Shear modulus of porcine coronary artery: contributions of media and adventitia

X. Lu,1 J. Yang,2 J. B. Zhao,2 H. Gregersen,2 and G. S. Kassab1
1Department of Biomedical Engineering, University of California, Irvine, California 92697; and 2Center for Sensory-Motor Interaction, Aalborg University, and Department A, Aalborg Hospital, 9000 Aalborg, Denmark

Submitted 17 April 2003; accepted in final form 14 June 2003

The blood vessel wall is exposed to two distinct hemodynamic forces: 1) shear stress, the frictional force generated by blood flow, and 2) tensile stress or strain due to vessel wall distension by blood pressure. On the surface of the heart, however, the large coronary arteries experience these mechanical forces as well as marked extensions and torsion in the axial direction due to changes in the shape and size of the heart during the cardiac cycle (4, 12, 19). Therefore, the study of the shear properties of these vessels is a significant aspect of coronary physiology and pathophysiology. Although there have been a number of studies on the passive mechanical properties of the coronary arteries in the circumferential and longitudinal directions (see review in Ref. 10), there have been no studies on the shear properties of these vessels. One of the goals of the present study was to fill this gap. In the process, we determined the dependence of the shear modulus on pressure, circumferential stress, and longitudinal stretch and stress.

The second goal of this study was to model the coronary blood vessel wall as a two-layer composite (intima-medial and adventitial layers). Each layer has its own zero-stress state and its own elastic constants. We tested the coronary artery as an intact vessel followed by dissection of either the adventitia or the media. A biomechanical analysis was proposed to compute the shear modulus of the adventitia from that of the intact vessel and media or the media from the intact vessel and adventitia. We found a simple relationship between the modulus of the intact vessel and that of its two layers. The results are discussed along with the assumptions and implications.

MATERIALS AND METHODS

Triaxial torsion machine. Figure 1 shows a schematic of the triaxial machine. The arterial specimen is mounted on the cannula horizontally on both ends. The cannula on the left is connected to the torque transducer as shown in Fig. 1. The right cannula is connected to a load cell (Sensotec model; Sensotec error at 0.15–0.25% at full scale), and the load cell is fixed with a servo motor (type SDS 601, Parker Hannifin) that twists the specimen at an angle θ. The organ bath chamber is designed to keep the specimen immersed in the physiological solution and to eliminate any friction between the cannulas and the wall of chamber. The cannulas are made to pass through the holes on the side walls of the chamber, and then a circulative pump is used to maintain the volume of the solution in the chamber. The right cannula is also connected with a pressure transducer (Summit disposable pressure transducer, Baxter Healthcare; error of ±2% at full scale) through a Y tube. A pressure regulator is used to control the luminal pressure in the arterial specimen. The torque transducer on the left and the rotation motor on the right are mounted on the linear stage (Daedal positioning...
Heart preparation. Twelve hearts of Danish Landrace-Yorkshire pigs with body weight in the range of 90–95 kg were obtained at a local abattoir. The hearts were transported to the laboratory in 4°C Krebs solution within 45 min after the animal was killed. A 20- to 30-mm segment of the left anterior descending artery (LAD) and of the right coronary artery (RCA) were dissected carefully from their emergence at aortic ostia, every bifurcation was identified, and each branch was ligated with 6-0 suture. The anterior surfaces of the LAD and RCA segments were marked with water-resistant ink. The loose connective tissue around the faces of the LAD and RCA segments were marked with water-resistant ink. Two rings (length 1–2 mm) were cut each from proximal and distal LAD and RCA. The cross section of rings was videotaped to measure the internal and external circumference and wall area in the no-load (zero transmural pressure) state. To obtain the zero-stress state, all rings were cut radially at the anterior surface. The digital photographs of all sections at the zero-stress state were saved in a computer and measured with Sigma image software.

Mechanical test. The remaining segment (15–20 mm) was mounted on the cannulas of the triaxial machine as shown in Fig. 1. Microbeads (stainless steel, 60–100 μm in diameter) were dispersed on the outer surface of the segment, which were videotaped during triaxial testing to measure displacement and compute strain. The segment was immersed in Krebs solution in the organ bath, which was aerated with 95% O₂–5% CO₂ at room temperature (∼22°C). The segment was preconditioned several times to obtain reproducible mechanical data. Briefly, preconditioning was performed as follows. The pressure was set at zero, the axial stretch ratio was ramped from 1 to 1.4 for four cycles, the stretch ratio was then fixed at 1.4, and the arteries were ramped from 0 to 18.7 kPa (140 mmHg) for four cycles.

In the protocol of triaxial measurements, the longitudinal stretch ratio ($\lambda_L$) was varied from 1 to 1.4 in increments of 0.1. The transmural pressure ($P$) was set at 0, 3, 5, 8, 10.7, 13.3, 16, and 18.7 kPa at every $\lambda_L$. At each $\lambda_L$ and pressure, a ramp of twist was performed from 0° to −25° and from 0° to 25°. For example, at $\lambda_L = 1.2$ and $P = 8$ kPa (60 mmHg), the twist angle was varied between −25° and 25°; however, when the stretch ratio was small ($\lambda_L \leq 1.2$), the segment became curved at higher pressures (≥10.7 kPa). Curved segments were not included in the analysis. The vessel was also preconditioned to twist before measurements.

The segment was removed from the triaxial machine and then transferred to a dish in cold Krebs solution. In eight hearts, the adventitia of the arterial segments was carefully dissected away from the media at the external elastic laminae with the aid of a stereomicroscope. The intima-medial layer of the arterial segments remained intact and was tested in the triaxial machine according to the same protocol used for the intact wall. In an additional four hearts, the vessel segment was inverted inside out and the media was dissected away, leaving the adventitia intact. The adventitia was then reinverted and tested in the triaxial machine with the protocol described above.

Histological preparation. The tissue specimens were fixed in formalin solution over 24 h and embedded in paraffin. Five-micrometer-thick sections were cut and stained with hematoxylin and eosin to examine the changes in the media or adventitia due to dissection of the adjacent layer. The thickness of media both in the intact arterial rings and in the rings after dissection was measured.

Biomechanical principles. The coronary artery is considered to be a two-layer cylinder. Because the intima is relatively thin in the normal artery, the intima-media is considered as the inner layer and the adventitia as the outer layer. Initially, the arterial wall is considered to be a homogeneous material so that we may obtain an “apparent” shear modulus. The artery is subjected to a transmural pressure ($P_i$), a longitudinal force ($F_L$), and a torque ($T$). The radii of the inner boundary of the intima, the interface of the media and adventitia, and the outer boundary of the adventitia are denoted by $r_i$, $r_m$, and $r_a$, respectively, as shown in Fig. 2. We consider a vessel segment of length $L$ undergoing a twist...
angle \( \theta \) and an angle of twist per unit length \( \theta/L \). The average shear stress in the vessel wall is \( \sigma_w \) for the intact artery. In the present experiments, we found that \( T \) is linearly proportional to \( \theta/L \) in the range of interest. Hence, \( \sigma_w \) is linearly proportional to \( \theta/L \) in this range. Because the shear strain \( (\varepsilon_{\theta\theta}) \) is, by definition, \( \varepsilon_{\theta\theta} = r \theta/2L \), the linearity implies that

\[
\bar{\sigma}_{\theta\theta} = 2G\varepsilon_{\theta\theta} = \frac{Gr\theta}{L}
\]

where \( G \) is the shear modulus of elasticity of the intact arterial wall. The torque is given by an integral of the product of the average shear stress and the moment arm and the wall area as

\[
T = 2\pi \int_{r_i}^{r_m} \frac{Gr\theta}{L} r^2 dr = \frac{\pi G r \theta}{2L} (r_m^3 - r_i^3) = GJ \frac{\theta}{L}
\]

where \( J \) is the polar moment of inertia of the intact vessel given by

\[
J = \frac{\pi}{2} (r_m^4 - r_i^4)
\]

Finally, we obtain the desired relationship between the torque and the shear modulus as given by

\[
T = GJ \frac{\theta}{L}
\]

To extend this analysis to a two-layer model, we assume that there is no slip between the medial and adventitial layers during torsion. This implies that the two layers have the same twist angle \( \theta \) during torsion. Let \( \bar{\sigma}_{\theta\theta}^m \) and \( \bar{\sigma}_{\theta\theta}^a \) denote the average shear stress in the intima-medial and adventitial layers, respectively. Hence, the relationship between the average shear stress and shear modulus takes on a form similar to Eq. 1, where \( G \) is replaced by \( G_m \) or \( G_a \) for the intima-medial or adventitial layer, respectively. The vessel wall force resultant is equal to the sum of the forces in the two layers

\[
F_\theta = \int_{r_i}^{r_m} \frac{G_m \theta}{L} r^2 dr + \int_{r_m}^{r_a} \frac{G_a \theta}{L} r^2 dr
\]

or

\[
F_\theta = \frac{2}{3} \frac{\pi \theta}{J} [G_m (r_m^3 - r_i^3) + G_a (r_a^3 - r_m^3)]
\]

The total force is calculated from the measured torque as follows

\[
F_\theta = \frac{T}{(r_i + r_m)^2}
\]

The desired relationship between the shear modulus of the intact vessel and that of its two layers can be obtained by combining Eqs. 3–5 to yield

\[
G = \frac{\pi}{3} \frac{r_i + r_m}{J} \frac{G_m (r_m^3 - r_i^3) + G_a (r_a^3 - r_m^3)}{GJ}
\]

For a thin-walled vessel where \( r_i \approx r_m \) and \( r_m \approx r_a \), Eq. 6 can be simplified to the form

\[
GJ = J_m G_m + J_a G_a
\]

Incidentally, Eq. 7 can be derived directly from considerations of membrane torque resultant. Because the intima-medial layer is tested mechanically after the adventitia is dissected, we can compute the shear modulus of adventitia with Eq. 6 or vice versa for the media.

The mean stresses in the circumferential \( (\sigma_\theta) \) and longitudinal \( (\sigma_z) \) directions are given by

\[
\sigma_\theta = \frac{Pr_i}{h}
\]

and

\[
\sigma_z = \frac{F_\theta}{(r_i + r_m)} + \frac{Pr_i^2}{h(r_i + r_m)}
\]

where \( F_\theta \) and \( h \) are the longitudinal force and wall thickness, respectively. The inner radius \( r_i \) of the vessel can be computed from the incompressibility condition for a cylindrical vessel as

\[
r_i = \sqrt{r_i^2 + \frac{A_0}{\pi h}}
\]

where \( r_m, A_0, \) and \( h \), are outer radii at the loaded state, the wall area in the no-load state, and the axial stretch ratio, respectively. Because all the quantities on the righthand side of Eq. 10 are measured, the loaded inner radius can be computed.

**Torsion of an angiographic catheter.** To determine the magnitude of the torque or shear stress induced by a slight twist of a conventional angiographic catheter, we tested two Monorail angioplasty catheters (2-Fr and 5-Fr) in torsion. A Tygon tube of \( \sim 3 \)-mm inner diameter was fixed onto the left cannula, which was connected to the torque transducer as shown in Fig. 1. The tip of the catheter was then inserted into the lumen of the tubing, and the balloon was inflated. Inflation of the balloon within the lumen of the tube rigidly fixed the catheter, i.e., the balloon did not slip against the wall of the tube. The catheter was attached to the right cannula of the torsion machine at various distances from the balloon.
Three different lengths of the catheter were tested; 50, 90, and 114 mm. The catheter was subjected to a maximum twist angle of \pm 10°. Subsequent to mechanical testing, a small ring was cut transverse to the length of the catheter and viewed with an optical microscope for measurements of inner and outer radii. The polar moment of inertia was computed from measurements of the geometry of the catheter.

Statistical analysis. Data are presented as means \pm SE unless otherwise indicated. Statistical significance was determined by the use of ANOVA or Student’s t-test. A probability of \( P < 0.05 \) was considered statistically significant.

RESULTS

The torque and twist angle were measured directly and recorded in the computer. These direct measurements show that the relation between torque and twist rate is linear at the inflation and longitudinal extensions examined for the intact wall, media, and adventitia. Figure 3 shows typical curves for the LAD. The polar moment of inertia (\( J \)) and the segment length (\( L \)) were constant during torsion for each coronary arterial segment at a given inflation and stretch. Therefore, the shear modulus of coronary arteries is equal to the slope of the line in Fig. 3 as obtained from a least-squares fit of the data. The slopes of the lines varied with pressure and longitudinal stretch ratio. Figure 4 shows the variation of shear modulus with pressure and circumferential stress for the LAD and RCA at various stretch ratios. Figure 5 shows the variation of shear modulus with longitudinal stretch and stress for the LAD and RCA at various pressures. Comparisons of measured shear modulus of intact wall and media and that of computed adventitial modulus are shown in Figs. 6, A–C, and 7 for the eight LAD and RCA, respectively. Table 1 summarizes the data on a linear regression between shear modulus and circumferential stress for the measured intact RCA and LAD and their media. Similarly, a comparison of measured shear modulus of intact wall and adventitia and that of computed medial modulus are shown in Fig. 6, D–F, for the four LAD. The empirical constant for a least-squares fit of the relationship between shear modulus and circumferential stress is summarized in Table 2 for the measured intact LAD and its adventitia.

The effect of direction of twist (clockwise vs. counterclockwise) is shown in Fig. 8. Figure 8A shows the experimental data with the clockwise twist in the upper quadrant and the counterclockwise twist in the lower quadrant. The solid line corresponds to a least-squares fit of the data for clockwise twist. It can be seen that there is a small angle between the curve fit and the data on the counterclockwise direction. The difference, however, is not statistically significant. Figure 8B provides a comparison between the shear modulus and the twist direction for various inflations at a given longitudinal stretch ratio. Again, we found no statistically significant differences in the direction of twist for
the range of pressures and longitudinal stretch ratios examined.

The viscoelastic properties of the coronary vessels were demonstrated through the relaxation of torque at a given twist angle. Figure 9 shows the time course of relaxation of the torque of the intact LAD and its media and adventitia for a twist angle of 25°. We observed an ~15% drop in the torque from the initial value to an asymptotic value after 5 min for both the intact wall and its media and adventitia at $\lambda = 1.3$. The time required to reach one-half of the amplitude of relaxation (time constant) was ~10 s for intact wall, ~12 s for media, and ~20 s for adventitia.

The intima-media thickness at the zero-stress state was measured from histological slides of the intact wall and of the intima-media segments where the adventitia was dissected away. For the LAD segments, the intima-media thickness was 293 ± 80.9 μm measured from the intact wall and 289 ± 46.4 μm measured from the dissected segments. For RCA segments, the thickness was 312 ± 41.2 and 306 ± 40.6 μm for the intact wall and media, respectively. No statistically significant differences in the medial wall thickness were caused by dissection. Also, the appearance of the edge of the media did not show any significant evidence of tearing or trauma.

Fig. 4. Relationship between the shear moduli of coronary artery and circumferential distension at various longitudinal stretch ratios. Distension is expressed in terms of pressure for the LAD (A) and right coronary artery (RCA; B). Distension is also expressed in terms of mean circumferential stress for the LAD (C) and RCA (D). A linear least-squares fit was used to describe the relationship between shear modulus ($G$) and circumferential stress ($\sigma_\theta$) as $G = \alpha + \beta \sigma_\theta$ for the LAD and the RCA as shown in Tables 1 and 2.

Fig. 5. Relationship between the shear moduli of the coronary artery and longitudinal distension at various distension pressures ($P_i$). Distension is expressed in terms of longitudinal stretch ratio of the LAD (A) and the RCA (B). Distension is also expressed in terms of mean longitudinal stress for the LAD (C) and the RCA (D).
The relationship between twist rate and torque for the angiographic catheters was also found to be linear, similar to Fig. 3. The shear modulus was found to be 220 \pm 23.8 and 267 \pm 20.9 MPa for the 2-Fr and 5-Fr catheters, respectively. There was no statistically significant difference between the three lengths of catheters tested. There was also no statistically significant difference in the direction of twist, i.e., the catheter is isotropic to the direction of twist.

**DISCUSSION**

Shear modulus of coronary artery. We have found that the shear stress is linearly related to the shear strain, i.e., the shear modulus does not depend on the shear stress or strain as shown in Fig. 3. The shear modulus does, however, vary with the circumferential and longitudinal stresses and strains (Figs. 4 and 5, respectively). These findings are consistent with the study on the shear modulus of the rat aorta (3). Furthermore, we found that the dependencies of the shear modulus on the circumferential and longitudinal stresses are linear but those on strains are nonlinear. We did not find any statistically significant differences in the values of shear moduli between RCA and LAD at \( \lambda_z = 1.4 \) (physiological longitudinal stretch).

**Comparison with other works.** There are no previous data in the literature on the shear modulus of the coronary artery or its individual layers. The only torsion data in the literature are on the aorta. Vossoughi and Tozeren (18) measured the shear modulus on a rectangular piece of excised aorta. They did not, however, determine the effect of circumferential or longitudinal stress on the shear modulus. Humphrey et al. (8) built a triaxial torsion machine but only showed illustratory data on the aorta and carotid artery. Deng et al. (3) invented a different triaxial torsion machine and used it to obtain the first systematic set of data on the shear modulus of an intact aorta at various pressures and longitudinal strains. They found that the shear modulus of the rat aorta is 183 \pm 25 kPa at physiological conditions (\( P = 16 \) kPa and \( \lambda_z = 1.3 \)). The shear modulus of the RCA and LAD at physiological conditions (\( P = 13.3 \) kPa and \( \lambda_z = 1.4 \)) is 210 \pm 46.5 and 231 \pm 55.1 kPa, respectively. Hence the porcine coronary artery is somewhat stiffer than the rat aorta in the longitudinal-circumferential direction under physiological conditions.

**A two-layer model.** A prominent feature of the blood vessel is the layered construction of its wall. The blood vessel wall consists of intimal, medial, and adventitial...
layers. For larger vessels for which the thickness of the intima is only a small fraction of that of the media, the two-layered model presented here can be considered to be sufficiently accurate. Each layer has its own zero-stress state and its own elastic constants including different shear moduli.

Classically, the vessel wall was considered as a homogeneous material and the no-load state was thought to be the zero-stress state. The paradigm changed in 1983 when Fung (5) and Vaishnav and Vossoughi (15) independently discovered that the geometry of the zero-stress state is a sector that is very different from the no-load state. This recognition removed the concept of stress concentration at the inner wall of the vessel. However, the homogeneous model of the vessel wall persisted until the 1990s, with the exception of the study by von Maltzahn et al. (16, 17). In the past decade, however, the vessel has been modeled as a shell of several layers, each of which has its own elasticity constants and its own state of zero-stress resultants and zero-stress moments (1, 2, 7, 13, 20, 21).

In the present study, we assume that the vessel is a two-layered structure: one layer of vascular smooth muscles and endothelial cells, elastin, and some collagen and another layer of collagen, fibroblasts, and elastin. These are the intima-medial and adventitial layers, respectively. We found the shear modulus of the adventitia to be greater than that of the intact vessel, which was greater than that of the media. This relationship was predicted by Eq. 7, which states that the product of polar moment of inertia and shear modulus of the intact vessel is equal to the sum of the products of polar moment of inertia and shear modulus of each of the two layers. This relationship was validated by experimental data.

Viscoelastic features of shear. The hysteresis loop of the torque rate of twist relationship as shown in Fig. 3 is fairly small. The relaxation of the shear stress at a constant angle of twist is also shown in Fig. 9 for the intact vessel, media, and adventitia. Only a 15% drop in the torque from the initial value to an asymptotic value was observed. Hence, the viscoelastic feature of shear in the epicardial coronary arteries is small.

Effect of direction of twist. In coronary artery (a muscular vessel), smooth muscle is a significant component of the vessel wall. The arterial vascular smooth muscle is reported as a helical structure in the media (14). To determine the effect of direction of twist on the shear modulus, the samples were twisted in clockwise and counterclockwise directions, respectively. We found that the shear moduli in the clockwise direction were slightly larger than the shear moduli in the counterclockwise direction at any longitudinal stretch ratio and transmural pressure. The differences, however, were not statistically significant (<5%). Hence, the porcine coronary arteries can be treated mechanically as a torsionally symmetrical cylinder.

Critique of methods. The dissection of a vessel wall into separate shells without injury is not always possible. Ideally, each layer can be separated without damage and tested for its mechanical property. Because dissection invites the criticism of injury, in vivo experiments are important. Fung and Liu (6) published a method to measure the elastic constants of the two layers of the arteries in vivo that was a breakthrough. The methods proposed, however, are very difficult to use on the coronary arteries because of the motion of the blood vessel and the associated forces during the cardiac cycle. In the present study, we opted to preserve one layer while dissecting away the other layer. Indeed, a cleavage plane exists at the external elastic laminae where the dissection of the two layers is possible without significant damage to one of the layers. Figure 10 shows a histological
LAD and RCA. Values with superscript letters are significant to be linear (Fig. 3); hence, the value of shear modulus does not depend on the degree of twist. A more significant concern may be that the presence of bifurcation may impose constraints where the torsional strain or deformation is nonuniform, unlike the present experimental setup. In this case, knowledge of the strain distribution can still lead to calculation of shear stress through the propagation of the media after dissection of adventitia. There is no significant evidence of tearing or damage to the media. Furthermore, the difference in the thickness of the media measured from the intact wall and from the media where the adventitia was dissected was not statistically significant.

Isolation of the coronary artery segment for mechanical testing required the ligation and excision of side branches. The diameter of the side branches ranged from 10% to 30% of the diameter of the test segment. In the intact beating heart, these side branches may constrain the torsion of the vessel segment, i.e., the maximum twist angles of ±25° may not be realized in vivo. Despite this, however, we found the relationship between torque and rate of twist to be linear (Fig. 3); hence, the value of shear modulus measured does not depend on the degree of twist.

### Table 1. Linear regression parameters of relationship between shear modulus G and circumferential stress σ₀ as given by $G = \alpha + \beta \sigma_0$

<table>
<thead>
<tr>
<th></th>
<th>Measured Intact Wall</th>
<th>Measured Media</th>
<th>Computed Adventitia</th>
<th>Measured Intact Wall</th>
<th>Measured Media</th>
<th>Computed Adventitia</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda = 1.2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.553 ± 0.101†</td>
<td>0.522 ± 0.189</td>
<td>0.586 ± 0.247 ‡</td>
<td>0.732 ± 0.191†</td>
<td>0.501 ± 0.185†</td>
<td>0.877 ± 0.325‡</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>19.4 ± 2.87‡</td>
<td>11.1 ± 2.56c</td>
<td>27.2 ± 5.68§</td>
<td>16.5 ± 4.08§</td>
<td>15.3 ± 3.49</td>
<td>17.9 ± 5.99§</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.974 ± 0.030</td>
<td>0.990 ± 0.007</td>
<td>0.932 ± 0.076</td>
<td>0.964 ± 0.041</td>
<td>0.985 ± 0.025</td>
<td>0.953 ± 0.057</td>
</tr>
<tr>
<td>$\lambda = 1.3$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.825 ± 0.172‡</td>
<td>0.706 ± 0.242b</td>
<td>0.951 ± 0.193§</td>
<td>1.23 ± 0.271‡</td>
<td>0.824 ± 0.233†</td>
<td>1.44 ± 0.384‡</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>24.7 ± 3.86b</td>
<td>13.5 ± 3.15c</td>
<td>35.4 ± 7.29§</td>
<td>18.8 ± 3.37§</td>
<td>18.8 ± 5.92</td>
<td>22.1 ± 3.36§</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.990 ± 0.011</td>
<td>0.990 ± 0.007</td>
<td>0.964 ± 0.050</td>
<td>0.959 ± 0.033</td>
<td>0.983 ± 0.016</td>
<td>0.929 ± 0.051</td>
</tr>
<tr>
<td>$\lambda = 1.4$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>1.47 ± 0.369*</td>
<td>0.916 ± 0.287b</td>
<td>2.02 ± 0.559§</td>
<td>1.95 ± 0.642†</td>
<td>1.12 ± 0.207†</td>
<td>2.45 ± 0.787†</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>33.1 ± 7.98*</td>
<td>20.7 ± 4.01a</td>
<td>45.1 ± 16.4a</td>
<td>32.9 ± 7.61†</td>
<td>24.7 ± 6.79†</td>
<td>37.9 ± 11.7†</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.993 ± 0.004</td>
<td>0.998 ± 0.002</td>
<td>0.986 ± 0.008</td>
<td>0.973 ± 0.032</td>
<td>0.993 ± 0.006</td>
<td>0.961 ± 0.023</td>
</tr>
</tbody>
</table>

### Table 2. Coefficients of linear regression of relationship between shear modulus G and circumferential stress $\sigma_0$ as given by $G = \alpha + \beta \sigma_0$

<table>
<thead>
<tr>
<th></th>
<th>Measured Intact Wall</th>
<th>Measured Media</th>
<th>Computed Adventitia</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda = 1.2$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.476 ± 0.168</td>
<td>0.378 ± 0.141</td>
<td>0.532 ± 0.252</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>13.8 ± 4.06a</td>
<td>5.48 ± 1.93c</td>
<td>21.7 ± 6.51</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.918 ± 0.089</td>
<td>0.953 ± 0.052</td>
<td>0.955 ± 0.064</td>
</tr>
<tr>
<td>$\lambda = 1.3$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.744 ± 0.233</td>
<td>0.666 ± 0.186</td>
<td>1.06 ± 0.279</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>20.1 ± 5.21b</td>
<td>6.64 ± 2.69a</td>
<td>27.6 ± 8.98</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.966 ± 0.025</td>
<td>0.917 ± 0.124</td>
<td>0.932 ± 0.098</td>
</tr>
<tr>
<td>$\lambda = 1.4$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>1.25 ± 0.412</td>
<td>0.843 ± 0.323</td>
<td>1.81 ± 0.627</td>
</tr>
<tr>
<td>$\alpha$, kPa</td>
<td>43.9 ± 12.92</td>
<td>30.2 ± 11.5</td>
<td>54.8 ± 18.8</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.970 ± 0.022</td>
<td>0.905 ± 0.064</td>
<td>0.973 ± 0.039</td>
</tr>
</tbody>
</table>

Parameter values are presented as means ± SD. Data were obtained from 4 animals for which the intact vessel and adventitia of the LAD were measured directly and the medial properties were computed according to Eq. 7. Values with superscript letters are significantly different ($P < 0.05$) from values with same superscript letters in Table 1.
posed constitutive relation, i.e., torsional stress-strain relation.

Finally, the dissection of vessel segments may also disrupt the vasa vasorum and its blood perfusion (or distension). Because the vasa vasorum is most abundant in the adventitia (11), this may lead to a reduction in the transmural (internal/external) pressure on the vessel wall. Our results show that the shear modulus increases linearly with the transmural pressure (Fig. 4). Hence, a local reduction in transmural pressure would cause a proportional decrease in shear modulus. The present data allow us to make the correction when the state of transmural pressure is known.

Clinical significance of study. Knowledge of the individual properties of coronary artery layers is necessary to understand the physiology and pathology of the arterial wall. For example, the two layers are innervated by baroreceptors and perfused by vasa vasorum. Shear forces at the media-adventitia border may stimulate the mechanoreceptors by mechanical deformation as well as affecting the vascular geometry of the vasa vasorum and hence the blood perfusion of the vessel wall. Kwon et al. (11) used micro-CT to study the anatomy of the vasa vasorum in the porcine coronary artery. They demonstrated that the vasa vasorum originates from the lumen of the coronary artery and runs longitudinally along the media-adventitia border. Hence, if the transmural forces at the border become abnormally high, they may collapse the vasa vasorum and cause ischemia of the vessel wall, which may lead to coronary artery disease or arteriosclerosis. Furthermore, significant differential torsional stresses at the media-adventitia border may lead to coronary artery dissection.

Catheter-induced dissection of the coronary artery is an important concern in invasive cardiology (9). The observations made in the present study may offer some guidance to minimize the occurrence. The data show that the shear modulus increases with pressure and longitudinal stretch and the difference between the shear moduli of the layers increases with an increase in pressure and stretch. When a balloon is used to distend a plaque or deploy a stent, the inflation should be done without any twist of the catheter because this would impose large differential torsional stresses at the media-adventitia border where dissection occurs. The measurements of shear modulus show that the catheter is three orders of magnitude larger than the blood vessel and any slight twist of the catheter would induce large shear stress on the vessel wall. Hence, if it is necessary to turn or twist the catheter, this should be done with a deflated balloon. Although most cardiologists may follow these practices, this study indicates possible mechanical consequences.

DISCLOSURES

This research was supported in part by National Heart, Lung, and Blood Institute Grant 5-R29-HL-55554 and American Heart Association (AHA) Grant 0140036N. G. S. Kassab is the recipient of the National Institutes of Health Young Investigator Award and the AHA Established Investigator Award.

Fig. 9. The temporal variation of shear stress, at a constant twist angle (25°), of LAD and its media (A) and LAD and its adventitia (B). The measurements were made at a longitudinal stretch ratio of 1.3 and a transmural pressure of 11 kPa. The corresponding circumferential and longitudinal stresses ($\sigma_\theta$ and $\sigma_z$) are indicated.

Fig. 10. A histological section of intact coronary artery vessel wall (A) and media after dissection of adventitia (B). IEL, internal elastic laminae; EEL, external elastic laminae. The thickness of the media (distance between IEL and EEL) is $\sim$300 $\mu$m.
REFERENCES