Effect of passive myocardium on the compliance of porcine coronary arteries

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The mechanical properties of coronary vessels play an essential role in understanding the physiological functions of the vessels, and as a result, have direct clinical implications in the diagnosis and treatment of patients with coronary artery disease and atherosclerosis (22, 27). Anatomically, the coronary arteries originate from the aortic ostia, just above the aortic valve, and continue along the surface of the heart as they penetrate into the myocardium where they deliver blood throughout the thickness of the heart (16). The posterior aspect of the proximal coronary artery is partially embedded into the myocardium, whereas the anterior portion is surrounded by the serous visceral pericardium. As the coronary artery descends along the ventricle, it becomes fully embedded into the myocardium.

A number of previous studies (1, 2, 9, 10, 13, 15, 21) have examined the mechanical properties of coronary arteries under in vitro conditions; i.e., after dissection of the vessels from the myocardium. For example, Patel and Janicki (21) determined the in vitro pressure-diameter relationship for isolated segments of the dog's left circumflex. The pressure-diameter relationship of excised coronary arteries from dogs and humans was measured by Gow et al. (10) and Gow and Hadfield (9), respectively. More recently, several in vitro inflation and extension tests on isolated passive human, porcine, and bovine coronary arteries have been performed by Carmines et al. (1) and Kang et al. (15). Although those studies provide a wealth of data on the compliance and material properties of blood vessels, they do not take into account the mechanical contribution of the surrounding medium. Our hypothesis is that the mechanical properties of the coronary artery stems not only from the intrinsic properties of its wall (collagen, elastin, ground substance, etc.) but also stems from the surrounding medium (myocardium including serous pericardium, fat tissue, etc.). It has generally been difficult to determine the compliance of the same blood vessel both with (in situ) and without (in vitro) the surrounding tissues. Consequently, very little data can be found in this regard.

Furthermore, the compliance of the coronary arteries has been previously determined primarily under distension. We are unaware of any data on the compressive mechanical properties of the coronary arteries. This is surprising because it is well recognized that the myocardium may exert compressive stresses on the embedded blood vessels during the cardiac cycle. Indeed, the compression between the heart muscle and coronary blood vessels may be an important determinant of the zero-flow pressure in the coronary circulation. Hence, in the present study, we wanted to determine the effect of passive myocardium on the mechan-
ical properties of coronary arteries both under distension and compression. Specifically, our objectives are 1) to determine the cross-sectional area (CSA) of the first several generations of coronary arteries in the range of −150 to +150 mmHg pressure difference (ΔP); 2) to determine the ΔP-volume relationship of the proximal coronary arterial tree (vessels >0.5 mm in diameter) under distension and compression; and 3) to compare the compliance of the proximal coronary artery with and without the myocardium.

METHODS

All experiments were performed in accordance with national and local ethical guidelines, including the Institute of Laboratory Animal Research (ILAR) Guide, Public Health Service policy, Animal Welfare Act, and University of California Institutional policies regarding the use of animals in research.

Isolated heart preparation. The studies were performed on six male Duroc swine weighing 34 kg ± 5 kg (range 30–39 kg). Surgical anesthesia was induced with ketamine (20 mg/kg im) and atropine (0.04 mg/kg im) and maintained with isoflurane (1–2%). Ventilation with 100% O2 was provided. Blood gas values were measured, and ventilation was adjusted to maintain normal values of PO2 and PCO2. A midline sternotomy was performed, and an incision was made in the pericardium to support the heart in a pericardial cradle. Anticoagulation was induced with heparin (100 U/kg) followed by the injection of pentobarbital (80 mg/kg iv) and then followed by a saturated KCl solution, through the jugular vein, to euthanize the animal and arrest the heart. The heart was then excised, and the aorta was clamped to keep air bubbles from entering the coronary arteries. The right coronary artery and the left circumflex were ligated, while the left anterior descending (LAD) was cannulated while immersed under saline to avoid air bubbles. Immediately afterward, an isosmotic cardioplegic rinsing solution (composed of 6% dextran in saline, including 80 mg/l of adenosine and 1.5 g/l of 2,3-butanedione monoxime) was perfused through the LAD artery to keep the myocardium relaxed and the vasculature vasodilated.

The heart was then placed into a saline-filled Lucite box with dimensions of 20 cm × 20 cm × 10 cm. A schematic of the experimental setup is shown in Fig. 1. Before the heart was placed into the box, paper towels were added to fix the position of the heart to ensure a nonoverlapping projection of the LAD arterial tree. The LAD artery was positioned to face the bottom of the box to prevent it from being pushed up against the top of the box as the box pressure increased. We maintained some air in the ventricles of the heart to make it buoyant so that the LAD artery was not compressed by the heart weight. The Lucite box contained two side openings and a third opening on the top cover. The coronary artery cannula was connected to one of the side openings and was used to regulate the intravascular pressure. The second side opening was used to regulate and measure the box pressure. The top cover of the box contained a ventilation hole, connected to a stopcock, which was normally closed during pressurization of the box. The stopcock was only opened to the atmosphere before the imaging process when the box pressure was set equal to zero or to remove air bubbles from the box. The post-mortem imaging experiments were completed within 1 h of euthanasia.

Determination of ΔP-CSA relationship. The elasticity of the coronary arteries with in situ diameters >0.5 mm was determined using quantitative coronary angiography. After perfusion with cardioplegic solution, the LAD was filled with iodinated contrast material (Omnipaque; Nycomed Amer- sham; Princeton, NJ) and 3% Cab-O-Sil (Eastman Kodak). Because Cab-O-Sil is a colloidal silica that forms agglomerated particles with effective diameters exceeding those of the capillaries, it was used to prevent the flow of the iodinated contrast material into the capillaries, thus ensuring the uniformity of the imposed pressure throughout the imaged coronary arterial tree (18).

To vary the ΔP (intravascular pressure – box pressure), the box pressure was, in turn, set at four different pressures (0, 50, 100, and 150 mmHg), whereas the LAD pressure was ramped between 0 and 150 mmHg in a triangular form with a slope of ~3 mmHg/s. Hence, there was some overlap in the range of ΔP achieved at different box pressures. Because the results depend only on the ΔP, different box pressures were used to allow the generation of a range of ΔP from −150 mmHg to +150 mmHg. To ensure the reproducibility of the mechanical properties of the arteries, the vessels were preconditioned with several cyclic changes in pressure between 0 and 150 mmHg (6). Coronary arteriograms were acquired at 1 frame per 5 s, as described in Kassab and Molloi (17). The pressure imposed and the X-ray tube voltages were recorded continuously (Biopac MP100 Systems; Santa Barbara, CA), thus the intravascular and box pressures for each acquired image were determined.

For calibration purposes, a cylindrical vessel phantom, which consists of contrast-filled plastic tubing with different inside diameters (between 1.01 and 3 mm), was imaged on top of the Lucite box over the heart region. The integrated gray levels in the vessel profiles were related to the known CSA of the vessel phantoms, thus the integrated gray levels were directly converted to CSA values for the coronary angiograms. Corrections were made for magnification differences between the calibration phantom and the arterial segment of interest.

Determination of ΔP-CSA relationship for the proximal artery in vitro. After the completion of the in situ mechanical testing, the heart was removed from the Lucite box and placed in a saline bath. A 1.5- to 2-cm proximal segment of the LAD artery was dissected out from the heart, and every bifurcation was identified and each branch was ligated with 6-0 suture. Before dissection, a suture was used to measure the length of the LAD artery by tracing along the vessel’s longitudinal axis. The cannulated vessel was then stretched to its in situ length and anchored to the two canulas in line with the two side holes of the saline-filled Lucite box, where the above mechanical testing procedure was repeated. The
same iodine 3% Cab-O-Sil solution was used as the contrast agent for imaging of isolated coronary artery.

**Determination of the ΔP-V relationship.** Digital angiography was used to determine the coronary arterial volume of all vessels with diameters >0.5 mm, which is the approximate resolution of the imaging system (20), as shown in Fig. 2B. After the images were corrected for scatter and veiling glare, temporal subtraction images were formed. A manually drawn region of interest (ROI) approximately outlined the epicardial arteries as shown in Fig. 2B. A second narrow shell (a background ROI) was drawn outside the arterial ROI (Fig. 2B). The background ROI was used to correct the iodine signal in the myocardium. The system iodine-calibration curve was used to convert the integrated video densitometric signal to iodine mass, which was then converted to volume by using the known iodine concentration of the contrast material (20). The in situ pressure-volume relationship of the entire LAD arterial tree (vessels >0.5 mm in diameter) and the pressure-volume relationship of the main LAD trunk (vessels >1.0 mm in diameter) were determined.

**Image acquisition and processing.** All images were acquired using a conventional X-ray tube (Dynamax 79-45/120, Machlett Laboratories; Stamford, CT), a constant potential X-ray generator (Optimus M200, Philips Medical Systems; Shelton, CT), a 23/15 cm CsI image intensifier, a focused grid (8:1 grid ratio, 36 lines cm⁻¹), and a CCD camera (Multicam MC-1134GN, Texas Instruments; Dallas, TX). An adjustable aperture controlled the camera’s light intensity. A Matrox Pulsar frame grabber (Matrox Electronics Systems; Dorval, Quebec, Canada) and a Pentium III computer were used to linearly digitize the video signal to 640 × 480 × 8-bit precision (17).

The images were obtained by using the large (1.2 mm nominal) focal spot and the 15-cm image-intensifier mode. A convolution filtering technique was used to estimate the scatter-glare distribution in images. Exposure parameters and the detected intensity distribution were used to estimate the scatter-glare intensity by predicting the total thickness at every pixel in the image. The thickness information was used to estimate scatter glare on a pixel-by-pixel basis (4).

**Zero-stress state.** After the completion of the in vitro mechanical testing, the proximal segment of the coronary artery was cut into several consecutive rings. Methods for the determination of coronary zero-stress state have been previously described in our laboratory (5). After a ring is cut, it was transferred to a Ca²⁺-free Krebs solution (composition in mM: 117.9 NaCl, 4.7 KCl, 1.2 MgCl₂, 25 NaHCO₃, 1.2 NaH₂PO₄, 0.0027 EDTA, 0.1 ascorbic acid, and 11 glucose) bath aerated with a gas mixture of 95% oxygen-5% carbon dioxide at room temperature. This represents the no-load state of the vessel. One more cut was then made radially, which caused the ring to open into a sector that represents the zero-stress state of the vessel. The opening angle of each sector, defined as the angle subtended by two radii connecting the midpoint of the inner wall, was measured from photographs using an image analysis system (Optimas). The morphological measurements of inner and outer circumference, and area in the no-load and zero-stress state were also made and used for the analysis of arterial mechanics as outlined below.

**Analysis of stress and strain.** The internal diameter was calculated from the CSA measurements \( D = \sqrt{4 \times \text{CSA}/\pi} \) where \( D \) is the luminal dimension) for the in vitro segment assuming that the coronary artery is cylindrical. The wall thickness \( (h) \) was also calculated based on the following assumptions: 1) the wall is incompressible; i.e., the volume of the wall does not change during distension, and 2) the shape of the vessel is cylindrical. The total wall area \( (A_w) \) was measured from the no-load pictures of the rings. The incompressibility condition for a cylinder was used to compute \( h \) as given by

\[
 h = r_o - r_i = \sqrt{r_i^2 + A_o/\pi h_o} - r_i \quad (1)
\]

where \( r_i \) and \( r_o \) are the inner and outer radii at the loaded state, respectively; and \( A_o = l l_o \), where \( l \) and \( l_o \) are the vessel lengths in the loaded and no-load state, respectively.

The circumferential strain \( (\varepsilon) \) is defined according to Green (see Fung in Ref. 6)

\[
 \varepsilon = \frac{1}{2}(\lambda_o^2 - 1) \quad (2)
\]

where \( \lambda_o \) is the circumferential stretch ratio calculated at the midwall as the ratio of the circumferences in the pressurized state to that in the zero-stress state. The circumferential stress \( (S) \) is expressed by Kirchhoff stress as

\[
 S = \frac{P r_i}{h \lambda_o^2} \quad (3)
\]

where \( P \) is the luminal pressure.

Fig. 2. A: typical arteriogram used to obtain cross-sectional area (CSA) and lumen volume of the LAD artery and its branches. B: arterial and background regions of interest (ROIs) used for lumen volume measurements are superimposed on image.
P-CSA relationship in the range of measurements were taken for seven segments along the main Kassab et al. (17). For each experiment, the vessels with diameter \( /H11022 \text{mm} \) were determined. The vessels were grouped in the following diameter ranges: 0.5–1.0 mm, 1.01–2.0 mm, and 2.01–3.5 mm, which roughly correspond to orders 9, 10, and 11, respectively, as previously reported by Kassab et al. (17). For each experiment, the \( \Delta P \)-CSA measurements were taken for seven segments along the main LAD trunk and three segments along the side branches. The \( \Delta P \)-CSA relationship in the range of \(-150 \) to \(+150 \text{ mmHg} \) pressure difference were curve fitted using nonlinear regression, according to the following relationship

\[
\text{CSA} = \frac{\alpha}{1 + e^{\gamma \Delta P}} + \delta
\]

where CSA of the vessel is at a given pressure difference \( \Delta P \) (intravascular pressure – box pressure), and \( \alpha, \beta, \gamma, \) and \( \delta \) are curve-fit constants. Equation 4 can be expressed in terms of four physical constants as

\[
\text{CSA} = \frac{(\text{CSA}^+ - \text{CSA}^-)}{1 + (\text{CSA}^+ - \text{CSA}^-) \times e^{(\text{CSA}^+ - \text{CSA}^-) \times \frac{\Delta P}{2\gamma}} + \text{CSA}^-
\]

where \( \text{CSA}^+ \) is the asymptotic value of CSA in the positive \( \Delta P \) direction (below yield pressure where the vessel may undergo plastic deformation and rupture), \( \text{CSA}^- \) is the asymptotic value of the CSA in the negative \( \Delta P \) direction, \( \text{CSA}^0 \) is the CSA value at \( \Delta P = 0 \), and \( \Delta P^{1/2} \) is the pressure difference corresponding to the average of \( \text{CSA}^+ \) and \( \text{CSA}^- [i.e., (\text{CSA}^+ + \text{CSA}^-)/2] \). The empirical curve fit constants \( \alpha, \beta, \gamma, \) and \( \delta \) are related to the physical constants \( \text{CSA}^+, \text{CSA}^-, \text{CSA}^0, \) and \( \Delta P^{1/2} \) as follows

\[
\text{CSA}^+ = \alpha + \delta
\]

\[
\text{CSA}^- = \delta
\]

\[
\text{CSA}^0 = \frac{[\alpha + 5(1 + e^{\delta})]}{1 + e^{\delta}}
\]

\[
\Delta P^{1/2} = \gamma
\]

The volume data were defined similarly where \( \text{CSA}^+, \text{CSA}^-, \) and \( \text{CSA}^0 \) were replaced with \( V^+, V^-, \) and \( V^0 \), respectively, with similar definitions. The \( \Delta P-V \) relationships of the entire LAD arterial tree, as well as that of the main LAD trunk were determined.

The compliance of the coronary arteries was determined as the change in luminal dimension \( (\Delta D, \Delta \text{CSA}, \text{or} \Delta V) \) per change in arterial pressure \( (\Delta P) \) (where box pressure = 0 mmHg; i.e., \( \Delta P > 0 \text{ mmHg} \)). In the negative pressure difference \( (\Delta P < 0 \text{ mmHg}) \) where the vessels were under compression, the compliance was not defined. The CSA compliance for the first several generations of the LAD artery was calculated, as well as the volume compliance of the total arterial tree (vessels >0.5 mm in diameter).

**Statistical analysis.** All data given in the text and tables were expressed as means \( \pm \) SD, whereas the data in the figures were expressed as means \( \pm \) SE. Analysis of variance was used to detect differences in compliance, as well as, in CSA and volume among the different-sized vessels within each heart and among various hearts. For all analyses, \( P < 0.05 \) level was used to indicate statistical significance.

**RESULTS**

The postmortem coronary angiogram, as shown in Fig. 2, was combined with digital subtraction angiography and video densitometry to measure the CSA and volume of the LAD arteries. The CSA and volume were determined from images corresponding to various \( \Delta P \). The loading \( \Delta P \)-CSA relationships for vessels representing the first several generations of the LAD artery of a single heart are shown in Fig. 3. A nonlinear equation was proposed (Eq. 4) to curve fit the data over the entire \( \Delta P \) range \((-150 \) to \(+150 \text{ mmHg}) \), and the empirical constants \( \alpha, \beta, \gamma, \) and \( \delta \) were determined. These constants were expressed in terms of \( \text{CSA}^+, \text{CSA}^-, \text{CSA}^0, \) and \( \Delta P^{1/2} \) according to Eq. 6 and are summarized in Table 1 for the three largest orders of vessels.

The CSA compliance of the LAD artery was also calculated \( \Delta \text{CSA}/\Delta P \) for values corresponding to box pressure of zero. The CSA-compliance values (at 100 mmHg) for the three largest generations of the LAD artery, from all six hearts, are summarized in Table 2. Figure 4 presents a comparison between the \( \Delta P \)-CSA

**Table 1. Values for empirical constants describing \( \Delta P \)-CSA relationship for the first several generations of coronary LAD arteries**

<table>
<thead>
<tr>
<th>Order</th>
<th>Diameter Range at 100 mmHg, mm</th>
<th>CSA0, mm²</th>
<th>CSA+, mm²</th>
<th>CSA−, mm²</th>
<th>( \Delta P^{1/2} ), mmHg</th>
<th>( R^2 )</th>
<th>( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>2.03–3.44</td>
<td>2.39 ± 0.9</td>
<td>5.0 ± 1.3</td>
<td>1.99 ± 0.9</td>
<td>34 ± 20</td>
<td>0.989 ± 0.005</td>
<td>27</td>
</tr>
<tr>
<td>10</td>
<td>1.03–1.93</td>
<td>1.07 ± 0.3</td>
<td>1.58 ± 0.7</td>
<td>0.53 ± 0.3</td>
<td>47 ± 33</td>
<td>0.988 ± 0.015</td>
<td>23</td>
</tr>
<tr>
<td>9</td>
<td>0.73–0.97</td>
<td>0.29 ± 0.1</td>
<td>0.64 ± 0.2</td>
<td>0.23 ± 0.1</td>
<td>33 ± 18</td>
<td>0.967 ± 0.045</td>
<td>10</td>
</tr>
</tbody>
</table>

Values are means \( \pm \) SD; \( n \), number of arteries. CSA, cross-sectional area; \( \Delta P \), pressure change (intravascular pressure – box pressure); LAD, left anterior descending. See text for further details.

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Table 2. Data for CSA compliance of three largest orders of LAD arteries

<table>
<thead>
<tr>
<th>Order</th>
<th>Diameter Range at 100 mmHg, mm</th>
<th>Average CSA, mm²</th>
<th>Compliance at 100 mmHg, mm²/mmHg</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>2.03–3.42</td>
<td>4.50±2.2</td>
<td>16.4±18</td>
<td>27</td>
</tr>
<tr>
<td>10</td>
<td>1.02–1.97</td>
<td>1.43±0.8</td>
<td>5.2±4.8</td>
<td>23</td>
</tr>
<tr>
<td>9</td>
<td>0.67–0.97</td>
<td>0.59±0.02</td>
<td>4.4±4.0</td>
<td>10</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, number of arteries.

The relationship of the proximal LAD artery in vitro (isolated segment) and in situ over the entire ΔP range. At 100 mmHg, the in situ mean CSA and CSA compliance are $4.26 \pm 1.8$ mm² and $4.85 \pm 3.8 \times 10^{-3}$ mm²/mmHg, respectively. These values are significantly smaller than their corresponding in vitro values of $7.12 \pm 1.6$ mm² and $16.5 \pm 6 \times 10^{-3}$ mm²/mmHg, respectively ($P = 0.014$ and $P = 0.009$, respectively). The CSA⁺, CSA⁻, CSA⁰, and ΔP₁/₂ for the proximal LAD artery in situ are $4.3 \pm 2.1$ mm², $1.09 \pm 0.6$ mm², $1.4 \pm 0.6$ mm², and $43 \pm 22$ mmHg ($R^2 = 0.988–0.999$). Their corresponding values in vitro are $7.24 \pm 1.6$ mm², $0.15 \pm 0.2 \times 10^{-3}$ mm², $1.3 \pm 0.7$ mm², and $21 \pm 3$ mmHg, respectively ($R^2 = 0.996–0.999$). The differences were statistically significant for CSA⁺ and CSA⁻ ($P = 0.02$ and $P = 0.007$, respectively), whereas the difference between the in situ and in vitro CSA⁰ and ΔP₁/₂ were not statistically significant.

The ΔP-V relationship was similar in shape to the ΔP-CSA relationship as shown in Fig. 5 for the arterial tree volume and the main trunk. Hence, a similar equation was employed, and the empirical constants were expressed in terms of V⁺, V⁻, V⁰ and ΔP₁/₂. It was found that V⁺, V⁻, V⁰, and ΔP₁/₂ have mean values of $1.41 \pm 0.3$ ml, $0.70 \pm 0.3$ ml, $0.85 \pm 0.3$ ml, and $24 \pm 13$ mmHg, respectively ($R^2 = 0.980–0.990$). The mean arterial volume at 100 mmHg is $136 \pm 0.3$ ml, which is approximately twice as large as the mean volume of the trunk ($75 \pm 0.2$ ml); and the differences are statistically significant ($P = 0.00007$). However, the mean arterial volume compliance at 100 mmHg ($2.6 \pm 1.8 \times 10^{-3}$ ml/mmHg) is found to be very similar to that of the trunk ($2.5 \pm 2.2 \times 10^{-3}$ ml/mmHg).

The circumferential stress-strain relationship for the in vitro vessel was computed according to Eqs. 2 and 3 and shown in Fig. 6. The tangent modulus of the vessel was calculated as the change of stress per change of strain from the data in Fig. 6. Our results show that the mean value of the tangent modulus at 100 mmHg is $220 \pm 74$ kPa ($2.2 \pm 0.74 \times 10^6$ dyn/cm²).

**DISCUSSION**

ΔP-CSA relationship: in situ properties. It is evident that the ΔP-CSA relationship is nonlinear over the full range of ΔP ($-150$ to $+150$ mmHg) and can be fitted by a nonlinear function (Eq. 4) as shown in Fig. 3. Our results, in the positive ΔP range, agree with those previously reported by Kassab and Molloy (17). However, the ΔP-CSA relationship in the negative ΔP range has not been previously determined. Generally, as the ΔP increases in the positive direction, the CSA of the coronary vessel reaches an asymptotic value CSA⁺. This pressure is well below the rupture pressure of the vessel. Moreover, as the ΔP increases in the negative direction, the CSA reaches an asymptotic value of CSA⁻. Our results show that the CSA for an intact vessel under compression is always nonzero; thus the large coronary arteries (diameter $>0.5$ mm) do not collapse. In two of six hearts, however, we did observe partial collapse of the most proximal artery. In those
cases, we confirmed that the proximal segment was more superficial; i.e., less tethered than the corresponding vessels of other hearts.

Similar to other vessels, the compliance of the coronary arteries decreases as the pressure is increased. We found that at 100 mmHg, the CSA compliance decreases as the vessel branching order decreases (Table 2).

Effect of myocardium on the CSA and compliance of coronary artery. To determine the effect of the myocardium on the CSA and compliance of the coronary artery, the ΔP-CSA relationship of the proximal LAD artery was compared in the in situ and in vitro states. Our data show that there are significant differences in the ΔP-CSA relationship between the two states, as shown in Fig. 4. In the positive ΔP range, the CSA attained in vitro is significantly larger than that in situ (P = 0.02). The in situ CSA⁺ is 41% smaller than that at the in vitro state. Similarly, at a pressure of 100 mmHg, the CSA in situ is 43% smaller than that at the in vitro state. Furthermore, the CSA compliance of the most proximal LAD artery in situ is 71% smaller than that of the in vitro state. Therefore, the myocardium limits the CSA expansion and compliance of the coronary artery in the positive ΔP regime.

One of the hypotheses of the present study was that the myocardium provides mechanical support for the blood vessels during compression. To test this hypothesis, the proximal artery was dissected away from the myocardium and its mechanical properties were retested. Our results show that in the negative ΔP regime, where box pressure exceeds intravascular pressure, the ratio of in vitro to in situ CSA reduces to zero. That is, in contrast to the in situ vessel, the isolated artery collapses under compression. Therefore, the myocardium tethers the vessel and prevents it from collapse.

ΔP-volume relationship. The relationship between ΔP and arterial volume for the coronary arterial tree (vessels >0.5 mm in diameter) is shown in Fig. 5. It can be seen that the LAD arterial tree retains a significant amount of volume (0.70 ± 0.3 ml) under external compression in an arrested, vasodilated heart. These results are consistent with the CSA data, which confirms that vessel collapse does not occur under compression. Furthermore, it is interesting to note that the two curves (arterial tree and trunk) become very similar when they are normalized by their respective volumes at zero pressure; i.e., the difference in compliance or distensibility is not statistically significant.

Comparison with other works. The diameter was computed from the CSA to calculate diameter-compliance values (ΔD/ΔP) for comparison with the literature. It is found that the in vitro diameter compliance of the proximal LAD is 6.51 ± 7.0 × 10⁻³ mm/mmHg (at 100 mmHg), which is in agreement with previously published data. For example, using microscopy, Patel and Janicki (21) obtained diameter compliance of a dog’s left circumflex coronary artery of 4 × 10⁻³ mm/mmHg (at a pressure range of 107–135 mmHg). Furthermore, Gow and Hadfield (9), using an electrical caliper, calculated the diameter compliance of the left common coronary artery (LCCA) in humans (D = 4.9 ± 0.3 mm) at pressure range of 70–110 mmHg and found it to be 10.8 × 10⁻³ mm/mmHg. However, because human arteries were stored overnight before experiments, it is difficult to make any direct comparison. Furthermore, the same investigators (10) calculated the diameter compliance in dogs (D = 3.1 mm) at a pressure range of 60–140 mmHg and obtained a value of 2.10 × 10⁻³ mm/mmHg. The variations may be due to species differences.

Tomoike et al. (26), using an ultrasonic dimension gauge, measured the diameter of a dog’s coronary arteries in situ in the beating heart and calculated the diameter compliance of LCCA as 2.50 × 10⁻³ mm/mmHg (at pressure range of 60–140 mmHg), which is in agreement with our in situ diameter-compliance value of 2.42 ± 2.3 × 10⁻³ mm/mmHg (at 100 mmHg) in the arrested heart. Furthermore, our data are in agreement with earlier swine studies in situ (17).

The in situ CSA compliance data determined in this study are also similar to those obtained in vivo studies on calves and human subjects (12, 22, 27). Gross et al. (12) used ultrasonic crystals to measure the coronary artery diameter changes during the cardiac cycle. They also made simultaneous measurements of coronary blood pressure and computed a pressure elastic modulus. Their modulus can be converted into a coronary arterial tree compliance to give an approximate value of 5 × 10⁻⁴ mmHg⁻¹. Williams et al. (27) obtained CSA compliance of ~20 ± 12 × 10⁻³ mm²/mmHg (at 100 mmHg) using intravascular ultrasound, which is similar to the values obtained in the present study (13.5 ± 9.7 × 10⁻³ mm²/mmHg, for order 11). Using a similar method, Shaw and colleagues (22) calculated the CSA-compliance at the diastolic blood pressure to be ~17.5 ± 5 × 10⁻³ mm²/mmHg.

Volume distensibility is defined as the volume compliance normalized with respect to its volume at zero pressure. We found the volume distensibility data to be in reasonable agreement with earlier studies. Gregg et al. (11) estimated the LAD arterial volume distensibility in a passively arrested dog’s heart to have a value of 5.4 × 10⁻³ mmHg⁻¹, and a mean pressure of 120 mmHg. Using a similar method, Patel and Janicki (21) obtained volume distensibility values of 4.5 × 10⁻³ mmHg⁻¹ at a mean pressure of 120 mmHg. Furthermore, using radiogram studies of LCCA under static distension in dogs, Douglas and Greenfield (3) evaluated the volume distensibility at a mean pressure of 100 mmHg to be 5.8 × 10⁻³ mmHg⁻¹. Those values are somewhat higher than those obtained in the present study (2.9 ± 1.3 × 10⁻³ mmHg⁻¹ at a pressure of 100 mmHg).

Elasticity of coronary artery and passive myocardium. It is well known that blood vessels in vivo are mechanically supported by the surrounding tissue. Previously, Fung et al. (8) evaluated the effect of mesentry on the elasticity of its capillary blood vessel by measuring the elasticity of the tissue and computing the contribution under the hypothesis that the vessel is...
in direct contact with the tissue. This formulation led to the well-known tunnel-in-gel concept; i.e., the elasticity of the capillary blood vessel is derived almost entirely from the surrounding tissue. Fung et al. (8) showed that the extent of tissue contribution on the elasticity of the blood vessel depends on the size of the tissue relative to the vessel. For a capillary vessel, the relative size of tissue to vessel is very large, and hence the contribution to elasticity is dominated by the tissue. For a coronary artery, the contribution may be smaller as demonstrated below.

An idealized version of the tunnel-in-gel model can be proposed to determine the relative elasticity of coronary artery and surrounding myocardium (8). The coronary artery is assumed to be uniform, isotropic, linear (i.e., obeys Hooke’s law), and infinitely long so that a plane state of strain exists. It follows from the infinitesimal theory of elasticity that the change of radius, \( R \), with internal pressure, \( P \), of a thin wall vessel is given by

\[
\frac{dR}{dP} = \frac{R^2}{hE_{\text{vessel}}} \tag{7}
\]

where \( E_{\text{vessel}} \) is Young’s modulus of the vessel. Similarly, for a cylindrical hole of radius \( R \) pressurized in an infinite elastic medium, the classic theory yields the rate of change of \( R \) with respect to \( P \) as follows [see Timoshenko and Goodier, p. 67 (25)]

\[
\frac{dR}{dP} = \frac{1 + \nu}{E_{\text{myo}}} R \tag{8}
\]

where \( \nu \) and \( E_{\text{myo}} \) correspond to the Poisson’s ratio and Young’s modulus of the myocardium, respectively. The ratio of these two rates is given by

\[
\frac{(dR/dP)_{\text{myo}}}{(dR/dP)_{\text{vessel}}} = \frac{(1 + \nu)E_{\text{vessel}}}{h E_{\text{myo}}} \tag{9}
\]

where \((dR/dP)_{\text{myo}}\) is a measure of the compliance of the vessel in situ and can be determined from the data in Fig. 4. Similarly, \((dR/dP)_{\text{vessel}}\) is a measure of the compliance of the vessel in vitro and can be computed from Fig. 4. As stated in the results, our data show that the mean value of \( E_{\text{vessel}} \) at 100 mmHg is 220 kPa. If we assume that \( \nu \) is 0.5 (i.e., an incompressible material), the computed mean value of \( E_{\text{myo}} \) (Eq. 9) at 100 mmHg is 140 kPa. These values are in agreement with the biaxial measurements of passive myocardium reported by Yin et al. (28) in the low stress-strain regime.

**Effect of myocardium on stress distribution in the coronary artery wall.** It is well accepted that fluid and solid mechanics of the blood vessel are important determinants of the health and disease of the cardiovascular system (7). One serious disease that seems to be uniquely associated with abnormal stress and strain is atherosclerosis. A compelling observation is that the epicardial arteries develop atherosclerosis, whereas the intramural arteries do not (19). Atherosclerotic changes involving the epicardial portion of the coronary artery abruptly stop at the point where the artery enters the myocardium. It has been previously proposed that the sites of prevalent atherosclerosis are sites of high wall stress (24). Hence, it would be expected that intramural vessels that have support from the myocardium would have a lower wall stress. In the context of the present study, we would hypothesize that the myocardial side of the epicardial artery would be less susceptible to atherogenesis. The hypothesis of circumferential variation of atherosclerosis in the epicardial coronary arteries remains to be tested.

**Physiological implications.** As the heart muscle contracts, the cells and collagen fibers bear stresses, whereas the fluid in the tissue compartments are exposed to hydrostatic pressure. The hydrostatic pressure in the soft tissue surrounding the myocardial fibers is referred to as the intramyocardial pressure (IMP) and may compress the coronary vessels. Numerous methods have been used to estimate hydrostatic pressure throughout the thickness of the heart muscle during the cardiac cycle. Although there is some disagreement about the absolute values measured, all studies observed a gradient in IMP across the wall during systole, with endocardial values being larger (see review in Ref. 14). Hence, the intramural arteries (orders \( \leq 10 \)) experience compression during the cardiac cycle. Although the mechanical properties of the coronary blood vessels are well understood under distention, there are no comparable data under compression. Such data are necessary to understand the physiology of coronary blood flow during the cardiac cycle. Both the vascular waterfall mechanism and the intramyocardial pump model presuppose the existence of an IMP acting on the external surface of the deformable vessel wall to explain the impediment of coronary flow during cardiac contraction [see review in Smith and Kassab (23)]. Although we do not suggest that the present preparation is a model for heart contraction, it is very interesting that the larger arteries are tethered by the passive myocardium and do not collapse under significant compression.

In summary, the passive myocardium limits the expansion of coronary arteries during distension and prevents collapse of vessels during compression. Hence, the myocardium is an important determinant of the mechanical properties of coronary arteries. This suggests that the results of in vitro measurements must be interpreted with caution. These conclusions apply to coronary arteries >0.5 mm in diameter. The vessel-myocardium interaction, however, may be even more significant for the smaller vessels, i.e., the microvasculature. Thus further studies are needed to understand the effects of the myocardium on the mechanical properties of smaller vessels. Furthermore, the active myocardium with its increased stiffness may affect the mechanical properties of coronary arteries to a greater extent. Finally, the effect of vessel tone may play an important role in vessel-myocardial interaction, which is not considered in the present study. These issues remain as topics for future studies.
DISCLOSURES
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