Regional Volume Distensibility of Canine Thoracic Aorta During Moderate Treadmill Exercise

Brian J. Gentile, C.J. Charles Chuong, and George A. Ordway

We characterized the in vivo mechanical properties of segments of upper descending thoracic aorta (UDTA) in terms of volume distensibility, which was derived from measurements of pulsatile intravascular pressure, inner wall radius, and length changes. Data for this analysis were obtained from six dogs at rest and during moderate treadmill exercise (8% grade, 4.5 miles/hr). Volume distensibility reflects the regional rheological properties of the UDTA at in vivo states. It was shown to be the sum of circumferential extensibility, longitudinal extensibility, and higher-order extensibilities. Circumferential extensibility and longitudinal extensibility are linear expressions of vessel kinematic changes which represent percent volume changes per pulse pressure and are due to circumferential and longitudinal dimensional changes alone. The higher-order extensibilities (second and third order), however, account for the coupling effect, which is the percentage volume change per millimeter mercury pulse pressure due to the interactions among radial, circumferential, and axial dimensional changes. The volume distensibility of the UDTA during exercise was significantly less than that at rest (0.67±0.12 vs. 0.91±0.11 %/V/mm Hg pressure). This was the result of a significant decrease in circumferential extensibility and higher-order extensibility in response to exercise with no change in longitudinal extensibility. The higher order extensibilities were also important since the volume distensibility of the UDTA was underestimated by 10% for both rest and exercise when they were ignored. We also evaluated radial extensibility by using pressure and wall thickness data and showed that this variable did not change in response to exercise. (Circulation Research 1988;63:1012-1019)

The arterial wall is anisotropic because of structural nonhomogeneity. Therefore, the study of its mechanical properties should include simultaneous analyses of stresses and strains in the circumferential, longitudinal, and radial directions. This is especially important when the mechanisms of arterial disease or the design criteria for cardiovascular prosthetic devices and grafts are studied or hemodynamic responses associated with them are examined. The effects of exercise on aortic wall properties in health and disease are also obscured by the lack of appropriate measurement techniques. The stress of exercise introduces a whole new set of hemodynamic conditions that must be evaluated.

In the present study, the in vivo mechanical responses of a segment of the upper descending thoracic aorta (UDTA) are described in terms of volume distensibility, which was derived from measurements of intravascular pressure, inner wall radius, and length changes at rest and during moderate treadmill exercise. This volume distensibility index can be written as the sum of circumferential and longitudinal extensibilities, plus the higher-order extensibility terms that account for the interactions among radial, circumferential, and longitudinal dimensional changes. A radial extensibility index that accounts for the wall thinning from diastole to systole is also evaluated through calculated vessel wall thickness and pulse pressure.
FIGURE 1. Schematic representation of sonomicrometer placement on the upper descending thoracic aorta segment (S) and the location of the manometer (P) are shown. Arrows between sonomicrometers across segment diameter and length depict the direction of ultrasound transmission.

Materials and Methods

Instrumentation and Experimental Procedure

Six adult mongrel dogs weighing from 15 to 26 kg were used in this study. All dogs were trained to run freely on a motor-driven treadmill prior to instrumentation. Acepromazine maleate (0.5 mg/kg) was administered intramuscularly as the preanesthetic agent. Surgical preparation and tracheal intubation were performed after intravenous administration of thio- pental sodium (10–15 mg/kg). A surgical plane of anesthesia was maintained with a veterinary anesthesia apparatus, appropriate concentrations of methoxyflurane, and a positive pressure ventilator. With aseptic technique, a left thoracotomy was performed through the fifth intercostal space. A high-fidelity strain gauge manometer (model P22, Konigsberg Instruments, Pasadena, California) was implanted through the wall of the descending aorta for measurement of aortic pressures. A fluid-filled Tygon catheter was implanted adjacent to the Konigsberg manometer for in vivo cross-calibration and zeroing to atmospheric pressure. A strain gauge pressure transducer (model P50, Gould Electronics, Cleveland, Ohio) was used for this purpose. Another Tygon catheter was inserted into the pulmonary artery for indocyanine green dye injection for cardiac output measurements.

A 10–15 mm segment of the UDTA was identified for sonomicrometer placement 3–4 cm proximal to the Konigsberg manometer (Figure 1). This was done to minimize the manometer’s effects on wall motion in the proximal segment. A relatively short segment was used for sonomicrometer attachment to limit the effects of tapering, to limit the effects of variations in structural properties along the length of the aorta, and to study localized aortic mechanical properties. The ultrasonic transit-time dimension system we used is capable of accurately measuring distances between ultrasound crystals in the range of 6 mm up to several centimeters. Two pairs of 5 MHz titanate-zirconate piezoelectric crystals (thickness, 0.5 mm; diameter, 4.0 mm) were sutured to the aortic wall with 3.0 metric braided polyester suture. The transmitters consisted of two ultrasonic crystals glued to each other at a right angle: one for transmitting to the diameter receiver and one for transmitting to the length receiver. Both receivers were sutured directly across from their respective transmitters. The alignment of the crystals was verified by observation of the received ultrasound signals on an oscilloscope. Detailed descriptions of this dimension-measuring technique were published previously. 3,4

All wires and catheters were tunneled subcutaneously to the dorsal surface of the neck and externalized. The chest was closed, and the animal was allowed to recover. Nalbuphine hydrochloride (1 mg/kg) was used as a postsurgical analgesic. Procaine penicillin G (20,000 units/kg) was given postoperatively for 5 days. Additional antibiotics were administered when indicated.

After a 7–10 day recovery period, simultaneous measurements of pulsatile pressure, external diameter, and length were made in the UDTA at rest and during 3–5 minutes of moderate treadmill exercise (8% grade, 4.5 miles/hr). All measurements were recorded on a heat stylus oscillograph (model 7758A, Hewlett-Packard, Palo Alto, California). Values taken from 20 consecutive cardiac cycles were averaged for all calculations at rest and during exercise each time a dog was studied. In addition, we measured cardiac output and heart rate at rest and during exercise. Cardiac output was measured by the dye-dilution technique with indocyanine green. 5 Each dog was studied three to five times at rest and during exercise. Values from these studies that were within 10% of each other were averaged for each dog.

Calculations

After experiments, the dogs were euthanatized with an overdose of sodium pentobarbital (120 mg/kg i.v.). The segment of aorta delineated by sonomicrometer sutures was excised immediately, cleaned of perivascular connective tissue, and weighed. Segmental wall thickness, internal radius, and volume were then calculated.

The inner wall radius \( R_w \) is needed to determine the volume distensibility. It is computed from the following equation:

\[
V_w = \pi (R_0^2 - R_w^2) L
\]
where $V_w$ is the segmental wall volume, $R_i$ is the segmental external radius, and $L$ is the segmental axial length. We calculated the segmental wall volume from the measured weight by using a tissue density of 1.06 g/ml. Assuming incompressibility, we obtained inner wall radii for both diastolic and systolic states from sonomicrometer measurements of external wall radius and axial length.

Similar to Patel et al., we used intraluminal space volume distensibility to represent the local segmental mechanical properties. In addition to the linear extensibility terms, however, we retained the higher order extensibility terms and showed the degrees of underestimation when these higher order components were ignored.

The major steps of deriving the expressions for volume distensibility are as follows. The diastolic or reference volume of the intraluminal space is written as $V = \pi R_i^2 L$, where $R_i$ is the inner wall radius and $L$ is the axial length. In response to the cardiovascular loadings from end diastole to peak systole, the inner wall radius and axial length change by $\Delta R_i$ and $\Delta L$, respectively. The resulting systolic intraluminal volume $(v)$, in terms of inner wall systolic radius $(r)$, and length $(l)$, can be written as

$$v = \pi r^2 l$$

$$= \pi (R_i + \Delta R_i + AR_j L + AL)$$

$$+ \pi (L + \Delta L)$$

(2)

The volume change $(\Delta V)$ can be easily obtained by

$$\Delta V = v - V$$

$$= \pi (2R_i L + \Delta R_i + R_j^2 L)$$

$$+ \pi (L + 2\Delta L)$$

(3)

and the unit volume change written as

$$\frac{\Delta V}{V} = \frac{2\Delta R_i}{R_i} + \frac{\Delta L}{L} + \frac{2\Delta R_j}{R_j} + \frac{2\Delta L}{L} + \frac{\Delta R_j}{R_j} + \frac{\Delta L}{L}$$

(4)

Using pressure increments $(\Delta P)$ as the loading index, we defined the volume distensibility $(E_v)$ as the percentage volume change per millimeters mercury $\Delta P$. That is,

$$E_v = \frac{\Delta V}{V} \times 100$$

$$= \frac{\Delta R_i}{R_i} + \frac{\Delta L}{L} \times 100$$

(5)

On the right side of Equation 5, the first and second terms are linear expressions representing contributions due to dimensional changes in the circumferential and longitudinal directions, respectively. The third and fourth terms, which are second- and third-order extensibilities $(E_{C,3})$, account for the volume distensibility due to coupling effects among radial, circumferential, and longitudinal dimensional changes. If we define the circumferential $(E_C)$ and longitudinal $(E_L)$ extensibilities as

$$E_C = \frac{2\Delta R_i}{R_i}$$

and

$$E_L = \frac{\Delta L}{L} \times 100,$$

then we can rewrite Equation 5 as

$$E_v = E_C + E_L + \left(\frac{\Delta R_i^2}{R_i^2} + \frac{2\Delta R_i \Delta L}{R_i L} \right) \times 100$$

$$+ \frac{\Delta R_j^2 \Delta L}{R_j^2 L} \times 100$$

(6)

Whether one can drop out the higher-order terms depends on their relative magnitude.

A radial extensibility index $(E_r)$ is also calculated as the percentage change in segment wall thickness per millimeters mercury $\Delta P$ where

$$E_r = \frac{\Delta T}{T} \times 100$$

(7)

$T$ is the segmental wall thickness at diastole, and $\Delta T$ is the change in segmental wall thickness from diastolic to systolic states. Wall thickness is calculated from the external radius minus the internal radius, and $\Delta T$ is obtained by subtracting the diastolic thickness from the systolic thickness. Note that both $\Delta T$ and $E_r$ are negative because of the decrease in wall thickness from diastole to systole.

Stroke volume was calculated by dividing cardiac output by the concomitantly measured heart rate. Systemic vascular resistance was calculated as the ratio of mean arterial pressure to cardiac output.

**Statistical Analysis**

All measurements and calculated values are expressed as mean±SD. The paired-difference method was chosen to evaluate significant differences between rest and exercise for all measured and calculated variables. A value of $p<0.05$ was used to determine the statistical significance.

**Results**

Simultaneous measurements of UDTA segment pressure, diameter and length at rest and during exercise are shown in Figure 2. Pressure-dimension data obtained from these and similar recordings are summarized in Table 1. There was a significant increase in $R_i$ and a significant decrease in both $\Delta R_i$ and $\%\Delta R_i$ in response to exercise. These circumferential and radial dimensional changes were coupled with significant increases in both $\Delta L$ and $\%\Delta L$. 
during exercise. Wall thickness (t and T) and change in wall thickness (ΔT) were not altered by treadmill exercise. Mean aortic pressure and ΔP both increased significantly in response to exercise.

Calculated $E_v$, $E_c$, $E_L$, and $E_K$ are presented in Figure 3. During exercise, $E_v$, $E_c$, and $E_K$ decreased significantly from resting levels. Separately, the second- and third-order extensibility components calculated during exercise were significantly less than they were at rest. The second-order component decreased from $0.096±0.015\%ΔV/mm Hg ΔP$ at rest to $0.065±0.018 \%ΔV/mm Hg ΔP$ during exercise. The third-order component significantly decreased from $0.004±0.001 \%ΔV/mm Hg ΔP$ at rest to $0.002±0.001 \%ΔV/mm Hg ΔP$ during exercise. The $E_L$ component was essentially the same both at rest and during exercise. There were no significant differences for $E_R$ calculated from pulse pressure and wall thickness data between resting and exercising conditions. Heart rate, cardiac output, and stroke volume all increased significantly in response to exercise, whereas systemic vascular resistance decreased significantly (Table 1).

**Discussion**

The factors that contribute to the aortic mechanical responses seen during exercise are numerous and complex. The results of the present study indicate that, in addition to separate characterization of the pressure-dimension relations in the circumferential, axial, and radial directions, it is necessary to include their interactions. Physical meanings of these coupling higher-order terms are given in "Appendix." These coupling effects among circumferential, axial, and longitudinal dimensional changes (second and third order terms) account for approximately 10% of the total volume distensibility during both rest and exercise states. Therefore, use of the first-order expressions ($E_c$ and $E_L$) alone will result in underestimation of $E_v$ by this amount.

Using mechanical calipers in thoracotomized, anesthetized dogs, Patel et al.7 showed that the contributions of $E_L$ and $E_c$ to $E_v$ are 4% and 96%, respectively, at mean aortic pressures between 70 and 140 mm Hg. Further, they showed decreased volume distensibility at higher mean distending pressures and suggested that the reduction was chiefly due to circumferential extensibility. Our data show that the percentage contribution of $E_L$ and $E_c$ to $E_v$ during rest conditions are 21.3±7.9% and 67.5±7.3%, respectively, at mean distending pressures between 90 and 120 mm Hg. During exercise, the percent contribution of $E_L$ and $E_c$ to $E_v$ became 31.3±8.2% and 56.7±6.8%, respectively, at mean distending pressures between 110 and 150 mm Hg (Figure 3).

Our study of awake, exercising dogs shows a reduction in both volume distensibility and circumferential extensibility at higher mean aortic pressures, a finding which is similar to that of Patel et al.7 The relative percent contributions of $E_L$ and $E_c$ to $E_v$, however, are dissimilar to those presented by Patel et al.7 These differences might be accounted for by variations in measurement techniques, different pressure ranges, different protocols in inducing high mean pressure, and the differences in cardiovascular variables between awake and anesthetized dogs. In addition, the specific region of measurement may be different and may have partially contributed to the differences. For example, using similar technique, we have measured the in
vivo segmental regional differences in volume
distensibility from ascending aorta, upper descending
thoracic aorta, and middle descending thoracic
aorta. Furthermore, the second- and third-order
components of \( E_v \) were not analyzed in their study.
Our data show that these higher-order terms are
important in accurate determination of the regional
volume distensibility of a localized vessel segment.

In the present study, \( E_v \), \( E_c \), and \( E_k \) were shown
to decrease during exercise. Part of the reason can
be attributed to the increased mean aortic pressure.
At elevated aortic pressure, the vascular wall is in a
more distended state (the stiffer region of the non-
linear stress-strain curves) and the percentage of
circumferential and longitudinal elongations are less
for a unit loading change. This partially explains the
decreases of \( E_v \), \( E_c \), and \( E_k \) during exercise.

In addition to the circumferential and longitudinal
extensibilities, which are components of the regional
volume distensibility, we also computed the \( E_r \)
index, and measurements showed no significant
change between rest and exercise states. Essentially,
\( E_r \) index is a measure of the regional aortic
wall thinning from diastole to systole. We obtained
external wall radius from sonomicrometer measure-
ments and computed inner wall radius from Equa-
tion 1 for both diastolic and systolic states. We then
computed the percentage wall thickness changes
during pulse pressure increase. Perivascular tether-
ing may impose constraints on the wall motion. The
external diameter measurements from sonomicrom-
eter, however, will reflect any tethering constraints
on the wall motion. Furthermore, we can ignore any
shear deformation on the vascular wall due to
tethering. Sonomicrometer crystals are known to be
sensitive to their relative alignment. Yet we were
able to continuously receive signals from both dia-
metrical and longitudinal pairs throughout experi-
ments. This suggests that the orthogonal orientation
of the crystal pairs was retained and any possible
vascular wall shear deformation must be small.

The major determinants of the stresses and strains
involved in aortic rheology include heart rate, stroke
volume, myocardial contractility, peripheral vascu-
lar resistance, perivascular tethering effects, the
elastic properties of the arterial tree, and the asso-
ciated incident and retrograde reflected pressure
waves. Among others, intravascular pressure is the
most important factor causing mechanical stresses,
inside the vascular wall. We used \( E_v \) to characterize

\[
\begin{array}{lcccccc}
\text{TABLE 1. Upper Descending Thoracic Aorta Pressure-Dimension Values (Mean±SD) and Hemodynamic Variables of}
\text{Six Dogs at Rest and During Moderate Treadmill Exercise} \\
\hline
\text{Rest} & \text{Exercise} \\
\hline
r_i (\text{mm}) & 8.39±1.15 & 8.64±1.35 \\
R_i (\text{mm}) & 7.34±1.10 & 7.78±1.10* \\
\Delta R_i (\text{mm}) & 1.05±0.27 & 0.86±0.34* \\
%\Delta R_i & 14.35±3.31 & 10.96±3.64* \\
l (\text{mm}) & 13.15±2.44 & 13.26±2.41 \\
L (\text{mm}) & 12.11±2.21 & 11.87±2.20 \\
\Delta L (\text{mm}) & 1.05±0.37 & 1.38±0.43* \\
%\Delta L & 8.67±2.64 & 11.68±3.65* \\
t (\text{mm}) & 0.59±0.07 & 0.56±0.07 \\
T (\text{mm}) & 0.71±0.07 & 0.69±0.06 \\
%\Delta T & -0.13±0.01 & -0.13±0.01 \\
P (\text{mm Hg}) & 96±14 & 118±23* \\
\Delta P (\text{mm Hg}) & 47±7 & 58±11* \\
E_v (\%\Delta V/\text{mm Hg } \Delta P) & 0.91±0.11 & 0.67±0.12* \\
E_c (\%\Delta V/\text{mm Hg } \Delta P) & 0.62±0.14 & 0.38±0.11* \\
E_l (\%\Delta V/\text{mm Hg } \Delta P) & 0.19±0.06 & 0.21±0.08 \\
E_k (\%\Delta V/\text{mm Hg } \Delta P) & 0.10±0.02 & 0.07±0.02* \\
E_R (\%\Delta T/\text{mm Hg } \Delta P) & -0.40±0.05 & -0.33±0.07 \\
Heart rate (bpm) & 100±16 & 204±18* \\
Cardiac output (/min) & 4.12±1.13 & 8.94±0.70* \\
Stroke volume (ml) & 36.0±7.9 & 46.5±3.4* \\
Systemic vascular resistance (PRU) & 24.5±7.1 & 12.6±2.3* \\
\hline
\end{array}
\]
the rheological properties of the UDTA since it is a quantity that allowed us to assess directly the regional physiological functional capacity and its alteration during exercise. The AP was used as a loading index to help define $E_v$ since it is a variable that can be measured easily. Effects of perivascular tethering and relative motion of the heart are all included because they all partially contribute to the vascular deformation as recorded by the sonomicrometers.

The average stresses along circumferential and longitudinal directions can be calculated as in Fung et al.\textsuperscript{9} and Patel and Vaishnav.\textsuperscript{10} In addition to transmural blood pressure, shear stress can occur at the inner wall due to blood flow–arterial wall interactions. Furthermore, the motions of the beating heart can cause additional mechanical stresses in all directions.\textsuperscript{7,11} Knowledge of the stress gradient through the vessel wall is also important.\textsuperscript{12,13} All stress components should be included for a complete investigation of vascular wall rheological behavior under normal conditions, during exercise, and under any pathological state.

Stimulation of cardiac sympathetic afferents results in reflexes that modify aortic mechanical properties and may alter the sensitivity of aortic mechanoreceptors.\textsuperscript{14} Reduction in smooth muscle tone increases aortic baroreceptor activity, due to a dilation of the receptor area.\textsuperscript{15} Reflex increases in smooth muscle activity within the vessel wall may result in rearrangement of its structural components during exercise. This might partially explain the theory of reduced baroreflex sensitivity during exercise summarized previously.\textsuperscript{16} Although $E_v$ and $E_c$ for the UDTA decreased during exercise, no significant difference was seen for longitudinal extensibility between rest and exercise. The increase in pressure associated with treadmill exercise may not be sensed by the stretch receptors within the arterial wall. Therefore, changes in smooth muscle activity within the vessel wall itself might prevent or limit baroreceptor stimulation during exercise. The mechanical responses in the carotid sinuses and aortic arch need to be evaluated in this regard.

In conclusion, the regional $E_v$ of a segment of the UDTA was examined in dogs at rest and during moderate treadmill exercise. Dynamic exercise results in a significant decrease in $E_v$, $E_c$, and $E_k$ constituents. There is no significant change in either $E_L$ or $E_R$ from rest to exercise. All components should be included in the mechanical description of the arterial wall.

Appendix

The meaning of higher-order terms in the expression of the volume distensibility can be explained as follows:

1) Let's first consider the case when there is no longitudinal dimensional change. For a vessel segment with inner radius (R) and unit length, the volume increase from the original volume $\pi R^2$ is $2\pi R \Delta R + \pi (\Delta R)^2$ due to radial increment ($\Delta R$). Graphically, the incremental volume is represented by the incremental area (of unit length) between the shaded circle (radius, R) and the dashed circle (radius, R+$\Delta R$) (see Figure B-1, top). This incremental area is generated by contributions from $\Delta R$ and incremental circumference $\pi (\Delta R)$, respectively.

To illustrate the incremental area, we can replat the area of a circle as a rectangular region ABCD with side lengths R and $\pi R$ (see Figure B-1, bottom). Similarly, we can replat the area of the distended circle as the rectangular region AEGK with side lengths (R+$\Delta R$) and $\pi (R+\Delta R)$. Note that the area AEGK consists of four regions 1, 2, 3, and 4. Regions 2, 3, and 4 represent area increments from the original area $\pi R^2$ of Region 1. Region 2 is the incremental area due to $\Delta R$ (incremental radius) alone, Region 3 is that due to $\pi (\Delta R)$ (incremental circumference) alone, whereas Region 4 is the incremental area due to the coupling from both $\Delta R$ and $\pi (\Delta R)$.

![Figure 3. Mean values and standard deviations are presented for volume distensibility ($E_v$), circumferential extensibility ($E_c$), longitudinal extensibility ($E_L$), and combined second- and third-order extensibilities ($E_K$) at rest and during exercise. $E_v$ is the $%\Delta V/mm Hg$ pulse pressure ($\Delta P$). $E_c$, $E_L$, and $E_K$ respectively are the $%LWImm Hg$ AP due to change in radius, length, and combined second- and third-order components of $E_v$. Significant differences from rest are denoted by $\dagger$ (p<0.05).](image-url)
2) The intraluminal volume increase of a vessel segment with nonzero $\Delta R$ and nonzero $\Delta L$ can be explained in a similar way. The incremental volume is represented by the region between the shaded surface (radius, $R$; length, $L$) and the dash-lined surface (radius, $R + \Delta R$; length, $L + \Delta L$), see Figure B-2, top. This incremental volume is generated by contributions from dimensional changes in radial ($\Delta R$), circumferential $\pi(\Delta R)$, and longitudinal ($\Delta L$) directions. Similar to the previous case, the original intraluminal volume can be represented by the shaded parallelepiped of $\pi R^2 L$, whereas different subregions in dash-line represent the incremental volume from the original volume due to nonzero $\Delta R$ and $\Delta L$ (Figure B-2, middle). To facilitate interpretation for each part of the incremental volume, an exploded view is given in Figure B-2, bottom. Regions 2, 3, and 4 are the same as those in the previous case except $L$ equals 1 in Figure B-1, bottom. Region 5 is the incremental volume due to $\Delta L$ alone, Region 6 is that due to the coupling of $\Delta R$ and $\Delta L$ alone, and Region 7 is that due to the coupling of $\pi(\Delta R)$ and $\Delta L$. Region 8 represents the coupling among $\Delta R$, $\pi(\Delta R)$, and $\Delta L$.

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References


2. Dobrin PB: Mechanical properties of arteries. Physiol Rev 1978;58:397-460


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