Axial nonuniformity of geometric and mechanical properties of mouse aorta is increased during postnatal growth

Yi Huang, Xiaomei Guo, and Ghassan S. Kassab

Department of Biomedical Engineering, University of California, Irvine, California

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Huang, Yi, Xiaomei Guo, and Ghassan S. Kassab. Axial nonuniformity of geometric and mechanical properties of mouse aorta is increased during postnatal growth. Am J Physiol Heart Circ Physiol 290: H657–H664, 2006. First published September 19, 2005; doi:10.1152/ajpheart.00803.2005.—The hemodynamic conditions of the aorta during development as well as the relation between those changes and the mechanics of the aorta (1, 3, 15, 16, 24, 31, 33, 34, 36). These studies confirm the aorta to increase its lumen, wall thickness, and mechanical stiffness during development. Most of these studies, however, have focused mainly on the proximal aorta, and none have systematically characterized the geometric and mechanical properties along the entire length of the aorta.

Our major objective was to quantify the heterogeneity of geometry and mechanical properties along the length of aorta as the organ becomes more specialized during growth and development. Hence, we systematically documented the geometry and mechanical properties along the length of the mouse aorta at different age groups. We chose the mouse model because the mouse is being widely used in experimental studies of many aspects of cardiovascular health and disease. We focused on the C57BL/6J strain because it is the most widely used and best known of all inbred strains. Furthermore, it has substrains that are predisposed to hypertension, diabetes, and hypercholesterolemia, all of which are important risk factors for cardiovascular disease (6, 30). Our results show that the heterogeneity of geometry and material properties increases during development and underscore the structure-function relationship of the aorta during the postnatal period. Furthermore, the present data will serve as a reference state that defines normal growth for future studies of cardiovascular diseases in genetically manipulated mice.

METHODS

Animal preparation. 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.

Forty-nine homozygous inbred mice of both sexes (C57BL/6 strain) from ages 1 to 33 days were used in this study. The mice were divided into eight groups according to age. The mice were anesthetized with intraperitoneal injections of ketamine (80 mg/kg) and xylazine (8 mg/kg). The mice were placed on a heating pad to maintain body temperature. The carotid artery was cannulated for blood pressure measurement by using a heating, stretched catheter as previously reported (26, 28). Heparin (200 U/ml) was used to prevent blood clots in the heart and blood vessels via the carotid artery catheter. The mice were euthanized with an overdose of the combination of ketamine and xylazine, and the apex of the hearts was excised.

Pressure-diameter-length relationship. The ascending aorta was cannulated through the apex of the left ventricle. The aorta was then...
carefully exposed and perfused with 6% dextran solution to flush out the blood. Cab-O-Sil (Eastman Kodak; concentration range 0.25–0.36%) was then mixed into the dextran solution to prevent flow through the microvessels and, hence, to attain a zero-flow condition. Water-resistant carbon particles were used to mark the aorta, dividing it into a series of 10–15 short segments. The aorta was preconditioned with five cyclic changes in pressure from 0 to the maximum in vivo pressure for each age group. The perfusion pressure was increased in 10- to 20-mmHg increments. The external geometry of the aorta, at different pressurized states, was photographed to obtain the loaded outer diameter along the trunk of the aorta. The outer diameter-length-pressure relationship for each of the 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 described by Guo and Kassab (11).

**No-load and zero-stress state.** After the distension protocol, the aorta was then dissected and placed into Ca\(^{2+}\)-free Krebs solution (composition in mM: 11 d-glucose, 4.7 KCl, 120 NaCl, 25 NaHCO\(_3\), 1.2 KH\(_2\)PO\(_4\), 1.2 MgSO\(_4\), and 0.026 EDTA). The entire length of the aorta was then cut into 50–70 rings. Each ring was transferred to Ca\(^{2+}\)-free Krebs solution, aerated with 95%O\(_2\) and 5% CO\(_2\), and photographed in the no-load state. Each ring was then cut radially at the anterior position labeled with carbon black particles. The ring opened to a sector and gradually approached a constant opening angle as defined as the angle subtended by two radii connecting the midpoint of the inner wall. The cross section of the sectors was photographed 30 min after the radial cut was made. The morphological measurements of inner and outer circumference, medial wall thickness (bounded by internal and external elastic lamina), and area in the no-load and zero-stress states were made from the images by using a morphometric analysis system (Sigma Scan). We made four measurements at equal distance along the circumference of the ring and the sector to determine the medial wall thickness.

A local dimensional coordinate, a, was introduced along the unloaded vessel trunk, with a = 0 at the aortic valve and a = 1 at the point of common iliac bifurcation. The coordinates x and a were referred to as the fractional longitudinal position (FLP) in the loaded and no-load states, respectively (11).

**Biomechanical analysis.** The characterization of biomechanical properties along the length of aorta has been previously described in detail (11). Briefly, the incompressibility condition was used to compute the inner radius as

\[
r_i = \sqrt{r_o^2 - \frac{A_0}{\pi \lambda_z}} \tag{1a}
\]

where \(r_o\) and \(r_i\) are the outer and inner radii at the loaded state, respectively. \(\lambda_z = l/l_0\) is the axial stretch ratio, where \(l\) and \(l_0\) are the vessel lengths in the loaded and zero-stress states, respectively, and \(A_0\) is the wall area in the no-load state. The wall thickness (h) was computed as

\[
h = r_o - r_i = r_o - \sqrt{r_o^2 - \frac{A_0}{\pi \lambda_z}} \tag{1b}
\]

The wall thickness was computed based on measured quantities \(r_o, A_0,\) and \(\lambda_z\) for the intima-media.

The circumferential deformation of the artery may be described by Green strain (\(\varepsilon\)) as

\[
\varepsilon_h = \frac{1}{2} [\lambda_z^2 - 1] \tag{2a}
\]

where \(\lambda_z\) is the midwall circumferential stretch ratio (\(\lambda_z = C_{\phi}/C_{\phi}^{ZS}\)). \(C_{\phi}\) refers to the midwall circumference (average of inner and outer circumference) of the vessel in the loaded or no-load state, and \(C_{\phi}^{ZS}\) refers to the midwall circumference in the zero-stress state as described in *No-load and zero-stress state*. The axial Green strain (\(\varepsilon_h\)) is given as

\[
\varepsilon_h = \frac{1}{2} \left[ \frac{r_o}{h} - 1 \right] \tag{2b}
\]

where \(\lambda_z\) is defined as above. At an equilibrium condition, the average circumferential Cauchy and Kirchhoff stresses in the vessel wall were computed as

\[
\tau_h = \frac{P}{h} \quad \text{and} \quad \tau_h = \frac{P}{h \lambda_z^2} \tag{3a}
\]

The elastic modulus in circumferential direction was computed as

\[
E_h = \frac{\Delta \tau_h}{\Delta \varepsilon_h} \tag{4}
\]

The value was constant for all pressures, because the stress-strain relationship was found to be linear.

The lumen cross-sectional area (CSA) and the lumen volume (V) at different distention pressures were computed as CSA = \(\pi r_i^2\) and

\[
V = \int_{0}^{L} \text{CSA}(x) dx \tag{5}
\]

where \(r_i\) is the inner radii at the loaded state and \(L\) is the total length of the aorta (aortic valve to common iliac bifurcation). Similarly, the wall area (WA) and the wall volume (V) of the aorta at loaded state were computed as WA = \(2 \pi r_i h\) and

\[
V = \int_{0}^{L} \text{WA}(x) dx \tag{6}
\]

The CSA compliance, C_{CSA}, of the aorta is given as the slope of the pressure-volume relationship; i.e., \(C_{CSA} = \Delta \text{CSA}/\Delta P\). The volume compliance, CV, was defined similarly as CV = \(\Delta V/\Delta P\).

**Wall shear stress.** The wall shear stress, WSS, can be evaluated if the diameter and flow rate are known under certain assumptions. The volumetric flow rate is proportional to the cube of the vessel radius, assuming a laminar, incompressible Newtonian flow through a rigid cylindrical vessel as given by the following relationship:

\[
\text{WSS} = \frac{32 \mu Q}{\pi D^3} \tag{7}
\]

where Q and D represent the volumetric flow rate and diameter of vessel and \(\mu\) denotes the viscosity of blood. If we combine the present data on the diameter of the proximal aorta with the data on cardiac output (CO) or flow of the same mouse strain (35), we can determine the WSS. Using MRI, Wiesmann et al. (35) showed that the CO increased linearly in the first 4 wk, which was 1.1 ml/min at 3 days of age and 5.3 ml/min at 10 days (CO = 0.32 + 1.1; \(R^2 = 0.998\), where CO and t have units of ml/s and days, respectively). Similarly, the inner diameter of the ascending aorta, from the present study, was...
found to vary linearly with time and were curve fitted accordingly. If we assume a constant blood viscosity of 4 cP, we can compute the WSS at various time points of development, given the diameter and flow.

**Data analysis.** The position along the aorta was normalized with respect to the total length. The results were expressed in terms of the FLP, ranging from 0 to 1. We further divided the aorta according to anatomic regions; i.e., the thoracic aorta was divided into proximal, middle, and distal regions, whereas the abdominal aorta was divided into proximal and distal regions. Anatomically, the proximal, middle, and distal thoracic aorta correspond to the segment from the aortic valve to the first pair of intercostals arteries, from the first to the sixth pair of intercostals arteries, and from the sixth pair of intercostal arteries to the subcostal artery (diaphragm), respectively (11). The proximal and distal abdominal aorta corresponds to the segment from the subcostal artery to the left renal artery and from the left renal artery to the common iliac artery, respectively.

**Statistical analysis.** Either linear or nonlinear regression was used to curve fit the data. One-way and two-way ANOVA and Student’s t-test were used to detect the possible difference between different positions and groups of animals.

**RESULTS**

Figure 1 shows the increase of body weight, which has a linear relationship with age in the first 30 days of growth. The growth rate is 0.5 g/day, as summarized in Table 1. The mean arterial blood pressure of the mice increased from 30.6 ± 3.9 mmHg with respect to the no-load state (approximately equivalent to zero-stress state) as shown in Fig. 2. The variation of outer diameter and wall thickness for the various segments of the aorta at loaded state are shown in Fig. 3, A and B, respectively. The outer diameter of the mouse aorta increases linearly with age during the first 4 wk of life, with the proximal thoracic aorta growing the fastest (26.7 μm/day) and the distal abdominal aorta growing the slowest (9.7 μm/day). The wall thickness of the mouse aorta increases rapidly during growth and development, the body length (distance from nose to anus), coelom length (distance from clavicle to anus), and aorta length (distance from common iliac bifurcation) at the loaded state increases linearly with an increase in age, as shown in Fig. 4A. The body length grew the fastest (1.64 mm/day), whereas the aorta grew the slowest (0.72 mm/day), as shown in Table 1. The global stretch ratio is taken as the total length of the aorta at physiological pressure normalized with respect to the in vitro length at the no-load state (approximately equivalent to zero-stress state) as shown in Fig. 4B.

The global stretch ratio of mice did not change significantly during the first 2 wk of life ($P > 0.05$), but it did so when the mice were 3–4 wk old ($P < 0.05$).

The lumen volume of the aorta increased linearly with age, as shown in Fig. 5A, at a rate of 1.09 mm$^3$/day. The wall volume growth of the aorta also increased linearly at a rate of 0.14 mm$^3$/day, as shown in Fig. 5B. If the density of the aorta remains constant, this would represent the growth rate of the aorta (mass/time).

Figure 6 shows the variation of the Green strain and Cauchy stress with age at physiological pressure. The Green strain was uniform during the first 3 days of life and began to decrease thereafter, as shown in Fig. 6A. It reached a constant value when the mice were more than 2 wk old. The Green strain of the thoracic and abdominal aorta tended to be uniform when the mice were <2 wk old but became significantly different when the mice were >2 wk old, albeit the differences are relatively small. Conversely, the Cauchy stress of the aorta increased gradually with age. When the mice were 3 days old, the stress was uniform along the length of the aorta. The Cauchy stress of proximal aorta tended to be higher than the distal after 3 days of age ($P < 0.05$).

The variation of the circumferential and axial Green strain and Kirchhoff stress with pressure were computed for various segments of the aorta. The relationships were found to be linear up to physiological pressures. The variation of the circumferential elastic modulus showed no significant difference along the aorta ($P > 0.05$), and it increased with age, as shown in Fig. 7A. The modulus was low when the mice were younger (age within 3 days) and reached a plateau when the mice were older.

![Fig. 1. Variation in mouse body weight with age.](http://ajpheart.physiology.org/content/290/2/Fig1)

![Fig. 2. Variation of mouse mean arterial blood pressure with age.](http://ajpheart.physiology.org/content/290/2/Fig2)

Table 1. Growth rate for various parameters of mouse and aorta for the first 30 days of life

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Position</th>
<th>PTh</th>
<th>MTh</th>
<th>DTh</th>
<th>PAb</th>
<th>DAb</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, g/day</td>
<td></td>
<td>0.50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outer diameter, μm/day</td>
<td></td>
<td>26.7</td>
<td>23.4</td>
<td>22.8</td>
<td>15.8</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td>Inner diameter, μm/day</td>
<td></td>
<td>24.6</td>
<td>20.9</td>
<td>20.4</td>
<td>14.5</td>
<td>9.1</td>
<td></td>
</tr>
<tr>
<td>Body length, mm/day</td>
<td></td>
<td>1.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coelom length, mm/day</td>
<td></td>
<td>1.22</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Aorta length, mm/day</td>
<td></td>
<td>0.72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumen volume, mm$^3$/day</td>
<td></td>
<td>1.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall volume, mm$^3$/day</td>
<td></td>
<td>0.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall shear stress (WSS)</td>
<td></td>
<td>−0.76</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

$P$, $M$, $D$, proixmal, middle, and distal thoracic aorta, respectively; $PAb$ and $DAb$, proximal and distal abdominal aorta, respectively; WSS, wall shear stress calculated according to Eq. 7.
than 2 wk of age. The variation of lumen CSA with pressure for the various segments of aorta also was found to be linear. Figure 7B shows the CSA compliance of the aortic segments (i.e., slope of the P-CSA relationship). The CSA compliance was relatively uniform along the length of the aorta when the mice were younger (first 2 age groups, \( P > 0.05 \)) and became significantly different later in age (\( P < 0.01 \)).

The variation of lumen volume with pressure for the various segments of aorta also was found to be linear. Hence, the volume compliance was computed as the slope of the pressure-volume relationship, as shown in Fig. 8A. The volume compliance of various segments of aorta was relatively uniform in the first 3 days and became significantly different later in age (\( P < 0.01 \)). Figure 8B shows the volume compliance of thoracic (sum of proximal, middle, and distal thoracic aorta) and abdominal aorta (sum of proximal and distal abdominal aorta). It is clear that the difference in volume compliance of thoracic and abdominal aorta increases with age.

The strain measurements were based on the circumferences in the zero-stress state. Correspondingly, the opening angle of the zero-stress state was measured in the various age groups. In the thoracic aorta, the opening angles varied from 106.9 ± 7.2° to 85.0 ± 4.0° at 6 to 30 days of age, respectively. The opening angles of the abdominal aorta did not vary significantly at 110° during the same period of time. The measurements of opening angle were less accurate for the first several days because of the softness and twisting of the tissue.

The WSS was computed according to Eq. 7 and is shown in Fig. 9. The linearity of the change of WSS during development is quite apparent. The rate of change of WSS during development is summarized in Table 1. The negative sign denotes a decrease in WSS during development.
DISCUSSION

The results of this study both support and extend the previous studies on the remodeling of aortic geometry and mechanical properties during postnatal growth and development (1, 2, 4, 15). Changes of pressure and flow in arterial tissue introduce deformations in the axial, circumferential, and radial directions (17, 32). Hence, the aorta should manifest growth and remodeling in length, diameter, and wall thickness during development. The heterogeneity of those parameters along the entire length of the aorta, which has previously not been documented, was the primary focus of this study.

One to two wk of age: pressure- and flow-induced remodeling. The first 2 wk of the mouse life are characterized by simultaneous changes of blood pressure and CO. Our data show that the mean arterial pressure of the C57BL/6 mouse increased from 30 to 80 mmHg during postnatal development and reached the adult value at 2 wk of age (Fig. 2). Study of CO of the same strain of mouse with MRI showed that the CO increased linearly in the first 4 wk of life and was 1.1 ml/min at 3 days of age and 5.3 ml/min at 10 days age (35). Hence, in addition to the hormonal changes in the first 2 wk of life, the C57BL/6 mouse aorta experiences stress-induced remodeling introduced by changes in both blood pressure and blood flow, with the changes in flow (382% increase) being significantly higher than those in pressure (167%).

Numerous studies have demonstrated that changes in blood pressure are associated with changes in wall thickness. Aortic wall thickening was observed during development (3, 24, 27), which was attributed to the medial tissue accumulation of elastin, collagen, and smooth muscle cells. The wall thickness increases rapidly during the first 2 wk of the C57BL/6 mouse. We found that the growth of the wall thickness is not uniform along the aorta during development. The thoracic aorta grows faster than the abdominal aorta, where the proximal aorta grows the fastest and the distal aorta grows the slowest.

The major flow changes at the time of birth include a dramatic increase in pulmonary blood flow because of the postnatal loss of the placental circulation. Furthermore, there is a dramatic decline in blood flow in the abdominal aorta because of the closure of the umbilical arteries at birth (13). Langille et al. (18) found that the abdominal aortic external diameter in the period between 4 and 14 days postpartum was reduced significantly compared with in utero values. Our data show a linear relationship in the outer diameter (Fig. 3A) and the inner diameter of the aorta (data not shown) with age. The growth rates of both the outer and the inner diameters of thoracic and abdominal aorta are different during the first 2 wk of life. The thoracic aorta grows faster than the abdominal, where the proximal grows the fastest and the distal aorta grows the slowest, as shown in Table 1.

Three to four wk of age: flow-induced remodeling. The mean blood pressure reached the adult value when the mouse was 2 wk old, as shown in Fig. 2. Interestingly, Fig. 3B shows that the growth of the wall thickness of the aorta levels off when the mouse reaches 2 wk of age. This observation is consistent with the results of Langille et al. (18), who found that the abdominal aortic external diameter in the period between 4 and 14 days postpartum was significantly reduced compared with in utero values. Our data show a linear relationship in the outer diameter (Fig. 3A) and the inner diameter of the aorta (data not shown) with age. The growth rates of both the outer and the inner diameters of thoracic and abdominal aorta are different during the first 2 wk of life. The thoracic aorta grows faster than the abdominal, where the proximal grows the fastest and the distal aorta grows the slowest, as shown in Table 1.

Fig. 6. Variation of circumferential Green strain (A) and Cauchy stress (B) in mouse aorta with age. Th, thoracic aorta; Ab, abdominal aorta. *Significant difference compared with different segments along the aorta. #Significant difference for thoracic compared with abdominal aorta.

Fig. 7. Circumferential elastic modulus (A) and cross-sectional area compliance (B) for different segments of mouse aorta. *Significant difference compared with different segments along the aorta. #Significant difference compared with other age groups.
hypertension-induced wall hypertrophy verified by previous studies (19, 25). Similarly, we found that the growth of the wall thickness is not uniform along the aorta during development, where the proximal aorta grows the fastest and the distal grows the slowest, as shown in Table 1. It has been previously demonstrated that the growth rates of the medial CSA between the thoracic and the abdominal aorta were different (18). This suggests that the aorta radially transforms from a relatively thin cylindrical tube to a thicker structure, where the thickness tapers along the length of the aorta during postnatal growth.

Although the blood pressure plateaus, the CO continues to increase linearly through 3 (8.7 ml/min) and 4 wk of age (9.3 ml/min) (35). Figure 3A shows that the outer diameter of the aorta increases linearly with age within the first 4 wk of life. Similarly, we found that the growth of the diameter of the aorta is not uniform along the aorta during development, where the proximal aorta grows the fastest and the distal aorta grows the slowest (Table 1). This implies that the blood flow increases the most at the proximal aorta. This difference in flow circumferentially transforms the aorta from a relatively cylindrical tube to a tapering structure after birth.

These mice are fully mature sexually at 63–70 days, and their average life span is ~900 days (20). Hence, at 10 wk, it is unlikely that there are additional significant changes in hemodynamic parameters. The MRI measurements of CO by Wiesmann et al. (35) showed values of 15.7 and 14.3 at 10 and 16 wk, respectively. These differences were not statistically significant. Hence, the increase in the various parameters (body weight, diameter, length, lumen volume, and wall volume of aorta) would plateau because the hemodynamic stimuli become uniform. The remodeling process in senescence is, of course, a different issue.

Axial growth and remodeling. The length of the aorta increases linearly with age during normal development (Fig. 4B). It is well known that arteries are under axial traction and that the percent vessel retraction increases linearly with age (4). The retraction is due to axial prestretch that is imposed by attachments to contiguous tissue. Our data show that the variation in global stretch ratios of the aorta was not significantly different in the first 2 wk ($P > 0.05$). The global stretch ratio increased significantly, however, when the mice were >3 wk of age. During development, the body length grows faster than the aorta, as shown in Fig. 4A. This implies that the aorta is subjected to a distending axial force during growth that becomes significant after 3 wk of age.

In a recent study, Zhang et al. (37) showed that an increase in axial stretch tends to increase the axial stress and strain much more significantly than their circumferential and radial counterparts for both the porcine left anterior descending coronary (LAD) artery and rabbit aorta. For the coronary artery, a stretch ratio of 1.5 results in identical circumferential and axial stresses and strains. This is interesting, because the axial prestretch ratio for the LAD artery is ~1.4 (22). These results indicate that the circumferential and axial wall stresses and strains in the LAD artery become more uniform as the axial prestretch ratio increases. In other words, under the same physiological pressure, a more homogeneous stress state may be obtained by prestretching the vessel. Hence, the axial prestretch at the in vivo state may play a role similar to that of the circumferential residual strain, i.e., making the stress and strain more homogeneous in the vessel wall. Future studies should consider the effect of change in prestretch on the intramural stress and strain distribution during development.

Changes in opening angle during postnatal development. The zero-stress state often has been characterized by the opening angle, which is defined as the angle subtended by two radii connecting the midpoint of the inner wall (10). Fung (10) previously proposed that the remodeling of the zero-stress state is an index of the nonuniformity of growth and remodeling. Fung and Liu (8, 9, 21) showed that hypertension induces growth of intima that exceeds that of the adventitia. Consequently, the vessel sector, in the zero-stress state, shows an outward bend and, hence, an increase in the opening angle. Conversely, Lu et al. (23) showed that flow overload induces growth of adventitia that exceeds that of intima. Hence, the
vessel sector bends inward and decreases the opening angle. In summary, hypertension and flow overload have opposing effects on the opening angle. In models of simultaneous hypertension and flow overload, the effects of opening angle are nearly conciliatory (14).

Our present results are consistent with the previous findings if we consider the changes in pressure and flow. In the thoracic aorta, the change in flow dominates the change in pressure, and hence the opening angle decreases during development (from 107° to 85°). In the abdominal aorta, however, the changes in pressure and flow are fairly similar (approximately constant at 110°), and hence the effect is conciliatory. In future studies, it would be interesting to consider the effect of change in zero-stress state on the transmural distribution of intramural stress and strain.

Physiological implications of mechanical remodeling. Elastin, collagen, and smooth muscle cells are the main components of aorta. The elastin and collagen are thought to contribute to the elastic properties at low and moderate blood pressures and at high pressures, respectively (1, 32). The principal source of viscoelasticity is attributed to smooth muscle cells (34). During development, there was an uneven growth of each of the microstructured components, with increases in collagen > elastic laminae > muscle cells (27). The collagen content was higher and the elastic fiber content was lower in the thoracic compared with the abdominal aorta, which implies the thoracic aorta is more compliant than the abdominal aorta (7). The present data show that the strain-stress relationship of the mouse aorta is linear within the physiological pressure range in all age groups (10–50 mmHg for the newborn, 30–100 mmHg from >3 wk old); the relationship becomes nonlinear beyond the physiological pressure range. These results are consistent with our study on adult mice (11). The lines shift upward and to the left during development, suggesting increased stiffness.

At birth, when the pressure is low, the elastic modulus (Fig. 7A) and the compliance (Figs. 7B and 8, A and B) are small and fairly uniform along the entire length of the aorta. As the pressure increases, the aorta becomes more elastic. Furthermore, the aorta becomes mechanically heterogeneous, with the proximal region near the heart being the most compliant and the distal region least compliant. This is a functional adaptation, because the aorta’s elasticity must convert the heart’s pulsatile flow to steady flow in peripheral vessels. This is, of course, the well-known windkessel model.

Similarly, our data on circumferential Cauchy stress show uniformity along the aorta during the first postpartum period, which is consistent with previous studies (18); the stress imposed on the proximal aorta is higher than the distal abdominal aorta thereafter. Hence, the Cauchy stress becomes heterogeneous along the length of the aorta during postnatal growth and development.

Tendency for strain homeostasis. The present data, in conjunction with a recent study by Guo and Kassab (11) on mice 10 wk of age, can be used to explore the issue of mechanical homeostasis. Our present results are consistent with the previous findings (14); the stress imposed on the proximal aorta is higher than the distal abdominal aorta thereafter. Hence, the Cauchy stress becomes heterogeneous along the length of the aorta during postnatal growth and development.

WSS and strain appear to attain their homeostatic values earlier in life.

The finding that strain may be a homeostatic mechanical parameter is in agreement with the findings of Guo and Kassab (12). They recently determined the distribution of circumferential stress and strain along the porcine aorta and throughout the coronary arterial tree. They showed that the stretch ratio (circumference of the artery at physiological loading relative to the zero-stress state) and stress varied from 1.2–1.6 and 10–150 kPa, respectively, along the aorta and the entire LAD arterial tree (more than 3 orders of magnitude difference in vessel diameters). The relative uniformity of strain (50% variation) from the proximal aorta to a 10-μm arteriole implies that the vascular system closely regulates the degree of deformation. Additional studies have shown that the circumferential strain (computed in reference to the zero-stress state) responds faster and recovers more quickly than the circumferential stress in pressure overload and flow overload models (23, 29). The homeostasis of strain has important implications for mechano-transduction and for vascular growth and remodeling.

Implications. The aorta grows and remodels in the circumferential, axial, and radial directions during normal development. Although the aorta is a relatively uniform organ geometrically and mechanically at birth, it becomes transformed into a tapering organ with varying mechanical properties along its length within the first 30 days of birth in the mouse model. The structural and mechanical remodeling is consistent with the functional adaptation of the aorta during development. Furthermore, it appears that strain attains its homeostatic values earlier than other mechanical parameters. In addition to the foregoing implications, the present data will serve as a physiological reference state for understanding pathological change in this transgenic model.

GRANTS

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