in peripheral vessels. In 1733, Stephen Hales (17) reported his observations that the aorta expands to accommodate a large fraction of the stroke volume. Hales reasoned that the aorta serves as an elastic reservoir that distends with blood during the heart’s contraction and discharges blood through the peripheral resistance by elastic recoil while the heart refills. An analogy was made with a hand-pump fire engine, which smooths a pump’s pulsatile flow of water. In 1899, Otto Frank used this analogy to formulate the well-known wind-kessell theory.

The data on the elasticity of the aorta are enormous (see reviews in Refs. 11, 12, and 27). One of the reasons for the great interest stems from the observation that increased stiffness of large elastic arteries represents an early risk factor for cardiovascular diseases (2, 19). Specifically, increased aortic stiffness is associated with aging (3, 14, 28), hypertension (10, 18), diabetes (1, 26, 29), hyperlipidemia (23), atherosclerosis (6), heart failure (21), and smoking (25, 31). Furthermore, arterial stiffness has also been shown to be an independent risk factor for cardiovascular events such as primary coronary events, stroke, and mortality (5, 22). Therefore, the assessment of aortic mechanical properties is particularly important in understanding the mechanisms of cardiovascular disease.

Although many species have been studied (see review in Ref. 27), there are no data on the variation of mechanical properties along the entire length of the in situ aorta of any species. We are interested in such data in the mouse model because the mouse is being used with increasing frequency in experimental studies of many aspects of cardiovascular health and disease. In the present study, we focus on the C57BL/6J strain because it is the most widely used and hence the best known of all inbred strains. Furthermore, it has substrains that are predisposed to hypertension, diabetes, and hypercholesteremia, all of which are important risk factors for coronary artery disease (9, 28). The major goal of the present study is to characterize the mechanical properties of the mouse aorta to understand its physiological implications. Furthermore, the present study provides a phenotypic model for genotypic manipulation.

METHODS

Animal Experiments

A group of seven homozygous inbred male mice (C57BL/6 strain) with body weight of 24.7 ± 1.49 g and age 68.3 ± 3.2 days was used in this study. The mice were preanesthetized with intraperitoneal injections of ketamine (56.2 mg/kg) and midazolam (3.75 mg/kg) to achieve requisite immobilization. The mice were then anesthetized with an intraperitoneal injection of pentobarbital sodium (40 mg/kg). Aortic blood pressure was measured by a catheter inserted into the common carotid artery. Heparin

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(200 U/ml) was used to prevent blood clots in the heart and the vessels via a jugular vein catheter. A tracheostomy was performed, and the mouse was ventilated with a rodent respirator. The chest was opened with a midline sternotomy. The mouse was euthanized with pentobarbital sodium (120 mg/kg iv), and the apex of the heart was excised. All experiments were performed in accordance with national and local ethical guidelines, including the Institute for Laboratory Animal Research Guide, National Institutes of Health Policy, Animal Welfare Act, and University of California Institutional policies regarding the use of animals in research.

**Pressure-Diameter-Length Relation**

The ascending aorta was cannulated by a 23-gauge needle through the apex of the left ventricle. The aorta from the aortic valve to the common iliac bifurcation was then carefully exposed on the anterior portion (dissected away the surrounding connective tissue) leaving the posterior portion attached. The aorta was then perfused with 6% dextran solution at the various perfusion pressures. Cab-O-Sil (0.35% by weight), a colloidal silica, was mixed into the Dextran solution to prevent flow through the microvessels and hence attain zero-flow distensions. Water-resistant carbon particles were used to mark the aorta, dividing it into a series of 10 short segments (about 3–4 mm per segment). The aorta was preconditioned with three cyclic changes in pressure from 0 to 150 mmHg in a triangular form. The perfusion pressure was increased in 30-mmHg step increments from 0 to 150 mmHg in a staircase pattern. The external geometry of each segment of the aorta, at the pressurized state, was photographed to obtain the loaded outer diameter along the trunk of the aorta. The outer diameter-length-pressure relation for each of the 11 segments was measured serially. A local dimensional coordinate \( x \) was introduced along the loaded vessel trunk, with \( x = 0 \) at the aortic valve and \( x = 1 \) at the point of common iliac bifurcation as shown in Fig. 1. The coordinate \( x \) represents the length measured from the aortic valve, along the centerline of the aorta, divided by the total length at the pressurized state.

**No-Load and Zero-Stress State**

After the mechanical testing, the aorta was carefully dissected and placed into a Ca\(^{2+}\)-free Krebs solution (composition in mM: 117.9 NaCl, 4.7 KCl, 1.2 MgCl\(_2\), 25 NaHCO\(_3\), 1.2 NaH\(_2\)PO\(_4\), 0.0027 EDTA, 0.1 ascorbic acid, and 11 glucose). The anterior position of the aorta was marked with carbon from the aortic valve down to the common iliac artery. The entire length of the aorta was then cut into 50–60 segments. Each segment was a ring with length of 0.3–0.5 mm (thoracic aorta: 0.4–0.5 mm, abdominal aorta: 0.3–0.4 mm). Each ring was transferred to a Ca\(^{2+}\)-free Krebs solution, aerated with 95% O\(_2\)-5% CO\(_2\), and photographed in no-load state. Each ring was then cut radially by a scissor at the anterior position labeled with carbon black particles. The ring opened into a sector and gradually approached a constant opening angle defined as the angle subtended by two radii connecting the midpoint of the inner wall. The cross section of each sector was photographed 30 min after the radial cut. The morphological measurements of inner and outer circumference, wall thickness, and area in the no-load and zero-stress state were made from the images using a morphometric analysis system (Sigma Scan). The length of each ring was measured at the no-load state, and a local dimensional coordinate \( a \) was introduced along the vessel trunk, with \( a = 0 \) at the aortic valve and \( a = 1 \) at the bifurcation of the common iliac artery as shown in Fig. 1. The coordinates \( x \) and \( a \) are referred to as the fractional longitudinal position (FLP) in the loaded and no-load states, respectively (20).

**Biomechanical Analysis**

**Incompressibility condition.** The incompressibility condition for a cylindrical vessel can be expressed as

\[
\frac{r_2}{r_0} = \frac{A_0}{\pi \lambda_0} \quad (1a)
\]

where \( r_0 \) and \( r_1 \) are the outer and inner radii at the loaded state, respectively; \( \lambda_0 \approx l/l_0 \) is the stretch ratio in the axial direction where \( l \) and \( l_0 \) are the vessel length in the loaded and zero-stress state, respectively; and \( A_0 \) is the wall area in the no-load state. The vessel length \( l \) may correspond to either a segment (each of the 11 segments marked along the length of the aorta) or to the entire length of the aorta (distance from aortic valve to common iliac bifurcation). In the former we define a local and in the latter a global longitudinal stretch ratio.

It should be noted that \( r_1 \) and \( A_0 \) are functions of coordinate axes \( x \) and \( a \), respectively. Because \( a = x/l_0, \) Eq. 1a can be rewritten as

\[
\frac{r_2}{r_0} = \frac{A_0[x/\lambda_0(x)]}{\pi \lambda_0(x)} \quad (1b)
\]

**Equation 1b** was used to compute the variation of inner radius along the aorta at various distension pressures (15).

**Strain and stress.** The circumferential deformation of the artery may be described by the Green strain (\( \varepsilon_\theta \)), which is defined as follows

\[
\varepsilon_{\theta i,o} = \frac{1}{2} [\lambda_{\theta i,o} - 1] \quad (2a)
\]

where \( \lambda_{\theta i,o} \) is the inner or outer circumferential stretch ratio (\( \lambda_{\theta i,o} = c_{i,o}\varepsilon_{\theta i,o} \); \( c_{i,o} \) refers to the inner or outer circumference

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**Fig. 1.** Schematic of the aorta in the loaded (left) and no-load state (right). Coordinate systems \( x \) and \( a \) are shown for the loaded and no-load states, respectively.

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of the vessel in the loaded or no-load state; and $c_{sw}$ refers to
the inner or outer circumference in the zero-stress state as
described in the previous section. In the no-load state, the
strain given by $\varepsilon = \frac{1}{2} (\lambda^2 - 1)$
is referred to as the residual strain. Similarly, the longitudinal
Green strain is given by
$$\varepsilon_z = \frac{1}{2} (\lambda_z^2 - 1)$$
(2b)
where $\lambda_z$ is the local longitudinal stretch ratio as defined
above.

At an equilibrium condition, the average circumferential
Kirchhoff stress in the vessel wall was computed, with an
assumption that the shape of the artery is cylindrical
$$\tau_0 = \frac{P r_i}{h z_o^2}$$
(3a)
where $P$ is the luminal pressure and $\lambda_0$ and $h$ are the
circumferential stretch ratio and wall thickness of the vessel,
respectively. The longitudinal Kirchhoff stress, under similar
assumptions, is given by
$$\tau_z = \frac{P r_i}{(r_i + r_o) z_o^2}$$
(3b)

Equations 2 and 3 allow us to compute the circumferential
and longitudinal stresses and strains, respectively, for dif-
ferent pressure distensions.

Elastic moduli. A pressurization of a blood vessel induces
biaxial (circumferential and longitudinal) stresses and
strains. The increase in the circumference during pressuriza-
tion will tend to shorten the vessel longitudinally because of
incompressibility (Eq. 1a) but also tend to lengthen the vessel
because of the longitudinal stress arising from pressuriza-
tion (Eq. 3b). The Poisson’s ratio ($\nu = -\frac{\Delta h/\Delta h}{\Delta d/\Delta d}$) and the elastic
moduli ($E_0$ and $E_z$) determine whether the vessel shortens or
lengthens. In analogy to an isotropic tube, Dobrin and Doyle
(8) expressed the relationship between the circumferential and
longitudinal strains for an anisotropic vessel as
$$\Delta \varepsilon_z = \frac{\Delta \varepsilon_z}{E_z} - \frac{\Delta \varepsilon_z}{E_z}$$
(4a)
and
$$\Delta \varepsilon_z = \frac{\Delta \varepsilon_z}{E_z} - \frac{\Delta \varepsilon_z}{E_z}$$
(4b)
where $\Delta$ signifies a change in a quantity. Equations 4a and 4b
can be solved for the respective moduli as
$$E_z = \frac{\Delta \varepsilon_z}{\Delta \varepsilon_z} + \left(\frac{\Delta \varepsilon_z}{\Delta \varepsilon_z}\right)^2 \frac{\Delta \varepsilon_z}{\Delta \varepsilon_z}$$
(5a)
and
$$E_z = \frac{\Delta \varepsilon_z}{\Delta \varepsilon_z} \left[ \frac{1}{\Delta \varepsilon_z} \frac{\Delta \varepsilon_z}{\Delta \varepsilon_z} \right]$$
(5b)

It should be noted that as $E_z$ tends to infinity, $E_0$ tends to
$\Delta \varepsilon_z/\Delta d_0$, which is the definition of the tangent modulus (or
Young’s modulus if the stress-strain relation is linear) for a
uniaxial experiment.

Compliance. The lumen cross-sectional area (CSA) was
computed from the lumen radius as given by Eq. 1b (CSA =
$\pi r_i^2$). The lumen volume ($V$) of the entire aorta can be conse-
quently computed as
$$V = \int_0^L \text{CSA}(x) \, dx$$
(6)
where $L$ is the total length of aorta (aortic valve to common iliac bifurcation).

The volume compliance ($C_V$) of the aorta is given as the
slope of the pressure-volume relationship; i.e., $C_V = \Delta V/\Delta P$.
The CSA compliance ($C_{CSA}$) is defined similarly as $C_{CSA} =
\Delta \text{CSA}/\Delta P$. The relationship between $C_V$ and $C_{CSA}$ can be expressed
through the chain rule of differentiation as
$$C_V = C_{CSA} L + \text{CSA} \frac{\Delta L}{\Delta P}$$
(7)

Constitutive equation. A strain-stress relation for an artery
can be determined from a strain energy function, which
represents stored energy per unit volume of arterial wall. For
a linear stress-stain relation, the strain energy function, in
a two-dimensional analysis, can be expressed as a simple
second-order polynomial
$$E = b_0 W + b_1 W^2 + b_2 W^3 + b_3$$
(8)
where $p_0$ is the mass per unit volume of the artery, $W$ is the
strain energy per unit mass, and the constants $b_1$, $b_2$ and $b_3$
are material coefficients. Under the assumptions that the
arterial wall is homogeneous and pseudoelastic (i.e., the
loading and unloading curves of the stress-strain relation are
considered to represent properties of two materials with
different elasticity), the strain energy function can be applied
to loading and unloading processes separately, and stress
components are expressed as follows
$$\tau_0 = \frac{\partial (p_0 W)}{\partial E_z}$$
(9)
where $\tau_0$ and $E_z$ are components of Kirchhoff stress and
Green strain, respectively. The stress and strain components
are measured experimentally, and the coefficients of the
strain energy function, $b_1$, $b_2$, and $b_3$ can be determined
by using a linear least square fit as outlined in the APPENDIX.

Data Analysis

The position along the aorta was normalized with respect to
the total length. Hence, the results were expressed in terms of the FLIP, ranging from 0 to 1. The data for both the
independent (FLP) and dependent variables (diameter, wall
thickness, area, stress, etc.) were then divided into 10 equal
intervals: 0–0.1, 0.11–0.2, 0.21–0.3..., 0.91–1.0. The results
are expressed as means ± SD over each interval. In some
cases, we further combined the intervals into anatomic re-

gions. The thoracic aorta was divided into proximal, middle,
and posterior regions, whereas the abdominal aorta was
divided into proximal and distal regions. Anatomically, the
proximal, middle, and posterior thoracic aorta corresponds
to the following: aortic valve to first pair of intercostal arteries,
first pair to sixth pair of intercostal arteries, and sixth pair
of intercostal arteries to subcostal artery (diaphragm), respec-
tively. The proximal and distal abdominal aorta corresponds
to the subcostal artery to the left renal artery and the left
renal artery to the common iliac artery, respectively.

Either linear or nonlinear regressions were used to curve
fit the data. The longitudinal variations were examined with
a one-way ANOVA. Student’s $t$-test was also used to detect
possible differences between animals.
MECHANICAL PROPERTIES OF AORTA IN MICE

A

Fig. 2. A: variation of the local longitudinal stretch ratio with the location along the long axis of the aorta (fractional longitudinal position, FLP) at the different pressures. AA, PTh, MTh, DTh, PAb, and DAb represent ascending aorta, proximal thoracic, middle thoracic, distal thoracic, proximal abdominal, and distal abdominal, respectively. B: variation of the global longitudinal stretch ratio of the aorta ($\lambda_l$) with the pressures ($P$). Solid line is a linear least-squares fit of the form $\lambda_l = 6.82 \pm 10^{-4} P + 1.33, R^2 = 0.953$.

RESULTS

The mean arterial blood pressure of the seven mice was 96.4 ± 9.62 (means ± SD) mmHg. The longitudinal stretch ratios of the aorta in situ were obtained by direct measurement of the segmental lengths between carbon marks at various pressures and relative to the zero-stress state after excision. Figure 2A shows the variation of the local longitudinal stretch ratio along the length of the aorta at different distension pressures. The anatomic correlates of the FLP are also shown (e.g., ascending aorta; proximal, middle, and distal thoracic aorta; and proximal and distal abdominal aorta). At all distension pressures, the local longitudinal stretch ratio increased along the length of the aorta ($P < 0.01$). The data were fitted by a third-order polynomial, and the constants of a least fit are summarized in Table 1. Figure 2B shows the variation of the global longitudinal stretch ratio of the aorta as a function of pressure. The global stretch ratio is taken as the ratio of the total length of the aorta at a given pressure normalized with respect to the in vitro length at no-load state (approximately equivalent to zero-stress). As the pressure increases, the global longitudinal stretch ratio shows a significant increase ($P < 0.01$). The curve is fitted by a linear least square, and the empirical constants are summarized in the legend of Fig. 2B.

The outer diameter increases linearly with an increase in pressure for all aortic regions. The data for each region were fitted by a linear least-square fit, and the empirical constants are summarized in Table 1. The loaded inner radius was fitted from the incompressibility condition (Eq. 1). The wall thickness at the loaded state was computed as the difference between the outer and inner radius of the vessel at different pressures. The wall thickness of the aorta decreases linearly with an increase in pressure, and the least-squares fit constants are also summarized in Table 1. The variations of diameter and wall thickness along the length of the aorta were found to be statistically significant as were the variations with pressure.

The open sector in the zero-stress state was characterized by the opening angle. The longitudinal variation of the opening angle is shown in Fig. 3A. The inner and outer strains were computed in reference to the zero-stress state. The variation of inner and outer residual strain, over the length of the aorta, at a given

Table 1. Regression coefficients for longitudinal stretch ratio, outer diameter, wall thickness and lumen cross-sectional area

<table>
<thead>
<tr>
<th>Pressure, mmHg</th>
<th>Local Longitudinal Stretch Ratio</th>
<th>Outer Diameter</th>
<th>Wall Thickness</th>
<th>Lumen Cross-Sectional Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\alpha, \beta, \gamma, \delta$</td>
<td>$\alpha, \beta$</td>
<td>$\alpha, \beta$</td>
<td>$\alpha, \beta$</td>
</tr>
<tr>
<td>0</td>
<td>$-2.797, 4.238, -0.982, 1.102$</td>
<td>0.871</td>
<td>62.662</td>
<td>0.343</td>
</tr>
<tr>
<td>30</td>
<td>$-2.909, 4.417, -1.065, 1.121$</td>
<td>0.982</td>
<td>53.182</td>
<td>0.273</td>
</tr>
<tr>
<td>60</td>
<td>$-3.043, 4.630, -1.146, 1.147$</td>
<td>0.989</td>
<td>45.541</td>
<td>0.205</td>
</tr>
<tr>
<td>90</td>
<td>$-2.720, 4.173, -1.079, 1.146$</td>
<td>0.994</td>
<td>44.647</td>
<td>0.197</td>
</tr>
<tr>
<td>120</td>
<td>$-2.572, 3.924, -0.887, 1.152$</td>
<td>0.993</td>
<td>44.334</td>
<td>0.196</td>
</tr>
<tr>
<td>150</td>
<td>$-2.157, 3.268, -0.622, 1.148$</td>
<td>0.992</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


PTh, proximal thoracic aorta; MTh, middle thoracic aorta; DTh, distal thoracic aorta; PAb, proximal abdominal aorta; DAb, distal abdominal aorta; $R^2$ represents the correlation coefficient of the curve fit. Local longitudinal stretch ratio: $\lambda_l = aFLP + \beta FLP^2 + \gamma FLP + \delta$ where FLP is fractional longitudinal position; outer diameter: $D_o = aP + \beta$ where $P$ is pressure; wall thickness: $WT = aP + \beta$; lumen cross-sectional area: $CSA = aP + \beta$.  

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The variation of lumen CSA with pressure for the various segments of aorta was found to be linear. The relationship is curve fitted with a linear least-square fit, and the empirical constants are summarized in Table 1. Figure 6 shows the $C_{CSA}$ of the various aortic segments (i.e., slope of the CSA-P relation). The pressure-volume relationship of the entire aorta is shown in Fig. 7A. The slope of the curve corresponds to the compliance of the aorta, which has a value of $2.67 \times 10^{-4} \text{ ml/mmHg}$. Finally, Fig. 7B shows the volume compliance of thoracic (sum of proximal thoracic, middle thoracic, and distal thoracic) and abdominal (sum of proximal abdominal and distal abdominal) aorta.

### Table 2. Regression coefficients for circumferential and longitudinal green strain and Kirchhoff’s stress and strain energy function

<table>
<thead>
<tr>
<th>Position</th>
<th>$\alpha$, l/mmHg</th>
<th>$\beta$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Circumferential</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTh</td>
<td>$1.03 \times 10^{-2}$</td>
<td>$1.94 \times 10^{-2}$</td>
<td>0.997</td>
</tr>
<tr>
<td>MTh</td>
<td>$1.43 \times 10^{-2}$</td>
<td>$-7.98 \times 10^{-2}$</td>
<td>0.996</td>
</tr>
<tr>
<td>DTh</td>
<td>$9.56 \times 10^{-3}$</td>
<td>$-1.46 \times 10^{-1}$</td>
<td>0.990</td>
</tr>
<tr>
<td>PAb</td>
<td>$1.02 \times 10^{-2}$</td>
<td>$-2.77 \times 10^{-2}$</td>
<td>0.980</td>
</tr>
<tr>
<td>DAb</td>
<td>$9.94 \times 10^{-3}$</td>
<td>$-2.19 \times 10^{-2}$</td>
<td>0.956</td>
</tr>
<tr>
<td><strong>Kirchhoff’s stress, ( \tau (\text{kPa}) = \alpha P + \beta )</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTh</td>
<td>0.708</td>
<td>$-2.84$</td>
<td>0.999</td>
</tr>
<tr>
<td>MTh</td>
<td>0.803</td>
<td>$-2.30$</td>
<td>0.999</td>
</tr>
<tr>
<td>DTh</td>
<td>0.977</td>
<td>$-2.88$</td>
<td>0.999</td>
</tr>
<tr>
<td>PAb</td>
<td>0.770</td>
<td>$-3.99$</td>
<td>0.998</td>
</tr>
<tr>
<td>DAb</td>
<td>0.630</td>
<td>$-2.19$</td>
<td>0.999</td>
</tr>
</tbody>
</table>

<p>| <strong>Strain Energy Function, ( \psi (\text{kPa}) = b_1 \varepsilon_1^2 + b_2 \varepsilon_2^2 + b_3 \varepsilon_3^2 )</strong> | | | |</p>
<table>
<thead>
<tr>
<th>Position</th>
<th>$b_1$, kPa</th>
<th>$b_2$, kPa</th>
<th>$b_3$, kPa</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTh</td>
<td>22.6</td>
<td>$-187$</td>
<td>121</td>
<td>0.999</td>
</tr>
<tr>
<td>MTh</td>
<td>25.8</td>
<td>$-32.6$</td>
<td>86.6</td>
<td>0.999</td>
</tr>
<tr>
<td>DTh</td>
<td>36.8</td>
<td>5.72</td>
<td>54.4</td>
<td>0.998</td>
</tr>
<tr>
<td>PAb</td>
<td>19.8</td>
<td>3.31</td>
<td>28.6</td>
<td>0.999</td>
</tr>
<tr>
<td>DAb</td>
<td>21.2</td>
<td>4.13</td>
<td>20.6</td>
<td>0.998</td>
</tr>
<tr>
<td><strong>Green Strain, ( \varepsilon = \alpha P + \beta )</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Position</td>
<td>$\alpha$</td>
<td>$\beta$</td>
<td>$R^2$</td>
<td></td>
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<tr>
<td>----------</td>
<td>--------</td>
<td>--------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td><strong>Longitudinal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTh</td>
<td>$8.39 \times 10^{-4}$</td>
<td>$4.99 \times 10^{-2}$</td>
<td>0.937</td>
<td></td>
</tr>
<tr>
<td>MTh</td>
<td>$6.59 \times 10^{-4}$</td>
<td>0.194</td>
<td>0.960</td>
<td></td>
</tr>
<tr>
<td>DTh</td>
<td>$7.55 \times 10^{-4}$</td>
<td>0.509</td>
<td>0.990</td>
<td></td>
</tr>
<tr>
<td>PAb</td>
<td>$4.94 \times 10^{-4}$</td>
<td>0.764</td>
<td>0.994</td>
<td></td>
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<tr>
<td>DAb</td>
<td>$5.87 \times 10^{-4}$</td>
<td>0.778</td>
<td>0.926</td>
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</tbody>
</table>

<p>| <strong>Kirchhoff’s Stress, ( \tau (\text{kPa}) = \alpha P + \beta )</strong> | | | |</p>
<table>
<thead>
<tr>
<th>Position</th>
<th>$\alpha$</th>
<th>$\beta$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTh</td>
<td>1.147</td>
<td>$-27.0$</td>
<td>0.983</td>
</tr>
<tr>
<td>MTh</td>
<td>1.105</td>
<td>$-24.0$</td>
<td>0.983</td>
</tr>
<tr>
<td>DTh</td>
<td>0.742</td>
<td>$-17.6$</td>
<td>0.977</td>
</tr>
<tr>
<td>PAb</td>
<td>0.566</td>
<td>$-14.0$</td>
<td>0.971</td>
</tr>
<tr>
<td>DAb</td>
<td>0.426</td>
<td>$-10.3$</td>
<td>0.976</td>
</tr>
</tbody>
</table>

$R^2$ represents the correlation coefficient of the curve fit.
It was observed that portions of the in situ aorta become curved at higher distension pressures. The degree of curvature was estimated by the angle relative to the long axes of the aorta. Our results show that in comparing pressures of 150 to 90 mmHg, the curvature angles for the proximal thoracic, middle thoracic, proximal abdominal, and middle abdominal were 14°/11006 2.8, 6.2°/11006 0.96, 9.3°/11006 4.0, and 7.4°/11006 2.4°, respectively.

We found no change of curvature of the distal thoracic region during distension presumably because of the mechanical constraint from the diaphragm.

DISCUSSION

Compliance of Aorta and Its Physiological Implications

Numerous estimates of compliance have been made in vivo based on the windkessel model by calculation of the time constant (product of total arterial resistance and compliance) of pressure decay or some modification thereof (see review in Ref. 30). Data on the compliance of pig, dog, and rat have been reported as ~0.5 ml/mmHg (30), 0.1 ml/mmHg (32), and 5 × 10⁻³ ml/mmHg (24), respectively. In the dog experiment, the reported compliance corresponds to the proximal descending aorta, which accounted for 60% of the total arterial compliance. It should be noted, however, that one of the limitations of the windkessel model is that it does not account for wave reflections. This limitation should be taken into account when interpreting the data.

In the present study, we found the pressure-volume relationship to be linear as shown in Fig. 7A with a slope of 2.67 × 10⁻⁴ ml/mmHg. The slope corresponds to the static volume compliance of the entire aorta, which is independent of pressures in the range of 30–150 mmHg. We also evaluated the volume compliance of thoracic and abdominal aorta as shown in Fig. 7B. Because the volume compliance is additive, the total volume compliance, obtained from Fig. 7A, is equal to the sum of volume compliance of thoracic and abdominal aorta. It is interesting to note that the abdominal compliance is only 15% of the thoracic compliance.

Fig. 4. Circumferential (A) and longitudinal (B) stress-strain relationship.

Fig. 5. Variation of circumferential elastic modulus along the length of aorta.

Fig. 6. Cross-sectional area compliance (∆CSA/∆P) for the various segments of aorta. The differences between aortic regions were statistically significant.

Fig. 7. A: variation of total aortic lumen volume (V) with distension pressures (P). Solid line is a linear least-square fit of the form V = 2.67 × 10⁻⁴ P + 8.52 × 10⁻³, R² = 0.998. B: volume compliance (∆V/∆P) for the thoracic (Th) and abdominal aorta (Ab).
Alternatively, the compliance can be expressed in terms of CSA (ΔCSA/ΔP). It is much easier to measure the CSA compliance; particularly, in vivo. Hence, the majority of data in the literature is on the CSA compliance, and it is often used interchangeably with volume compliance. The relation between volume compliance and CSA compliance is given by Eq. 7. The general practice is to assume that the axial deformation with distension is negligible; i.e., ignore the second term in Eq. 7. In the present study, we found that the second term contributes ~10% to the volume compliance because the axial deformation with distension is small as confirmed in Figs. 1, A and B. Hence, as an approximation the volume compliance is the product of CSA compliance and length of the vessel. We should caution, however, that even when the axial deformation is small, the second term can be significant for a vessel that has a small length-to-CSA ratio. The results of the mouse CSA compliance are shown in Fig. 6. Both CSA and volume compliance show that the proximal aorta, near the heart, is most compliant with the compliance decreasing toward the distal aorta. Hence, the mouse aorta shows geometric and compliance taper similar to other species (27).

We can estimate the degree of accommodation that the aorta provides to each ejection of the heart. The stroke volume can be determined as the quotient of cardiac output and heart rate, whereas the change of volume of the aorta during each cardiac cycle can be estimated from the product of compliance and pulse pressure. For the mouse, at a cardiac output of 12.5 ml/min and heart rate of 622 beats/min, we obtain a stroke volume of 0.02 ml (4). For a pulse pressure of 25 mmHg, the computed compliance yields a change in aortic volume of 0.0067 ml. Hence, the aorta can accommodate about one-third of the stroke volume. It should be noted that this is an estimate because the dynamic compliance may be somewhat different, which would affect the value. Similar calculations for the pig yield a stroke volume of 20 ml assuming a cardiac output of 2 l/min and heart rate of 100 beats/min. The change in aortic volume during each cardiac cycle can be estimated as 12.5 ml assuming a pulse pressure of 25 mmHg and dynamic compliance of 0.5 ml/mmHg. Hence, the aorta accommodates about two-thirds of the blood pumped in one stroke. Incidentally, this is the same estimate made by Hales (17) nearly three centuries ago.

At physiological pressure, the mean aortic lumen volume (from aortic valve to common iliac bifurcation) of the mouse, with a mean body weight of 25 g, is ~0.035 ml. Hence, the aortic blood volume is equal to ~0.14% of the mouse body weight. Barbee et al. (4) have previously shown that the entire circulating blood volume is ~2 ml. Hence, only 2% of the entire mouse blood volume resides in the aorta.

Other Biomechanical Characteristics

The circumferential and longitudinal deformations were measured as a function of pressure along the entire length of the aorta. Figure 1A shows that the longitudinal stretch ratio increases along the length of the aorta (larger near the common iliac bifurcation) and increases with pressure at any longitudinal position. The former observation is very pronounced where the stretch ratio is near 1 at the ascending aorta and 1.6 near the common iliac bifurcation. This deformation is due to longitudinal stretch from the zero-stress state to the in situ state. Consequently, when the vessel is excised, the various regions will shorten according to Fig. 1A where the abdominal aorta shortens the most. Han and Fung (16) measured the longitudinal stretch ratio of canine and porcine aortas in situ (zero pressure) relative to the zero-stress state. The similarity of the longitudinal stretch ratio of the mouse aorta to that of dog and pig is striking. They did not examine the effect of pressure on the longitudinal stretch ratio, however, which was found to be fairly small in the present study (Fig. 1, A and B).

The linearity between pressure and various morphometric parameters (diameter, wall thickness, lumen CSA, and volume) in a large range of pressure (30–150 mmHg) is remarkable. The wall thickness decreases, whereas the diameter, lumen CSA, and volume increase distally toward the common iliac bifurcation. The pattern holds for all segments of the aorta. Similarly, the computed stress and strain vary linearly with pressure. The resulting stress-strain relationship is also linear in the pressure range of 30–120 mmHg. The observed simplicity of mechanical properties along the length of the aorta allows the use of a simple strain energy function (Table 2), which will simplify future mechanical modeling of the cardiovascular system of the mouse.

The linearity of the stress-strain relation is limited to the range of pressure used. Figure 8 shows the stress-strain relation for the middle thoracic and abdominal aorta in the pressure range of 30–210 mmHg. It can be seen that the relationship is linear up to 120 mmHg (i.e., physiological range) beyond which it becomes nonlinear. It is also interesting to note that the relationship in the two regions is essentially the same below 120 mmHg. Above this pressure, the abdominal aorta attains larger stresses and strains. This observation may be due to the fact that the abdominal aorta has fewer bifurcation constraints and is less tethered by surrounding tissue. This observation underscores an interesting possible correlation between higher stresses and strains with the predisposition of disease in the abdominal aorta in hypertension (7).

The circumferential and longitudinal moduli were computed along the length of the aorta. The circumferential stress-strain relation for the MTh and MAb aorta in the pressure range of 30–210 mmHg.
ential modulus attains its largest value near the diaphragm; i.e., the aorta is most stiff there. Thirty years ago, Tanaka and Fung (33) cut the aorta into strips along the length of the aorta. They tested each strip uniaxially either in the circumferential or longitudinal direction. In the process, they obtained the Lagrangian stress-stretch ratio relation, which was found to have an exponential character. The tangent modulus was computed (slope of the stress-strain relation) for the various segments. They showed a similar peak in the tangent modulus near the diaphragm, which is consistent with our present findings. The mean longitudinal modulus was found to be fairly constant along the length of the mouse aorta. The value of the longitudinal modulus was approximately two orders of magnitude larger than in the circumferential direction. It should be noted that the aorta is constrained along its entire length through numerous bifurcations. Hence, the measured modulus is not only of the aorta but also of the surrounding tissue.

Uniform Transmural Strain Hypothesis

The existence of the opening angle, as shown in Fig. 3A, makes the transmural strain distribution more uniform (13). This was previously demonstrated along the entire length of the mouse aorta at physiological pressure (15). In the present study, we can examine the effect of pressure on the uniformity of transmural strain. The difference between outer and inner strain $e_o - e_i$ was computed and shown in Fig. 3B. At zero pressure, the values correspond to the residual strain. Outer residual strain is tensile, whereas inner strain is compressive. Hence, the difference is fairly large as shown in Fig. 3B. As the vessel is pressurized, the outer strain remains larger than the inner strain at a pressure of 30 mmHg. At 60 mmHg, the difference in transmural strains is not statistically significant. This remains to be the case until the pressure is increased to a value of 150 mmHg where the inner strain exceeds the outer strain. These results have important implications for hypertension where the increase in pressure may be well above 150 mmHg. The resulting gradient in transmural strain may be a stimulus for growth and remodeling (20).

Future Studies

The structural components of the vessel wall are altered in the various conditions (e.g., aging, diabetes, hypercholesteremia, hypertension, smoke exposure, etc.) that pose a risk factor for arteriosclerosis due to the mechanical or metabolic abnormality through various mechanisms. One of the implications of the structural changes is the change in mechanical properties of the blood vessel; i.e., the compliance or modulus. Numerous studies on animal and human tissue have demonstrated increased vascular stiffness during these risk factors. In the present study, the mechanical properties of the entire aorta are described quantitatively. This model will serve as a physiological reference state for future studies of risk factors in the mouse model.

APPENDIX

If we neglect the radial and all shear components, the stress-strain relations of the aorta in both circumferential and longitudinal directions can be expressed by combining Eqs. 8 and 9 as

$$\tau_o = 2b_1E_o + b_3E_z$$

and

$$\tau_z = 2b_3E_z + b_2E_o$$

A residual or error, $e$, can be defined for the stress as the square of the difference of the curve fit and experimental value as

$$e = \sum_{i=1}^{n} (2b_1E_{i}^{o} + b_3E_{i}^{z} - \tau_{i}^{o})^2 + \sum_{i=1}^{n} (2b_3E_{i}^{z} + b_2E_{i}^{o} - \tau_{i}^{z})^2$$

where the summation is taken over the four pressures measurements (30, 60, 90, and 120 mmHg); i.e., $n = 4$. Our objective is to determine the values of $b_1$, $b_2$, and $b_3$ for which the error $e$ is a minimum. Mathematically, this can be satisfied if the derivatives of $e$ with respect to $b_1$, $b_2$, and $b_3$ vanish; namely,

$$\frac{\partial e}{\partial b_1} = 0 \quad \text{or} \quad 2b_1 \sum_{i=1}^{n} E_{i}^{o} + b_3 \sum_{i=1}^{n} E_{i}^{z} = \sum_{i=1}^{n} \tau_{i}^{o}$$

$$\frac{\partial e}{\partial b_2} = 0 \quad \text{or} \quad 2b_3 \sum_{i=1}^{n} E_{i}^{z} + b_2 \sum_{i=1}^{n} E_{i}^{o} = \sum_{i=1}^{n} \tau_{i}^{z}$$

$$\frac{\partial e}{\partial b_3} = 0 \quad \text{or} \quad 2b_2 \sum_{i=1}^{n} E_{i}^{o} + b_3 \sum_{i=1}^{n} E_{i}^{z} = \sum_{i=1}^{n} \tau_{i}^{o}$$

The above set of equations can be represented in terms of matrix algebra as follows

$$\begin{pmatrix}
2 \sum_{i=1}^{n} (E_{i}^{o})^2 & 0 & \sum_{i=1}^{n} (E_{i}^{o}E_{i}^{z}) \\
0 & 2 \sum_{i=1}^{n} (E_{i}^{z})^2 & \sum_{i=1}^{n} (E_{i}^{o}E_{i}^{z}) \\
\sum_{i=1}^{n} (E_{i}^{o}E_{i}^{z}) & \sum_{i=1}^{n} (E_{i}^{o}E_{i}^{z}) & \sum_{i=1}^{n} [(E_{i}^{o})^2 + (E_{i}^{z})^2]
\end{pmatrix} \times \begin{pmatrix}
b_1 \\
b_2 \\
b_3
\end{pmatrix} = \begin{pmatrix}
\sum_{i=1}^{n} \tau_{i}^{o} \\
\sum_{i=1}^{n} \tau_{i}^{z} \\
\sum_{i=1}^{n} [(\tau_{i}^{o})^2 + (\tau_{i}^{z})^2]
\end{pmatrix}$$

The solution to this problem yields values of $b_1$, $b_2$, $b_3$ for each set of experimental data on stress and strain. The set of constants for the strain energy function is summarized in Table 2 for each region of the aorta, respectively.

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DISCLOSURES

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