Relation between zero-stress state and branching order of porcine left coronary arterial tree

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1Skejby Hospital, Department of Cardiology, and 2Center of Biomechanics, Institute of Experimental Clinical Research, Aarhus University Hospital, DK-8200 Aarhus N; 3Institute of Pharmacology, Aarhus University, DK-8000 Aarhus C, Denmark; 4Cardiological Department, Imperial College School of Medicine, Hammersmith Hospital, London W12 ONN, United Kingdom; and 5Department of Bioengineering, University of California, San Diego, California 92093

Frøbert, Ole, Hans Gregersen, J esper Bjerre, Jens P. Bagger, and Ghassan S. Kassab. Relation between zero-stress state and branching order of porcine left coronary arterial tree. Am. J. Physiol. 275 (Heart Circ. Physiol. 44): H2283–H2290, 1998.—The left common coronary arterial trees of eight pig hearts were dissected. The zero-stress state (the state of the organ when the external loads are removed) of the coronary arteries was determined by first cutting the arteries into short, ring-shaped segments perpendicular to the longitudinal axis of the blood vessel and then making a radial cut. This procedure caused the ring to open into a sector whose opening angle (\(\theta\)), internal and external lengths (circumferences), and wall thickness were measured. Morphometric and \(\theta\) data were organized in the framework of a diameter-defined Strahler system. We investigated 4 rings from the left common coronary artery (LCCA), 185 from the left anterior descending artery (LAD) and its branches, and 159 from the left circumflex artery (LCX) and its branches. The inner circumferences of the rings ranged over six orders for the LAD arterial tree and five orders for the LCX arterial tree, corresponding to a diameter range of about one order of magnitude for both arteries. \(\theta\) demonstrates viscoelastic behavior and was measured 30 min after cutting. Our results show that the inner and outer circumference and the wall thickness increase as geometric sequences with the order number. \(\theta\) is found to decrease linearly toward the smaller orders with a slope of 7.3°/order in the range of the six largest orders. Strain calculations showed that the inner part of the arterial wall is in compression, whereas the outer part of the wall is in tension in the no-load (zero transmural pressure) state. This study provides basic data on the zero-stress state that are necessary for understanding the mechanics of the coronary artery.

biomechanics; diameter-defined Strahler system; opening angle; residual strain; vessel wall thickness

RECENT STUDIES on pressure-diameter relations in coronary arteries using intravascular ultrasound (1, 3, 12) and studies on stress distributions in coronary plaques (4, 26, 27, 30) emphasized the clinical role of the mechanical properties of blood vessels. Characterization of coronary artery mechanics requires data on the zero-stress state (the state in which all loads are reduced to zero), because all strain calculations must be referred to such a state. Previously, the vascular wall was considered stress free in the no-load state when the transmural pressure is zero. However, it was demonstrated that arterial rings, when cut radially, open into sectors (11, 14, 22, 33). The stress released when all external loads are removed is termed the residual stress. Residual stress can greatly alter the stress distribution in an organ at its normal in vivo state of function. If the residual stresses are zero, the most accurate analysis of the stress distribution in the arterial wall given by Chuong and Fung (6) yields the result that the circumferential stress at the inner wall is 6.5 times larger than the average value across the wall. On the other hand, if the effect of residual stress is taken into account, it can be shown that at a physiological blood pressure the circumferential stress is completely uniform. Hence, one physiological implication of residual stress is the reduction of the transmural stress gradient (29). The geometry of an arterial ring in the zero-stress state can be characterized by an opening angle defined as the angle subtended by two radii connecting the midpoint of the inner wall. The opening angle can be used in analysis of the stress-strain relationship of the arteries (6).

The opening angle has been shown to be a sensitive measure of tissue remodeling in response to aortic and pulmonary hypertension (9, 10, 23), diabetes (24), cigarette smoke (25), and age and atherosclerosis (31). Other cardiovascular studies have shown the existence of residual stress in systemic arteries of pigs and cows (14, 33), systemic veins of rats (38), and left ventricles of rats (29) and dogs (28). A brief description of zero stress in canine coronary arteries was also recently published (18). Furthermore, the guinea pig duodenum (13) and the trachea of pigs and dogs have been investigated (15). In describing the opening angle, all previous studies used the axial position as the independent variable. In this study, we describe the opening angle as a function of the order number (19, 21). The rationale is that because the coronary arteries are treelike, a statistical description of the various properties of the tree should be done in the framework of an ordering scheme. The use of the order number has the advantage of allowing comparison between vessels of different organs, species, or disease states. A description of the branching pattern of a vascular tree should ideally be based on a classification that organizes the different parts of the tree according to

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structural and functional similarity of the branches. Previously, characterization of branching patterns was based on Weibel's bifurcation model (36) and Strahler's rivulets model (32). Strahler's system is much more appropriate for ordering of asymmetric branching patterns than Weibel's generation scheme. The Strahler system was introduced for the geographical study of branching patterns of rivers into rivulets but has also been employed in coronary artery studies (34) as well as in studies of several other biological treelike structures (16, 37). Recently, Kassab et al. (19, 21) developed a diameter-defined Strahler system that uses a rule for assigning the order numbers of the vessels on the basis of diameter ranges.

In the present study we describe the zero-stress state of the pig left coronary arterial tree in relation to its branching pattern as described by the diameter-defined Strahler system. Complete left coronary arterial branches down to vessels of ~200 µm in diameter were investigated.

MATERIALS AND METHODS

Coronary artery preparation. Eight hearts from 70- to 90-kg Danish Landrace-Yorkshire pigs of either sex were obtained at a local slaughterhouse on the morning of the experiment. Immediately after the pigs were killed, the aorta was cannulated and the coronary circulation was perfused with 100 ml of a physiological salt solution (PSS) containing dextran (6%) at 5°C bubbled with 5% CO₂ in O₂. The hearts were then bathed in PSS and stored at 5°C. The PSS had the following composition (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. The PSS was made with analytical grade chemicals and twice-distilled water. Dissection of the left coronary arterial tree was performed under a stereo dissection microscope. The dissection was done in PSS continuously bubbled with 5% CO₂ in O₂ at 5°C and started no later than 2 h after the animals were killed. The arterial tree was divided into the left common coronary artery (LCCA), the left anterior descending artery (LAD) and its branches, and the left circumflex artery (LCX) and its branches. Vessels were classified as extramural if part of their circumference was not surrounded by myocardial tissue and as intramural if their entire circumference was embedded in myocardial tissue. The anterior surface of the arteries was spray marked with 10- to 50-µm dots of indelible blue ink in situ. Arterial segments (defined as the distance between 2 bifurcations) were excised randomly, deaned for periadventitial tissue, and cut perpendicular to the longitudinal axis into rings with segmental lengths of approximately one lumen radius. Care was taken to avoid arterial rings with bifurcations because of their complex three-dimensional geometry (11). Each ring was put into a separate petri dish submerged in PSS and bubbled with 5% CO₂–95% O₂ at room temperature, in which all measurements were made. The successive rings were arranged in series and photographed (no-load condition). Each ring was then cut radially at the anterior surface (at 90° relative to the horizontal plane) with a pair of microsurgery scissors, while in the solution, to obtain the zero-stress state. The rings opened into sectors and were photographed 30 min after cutting.

Morphometric measurements. The photographic negatives were analyzed with the aid of an Optimas image-processing system (version 5.2, Bioscan, Edmonds, WA). The inner and outer circumferences and the wall thickness (average of the measurements at 4 quadrants) were measured in the no-load and zero-stress conditions. The cross-sectional area was noncircular in the no-load state. However, we could calculate a diameter (D₉₅) that would correspond to a circular cross section as given by the equation

\[
D₉₅ = C/π
\]

(1)

In the open rings the opening angle (ii) was measured as the angle between two radii joining the midpoint of the arc of the inner wall of the vessel to the tips of the sector (Ref. 22; Fig. 1). All computer measurements were made by a technician who was blinded as to the location of the rings.

Effect of circumferential location of cut, additional cuts, time, and temperature on opening angle. The effect of cutting the rings at different circumferential locations [0°, 90° (anteri or surface), 180°, 270° (posterior surface)] was studied on 28 rings. The temporal change of u was studied to characterize the viscoelastic creep phase. We used the data on creep to define the time span between application of the radial cut and measurements of u. Ten additional cuts were photographed immediately after cutting and at 30 s and 2.5, 10, 30, 60, and 180 min.

We examined the effect of temperature on the opening angle by studying six pairs of rings each from the LAD and LCX. The location of each pair of rings was adjacent to each other. We randomly transferred each ring to a 37°C bath and its pair to a room temperature (20°C) bath.

Fig. 1. Schematic illustration of measurements obtained from coronary arterial rings. Left, coronary ring in no-load (nl) state. Cₒ, outer circumference; Cᵢ, inner circumference; WT, wall thickness. Right, ring has been cut radially and opened into a sector and is in zero-stress (zs) state. This state can be characterized by an opening angle (θ) defined as angle subtended by 2 radii connecting midpoint of inner wall. θ is a measure of difference between strain in nl state and zs state, and hence it is related to residual stress.
Strain. The residual strain ($e_i$) at the endothelial surface was computed as the difference between the circumference (C) in the no-load condition (n) and the zero-stress state (zs) at the inner coronary artery wall with reference to the circumference in the zero-stress state

$$e_i = \frac{C_{n1} - C_{zs}}{C_{zs}}$$

(2)

The residual strain ($e_o$) at the adventitial surface was computed similarly from circumferential values of the outer wall.

Ordering of vessel branches: diameter-defined Strahler system. Because only the first several largest generations of the left coronary arterial tree were dissected, we had to initially assign order numbers from proximal to distal starting with the LCCA in accordance with our previous study (20). At the aortic orifice, the left coronary artery is largest and was denoted as order N. Initially, we computed the inner circumference ratios of all the branches at all points of bifurcation. We used the inner circumference ratios instead of diameter ratios because of the noncircular shape of the arteries at zero transmural pressure. With the average value, we made a first round of assigning order numbers as follows. The order number of a coronary artery branch remained the same as long as the inner circumference ratio was smaller than the average. However, the order number was reduced by 1 when the inner circumference ratio was equal to or larger than the average. For example, the average inner circumference ratio between segments of orders N and N – 1 was found to be 2.1 (20). Inner circumference ratios < 2.1 classified a segment as order N and ratios > 2.1 classified a segment as order N – 1. When the first round of calculations was done, we computed the mean and SD of the circumferences of all the branches at all points of bifurcation. We used the average circumference instead of diameter ratios because of the noncircular shape of the arteries at zero transmural pressure. With the average value, we made a first round of assigning order numbers as follows. The order number of a coronary artery branch remained the same as long as the inner circumference ratio was smaller than the average. However, the order number was reduced by 1 when the inner circumference ratio was equal to or larger than the average. For example, the average inner circumference ratio between segments of orders N and N – 1 was found to be 2.1 (20). Inner circumference ratios < 2.1 classified a segment as order N and ratios > 2.1 classified a segment as order N – 1. When the first round of calculations was done, we computed the mean and SD of the circumferences of all the branches at all points of bifurcation. We used the average circumference instead of diameter ratios because of the noncircular shape of the arteries at zero transmural pressure. With the average value, we made a first round of assigning order numbers as follows.

One or two iterations was generally adequate for this purpose.

Statistics. The results in Table 1 are expressed as means ± SD; results in Figs. 2, 3, and 5–7 are presented as means ± SE. Each arterial ring was considered as an independent statistical sample. Between-branch and between-heart findings were compared by one-way ANOVA (35). ANOVA was also used to test the null hypothesis that the mean of a dependent variable is a linear function of the value of an independent variable. Bivariate associations were evaluated by least-squares regression. Intraobserver and interobserver inner circumference, outer circumference, wall thickness, and SD variability (all in the zero-stress state) differences were analyzed by the Bland and Altman technique (2). Analyses were carried out with BMDP Statistical Software (BMDP DYNAMIC Release 7.0, Cork, Ireland; Ref. 7). Significance was considered if P < 0.05.

RESULTS

In total, 348 arterial rings were investigated, 4 from the LCCA, 185 from the LAD and its branches, and 159 from the LCX and its branches. The LCCA was poorly defined in the hearts of the Danish Landrace-Yorkshire pigs. The length of the LCCA was usually <1 mm, making it difficult to avoid the nearby bifurcation of the LAD and LCX. Consequently, the results for the LCCA are presented separately.

Morphometry of coronary arterial tree. The left common coronary arteries examined had circumferences ranging over six orders corresponding to a diameter range of one order of magnitude. The morphometric data for the different order numbers of the LAD and LCX arterial trees are shown in Table 1. Figure 2 shows the relationship between the inner and outer circumference and the order number for the LAD and LCX. The curves can be fit by the equation

$$\log_{10} C_n = a + bn$$

(4)

where $C_n$ is the circumference in a ring of order n. Hence, mean arterial inner and outer circumferences

Table 1. Morphometric measurements of porcine coronary artery rings

<table>
<thead>
<tr>
<th>Order No.</th>
<th>n</th>
<th>$D_{\text{circum,}a}$</th>
<th>$D_{\text{circum,}i}$</th>
<th>$C_o$</th>
<th>$C_i$</th>
<th>WT</th>
<th>$C_o$</th>
<th>$C_i$</th>
<th>WT</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N – 1</td>
<td>26</td>
<td>2,438 ± 343</td>
<td>1,925 ± 290</td>
<td>7,658 ± 1,077</td>
<td>6,048 ± 911</td>
<td>223 ± 31</td>
<td>7,252 ± 931</td>
<td>7,156 ± 934</td>
<td>288 ± 37</td>
</tr>
<tr>
<td>N – 2</td>
<td>40</td>
<td>1,460 ± 217</td>
<td>1,105 ± 184</td>
<td>4,588 ± 684</td>
<td>3,470 ± 577</td>
<td>158 ± 52</td>
<td>4,120 ± 639</td>
<td>3,979 ± 744</td>
<td>194 ± 69</td>
</tr>
<tr>
<td>N – 3</td>
<td>66</td>
<td>798 ± 174</td>
<td>743 ± 136</td>
<td>3,073 ± 527</td>
<td>2,333 ± 427</td>
<td>99 ± 42</td>
<td>2,760 ± 445</td>
<td>2,591 ± 400</td>
<td>142 ± 53</td>
</tr>
<tr>
<td>N – 4</td>
<td>18</td>
<td>708 ± 98</td>
<td>484 ± 54</td>
<td>2,224 ± 308</td>
<td>1,521 ± 170</td>
<td>92 ± 42</td>
<td>1,962 ± 211</td>
<td>1,769 ± 238</td>
<td>123 ± 47</td>
</tr>
<tr>
<td>N – 5</td>
<td>28</td>
<td>507 ± 122</td>
<td>297 ± 48</td>
<td>1,593 ± 384</td>
<td>934 ± 152</td>
<td>94 ± 35</td>
<td>1,335 ± 309</td>
<td>1,149 ± 250</td>
<td>107 ± 60</td>
</tr>
<tr>
<td>N – 6</td>
<td>7</td>
<td>291 ± 33</td>
<td>192 ± 29</td>
<td>913 ± 103</td>
<td>603 ± 90</td>
<td>50 ± 34</td>
<td>790 ± 150</td>
<td>747 ± 158</td>
<td>57 ± 12</td>
</tr>
<tr>
<td>LCX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N – 1</td>
<td>19</td>
<td>2,337 ± 237</td>
<td>1,813 ± 252</td>
<td>7,341 ± 743</td>
<td>5,696 ± 791</td>
<td>229 ± 43</td>
<td>6,416 ± 706</td>
<td>6,229 ± 633</td>
<td>293 ± 32</td>
</tr>
<tr>
<td>N – 2</td>
<td>67</td>
<td>1,286 ± 293</td>
<td>1,003 ± 229</td>
<td>4,040 ± 920</td>
<td>3,152 ± 721</td>
<td>121 ± 37</td>
<td>3,694 ± 941</td>
<td>3,529 ± 933</td>
<td>167 ± 42</td>
</tr>
<tr>
<td>N – 3</td>
<td>52</td>
<td>679 ± 116</td>
<td>500 ± 93</td>
<td>2,134 ± 366</td>
<td>1,572 ± 292</td>
<td>73 ± 18</td>
<td>1,920 ± 293</td>
<td>1,786 ± 303</td>
<td>97 ± 19</td>
</tr>
<tr>
<td>N – 4</td>
<td>14</td>
<td>468 ± 60</td>
<td>321 ± 35</td>
<td>1,469 ± 188</td>
<td>1,010 ± 111</td>
<td>66 ± 22</td>
<td>1,295 ± 130</td>
<td>1,123 ± 149</td>
<td>82 ± 13</td>
</tr>
<tr>
<td>N – 5</td>
<td>6</td>
<td>303 ± 22</td>
<td>172 ± 15</td>
<td>950 ± 103</td>
<td>540 ± 56</td>
<td>60 ± 15</td>
<td>860 ± 75</td>
<td>820 ± 96</td>
<td>80 ± 10</td>
</tr>
</tbody>
</table>

Values, in micrometers, are means ± SD; n = no. of rings. LAD, left anterior descending artery; LCX, left circumflex artery; $D_{\text{circum,}a}$, calculated outer diameter; $D_{\text{circum,}i}$, calculated inner diameter; $C_o$, outer circumference; $C_i$, inner circumference; WT, wall thickness.
increase as a geometric sequence with the order number in accordance with Horton’s law (17). The relationship between mean arterial wall thickness in the no-load state and the order number for the left coronary (LAD and LCX) arterial tree is shown in Fig. 3. The wall thickness-to-inner circumference ratio decreased with an increase in the order number, i.e., smaller vessels had relatively thicker vessel walls.

Opening angle. An LAD ring in the no-load state and in the zero-stress state is shown in Fig. 4. Figure 5 shows the average creep of the opening angles of 10 arterial rings after the initial cut. The creep data could be fitted by an exponential function in the form of

$$\theta(t)/\theta(30\text{ min}) = 1/\alpha[1 - \eta \exp(-\lambda t)]$$  (5)

A least-squares fit was used to determine the constants $\alpha (0.971\text{ s}^{-1})$, $\eta (0.274\text{ s}^{-1})$, and $\lambda (1.17 \times 10^{-3}\text{ s}^{-1})$ with a correlation coefficient ($r$) of 0.996. $\theta$ was normalized to 100% at 180 min after cutting. The ratio $\theta(t)/\theta(180\text{ min})$ reached 97% at 30 min after cutting. Accordingly, we measured $\theta$ at 30 min after cutting.

The variation of $\theta$ in relation to order number is shown in Fig. 6. $\theta$ increased linearly from a mean value of $125^\circ$ in order $N - 5$ to $169^\circ$ in order $N$ as described by the equation $\theta = 64.1 + 9.7n$ (ANOVA, $P < 0.001$). $\theta$ of the four LCCA rings varied between 37 and $60^\circ$.

Cutting the rings at 0, 90, 180, and 270° did not produce systematic differences in $\theta (213 \pm 37, 204 \pm 30, 218 \pm 24$, and $207 \pm 60^\circ$, respectively; ANOVA, $P > 0.9$). The residual strain was not affected by additional cuts of the arterial rings [outer circumference after 1 cut: $8.12 \pm 1.52\text{ mm}$; combined outer circumference after 2 cuts: $8.76 \pm 1.73\text{ mm}$ ($P = 0.21$); inner circumference after 1 cut: $8.04 \pm 1.52\text{ mm}$; combined inner circumference after 2 cuts: $8.62 \pm 1.70\text{ mm}$ ($P = 0.25$)]. We also examined the effect of temperature on the opening angle and found no statistical significant difference between the opening angle at $20^\circ$C ($\theta = 193 \pm 24.2^\circ$) and $37^\circ$C ($\theta = 198 \pm 28.5^\circ$) ($P = 0.6$).

Residual strain. The variation of residual strain with order number is shown in Fig. 7. $\epsilon_i$ was consistently negative, whereas $\epsilon_o$ was consistently positive throughout the coronary arterial tree at the no-load state. This implies that the inner part of the arterial wall is in compression whereas the outer part of the wall is in tension in the no-load state. $\epsilon_i$ correlated negatively with the wall thickness-to-inner circumference ratio ($r = -0.44$, $P < 0.001$), and $\epsilon_o$ correlated positively with the wall thickness-to-inner circumference ratio ($r = 0.50$, $P < 0.001$). $\epsilon_i$ and $\epsilon_o$ showed no correlation with $\theta$ ($P > 0.2$ for both).

Measurement variability. Intraobserver (technician) and interobserver (technician and O. Frøbert) variability were assessed by analyzing 30 randomly selected images of the arterial rings in the zero-stress state. The mean difference in inner circumference between two blinded measurements made by the same person was $0.027 \pm 0.117\text{ mm}$ ($P = 0.21$). The mean difference between blinded measurements made by two different persons was $0.022 \pm 0.102\text{ mm}$ ($P = 0.24$). Similarly, the mean intraobserver difference in the assessment of outer circumference was $0.007 \pm 0.093\text{ mm}$ ($P = 0.68$), and the interobserver difference was $0.014 \pm 0.140\text{ mm}$ ($P = 0.59$). Wall thickness intraobserver difference was $0.003 \pm 0.016\text{ mm}$ ($P = 0.24$), and interobserver difference was $0.002 \pm 0.021\text{ mm}$ ($P = 0.64$). $\theta$ intraobserver difference was $2 \pm 15^\circ$ ($P = 0.52$), and interobserver difference was $1 \pm 14^\circ$ ($P = 0.59$). Plots of the
average values versus the differences of the inner circumference, outer circumference, wall thickness, and \( \theta \) (not shown) showed no relation between the difference and the mean.

**DISCUSSION**

The stress and strain that remain in an organ when the external load is removed are called residual stress and strain, respectively. They can be seen by cutting up the organ in such a way as to reveal the zero-stress configuration. The function of the organ depends on the residual strain. For a blood vessel, the zero-stress configuration is very different from that of the no-load condition and represents a reference state for the analysis of arterial strain and stress. It has been shown that the residual strain significantly reduces the stress concentration at the inner portion of the vessel wall in the in vivo state (11) so that no part demands more oxygen than the rest.

In accordance with previous findings (10, 14, 15, 29) we found the opening angle to have a slow creep phase that can be explained by a standard linear spring-

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Fig. 4. Arterial ring from the left anterior descending artery (LAD) cut in a plane perpendicular to course of the artery. A: arterial ring in nl state. B: 1 radial cut releases residual stress, and sector is now in zs state.
dashpot model. In their study of the pig aorta Han and Fung (14) found creep function constants very similar to ours: $\alpha$ (0.981 vs. our finding of 0.971 s$^{-1}$) and $\eta$ (0.263 vs. 0.274 s$^{-1}$). However, $\lambda$ has a larger value in the aorta ($3.31 \times 10^{-3}$ vs. $1.17 \times 10^{-3}$ s$^{-1}$ in the coronary artery), which implies that the opening angle of the aorta has a smaller time constant of creep than the coronary artery.

In line with previous vascular studies we found the effect of the angular position of the radial cut to be negligible (14). Additional radial cuts did not release further residual strains, which is in agreement with the notion that the first-order residual strains are by far the largest (15, 29). Because human coronary atherosclerosis is limited to the epicardial vessels (8) conceivably caused by hemodynamic factors, we examined the intramural and extramural vessels separately. However, we found no differences in the opening angles or strains between epicardial and intramural arteries.

The present study is the first to describe the opening angle as a function of order number. Variation of the opening angle was found to vary linearly from $125^\circ$ in order $N=5$ to $169^\circ$ in order $N$ as described by equation $\theta = 64.1 + 9.7n$ (ANOVA, $P < 0.001$).
opening angle increased from 130° at the larynx to 200° at its lower end when the cut was made at the anterior, cartilaginous position (15). When the trachea was cut at the posterior, muscular position the opening angle varied from 50° at the larynx to 70° at its lower end. In porcine tracheas the opening angle decreased from 15° at the laryngeal part to 5° at the lower end for both anterior and posterior cuts (15). In summary, the previous studies found complex relationships between opening angle and axial position. The relationship between opening angle and order number presented in this study is much simpler.

Kassab et al. (21) showed previously that the largest order of the coronary arterial tree, in a 30-kg pig, is 11. In the present study, we could not determine the largest order, N, of the coronary artery because of the partial analysis of the coronary arterial tree. The weight of the pigs in this study was significantly larger (70–90 kg) than that of the pigs studied by Kassab et al. (21). However, because the inner circumference of the LAD artery at the no-load state (Table 1) is not significantly larger than that of a 30-kg pig (G. S. Kassab, unpublished data), it is unlikely that N is >11. Whether N is 11 or 12, however, will not change the interpretation of the results of the present study.

The physiological implications of residual stress in the wall of a tubular structure are several. With the use of finite-element analysis, Richardson and co-workers (30) investigated stress distributions in coronary artery plaques from 85 patients. In a computer model they demonstrated that circumferential stress is highest at the intima and lowest on the outside of the adventitia. They also showed that an increase in intraluminal pressure raises circumferential stress disproportionately more in the inner than in the outer layers of the vessel wall (30). Their analysis did not take the residual stress into account, however. They assumed that the no-load state was the zero-stress state. The studies that have taken into account the residual stress in the wall of small blood vessels and left ventricles of rat hearts have shown a more uniform stress distribution under in vivo conditions (11, 28, 29).

It is tempting to relate the reduction in opening angle as the order number lessens to the blood pressure drop in the coronary arterial circulation. However, blood pressure may not be the only explanation for the reduction in opening angle. The pressure drop is fairly small over the larger arteries (probably 5–10 mmHg from the aorta to arteries with a diameter of 300 µm; Ref. 5), i.e., the reduction in pressure is not in proportion with the reduction in opening angle. What may be more relevant is the elasticity of the coronary blood vessels. Unfortunately, a complete set of data on the compliance of the various orders or coronary arteries does not exist. When these data are provided, it will be possible to correlate the opening angle to the Young’s modulus through mechanical analysis.

The residual stress affects the elasticity of the tissue because the stiffness of the tissue is increased with the level of stress. We demonstrated that the strains correlate with the wall thickness-to-inner circumference ratio. The stress distribution in the arterial wall depends on the wall thickness-to-inner circumference (or lumen diameter) ratio in a complex way (14). In our study adventitial surface strain increases whereas endothelial surface strain decreases with an increase in the thickness-to-circumference ratio. We found that the opening angle increases with vessel size whereas the strain is independent of it.

The present study did not include testing of the effect of various drugs on the opening angle. Previously, papaverine has shown little effect on the opening angles of the rat aorta (9). Also, potassium had little influence on rat and pig aorta opening angles (14). Epinephrine caused minor changes in the opening angle in small blood vessels in the rat, whereas EDTA decreased the opening angle in vessels <100 µm in diameter but had no effect on larger vessels (11). In our study the PSS was calcium free and contained EDTA, so the smooth musculature was completely relaxed. Hence, the passive elastic and viscoelastic properties were investigated. It has been suggested that the reason why drugs have relatively little effect on the opening angle is because these factors act on the smooth muscle cells, and the smooth muscles are located in the medial region of the blood vessel wall where the neutral axis lies (24).

In summary, we showed that the opening angle of the porcine left coronary artery tree varies linearly with the order number of its branches for the six largest orders. Furthermore, we obtained data on the residual strain that showed the inner part of the arterial wall is in compression whereas the outer part of the wall is in tension in the no-load state. This study provides the basic data necessary for understanding the stress distribution across the coronary artery wall and in future studies of coronary artery mechanics.

The authors thank Margit Nielsen and Edith Pallencaoe for excellent assistance during the experiments. Dr. Vibke E. Hjortdal is acknowledged for valuable advice regarding the microsurgical procedures.

The study was supported by the Danish Heart Foundation, the Danish Medical Research Council, Fonden til Lægevidenskabens Fremme, Karen Elise Jensens Fond, Kong Chr. d. XS’s Fond, L. F. Foghs Fond, the Novo Nordisk Foundation, Søster og Verner Lipperts Fond, and Yde’s Fond. Dr. Kassab is a recipient of the National Institutes of Health First Award.

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Received 11 February 1998; accepted in final form 31 August 1998.

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