Effects of myocardial constraint on the passive mechanical behaviors of the coronary vessel wall

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Liu Y, Zhang W, Kassab GS. Effects of myocardial constraint on the passive mechanical behaviors of the coronary vessel wall. Am J Physiol Heart Circ Physiol 294: H514–H523, 2008. First published November 9, 2007; doi:10.1152/ajpheart.00670.2007.—The large epicardial coronary arteries and veins span the surface of the heart and gradually penetrate into the myocardium. It has recently been shown that remodeling of the epicardial veins in response to pressure overload strongly depends on the degree of myocardial support. The nontethered regions of the vessel wall show significant intimal hyperplasia compared with the tethered regions. Our hypothesis is that such circumferentially nonuniform structural adaptation in the vessel wall is due to nonuniform wall stress and strain. Transmural stress and strain are significantly influenced by the support of the surrounding myocardial tissue, which significantly limits distension of the vessel. In this finite-element study, we modeled the nonuniform support by embedding the left anterior descending artery into the myocardium to different depths and analyzed deformation and strain in the vessel wall. Circumferential wall strain was much higher in the untethered than tethered region at physiological pressure. On the basis of the hypothesis that elevated wall strain is the stimulus for remodeling, the simulation results suggest that large epicardial coronary vessels have a greater tendency to become thicker in the absence of myocardial constraint. This study provides a mechanical basis for understanding the local growth and remodeling of vessels subjected to various degrees of surrounding tissue.

vessel mechanics; elasticity; myocardium; finite element; remodeling


WE USE THE TERM “ELASTICITY” TO DESCRIBE THE RELATION BETWEEN THE INCREASES OF RADIUS AND INTRAVASCULAR PRESSURE. THE RADIUS IS INCREASED MORE BY A SOFT VESSEL THAN BY A STIFFER VESSEL UNDER THE SAME PRESSURE; THUS THE SOFT VESSEL HAS GREATER ELASTICITY. SOME RECENT STUDIES (13, 16, 27, 50, 51, 57, 58) HAVE SHOWN THAT CONSTRAINT BY THE SURROUNDING TISSUES DRAMATICALLY REDUCES VESSEL ELASTICITY. LIU ET AL. (27) DETERMINED THE IN VIVO PRESSURE-RADIUS RELATIONS OF CAROTID AND FEMORAL ARTERIES WITH THE SURROUNDING TISSUE INTACT AND AFTER DISSECTION, RESPECTIVELY. IT WAS FOUND THAT THE SURROUNDING TISSUE TAKES UP ~50% OF THE INTRAVASCULAR PRESSURE AND REDUCES VESSEL ELASTICITY BY ~20%.

THE MECHANICS OF PARTIALLY TETHERED LARGE EPICARDIAL CORONARY ARTERIES ARE OF INTEREST IN THE STUDIES OF CORONARY HEMODYNAMICS (6, 45, 47, 55), WHERE THE VESSEL ELASTICITY IS CENTRAL TO THE PRESSURE-FLOW RELATION OF CORONARY CIRCULATION. THE MYOCARDIAL CONSTRAINT IS ALSO A DETERMINANT OF THE STRESS-STRAIN DISTRIBUTION IN THE VESSEL WALL AND AFFECTS MASS TRANSPORT THROUGH THE ARTERIAL WALL (11) AND GROWTH AND REMODELING (21). CHOY ET AL. (2) FOUND SIGNIFICANT INTIMAL HYPERPLASIA (IH) IN RESPONSE TO HYPERTENSION (BY VENOUS LIGATION) IN THE WALL OF CORONARY VEINS THAT ARE NOT TETHERED TO THE MYOCARDIUM. NO IH WAS OBSERVED IN VESSELS COMPLETELY SURROUNDED BY MYOCARDIUM. TO EXPLAIN THIS RESULT, THEY HYPOTHESIZED THAT THE REMODELING IS STIMULATED BY EXCESSIVE CIRCUMFERENTIAL WALL STRAIN OR STRESS IN HYPERTENSION, WHICH DOES NOT OCCUR IN THE TETHERED VESSEL WALL. SINCE AN ANALYTIC SOLUTION IS NOT AVAILABLE FOR ASYMMETRIC DEFORMATION OF PARTIALLY EMBEDDED LARGE EPICARDIAL VESSELS, IT HAS BEEN DIFFICULT TO PREDICT THE DEFORMATION AND STRESS-STRAIN DISTRIBUTION OF THESE VESSELS IN VIVO.

IN THE PRESENT STUDY, WE SIMULATE THE PASSIVE DEFORMATION OF LEFT ANTERIOR DESCENDING (LAD) ARTERIES EMBEDDED TO DIFFERENT DEPTHS IN THE MYOCARDIUM. OUR OBJECTIVE IS TO DETERMINE THE CHANGE OF ELASTICITY AND STRAIN DISTRIBUTION IN THE VESSEL DUE TO NONUNIFORM MYOCARDIAL CONSTRAINT. OUR FINITE-ELEMENT (FE) MODEL INCORPORATES ANISOTROPIC TISSUE PROPERTIES AND RESIDUAL DEFORMATION IN THE VESSEL WALL AND MYOCARDIUM. THE RESULTS SHOW NONUNIFORM VESSEL DEFORMATION IN RESPONSE TO PARTIAL TISSUE CONSTRAINT. THESE FINDINGS ARE IMPORTANT FOR UNDERSTANDING LOCAL MECHANICS OF EPICARDIAL CORONARY VESSELS IN HEALTH AND IN RESPONSE TO ALTERED LOADING.

MATERIALS AND METHODS

Geometric Model

A computational model of pig LAD artery is schematically illustrated in Fig. 1. The morphological data were obtained from previous in vitro experiments (53). The zero-stress configuration (ZSC; Fig. 1A) was obtained by cutting a vessel ring radially. The opening angle is 132°, the outer and inner radii are 4.66 and 4.27 mm, respectively. Two mechanically functional layers of the vessel, intima-media and adventitia, were considered. The outer radius of the media is 4.50 mm.

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The reference configuration (RC) for FE simulations was selected as the state subjected to an in vivo axial stretch ratio ($\lambda_3$) of 1.4 and zero intravascular pressure (Fig. 1B). As suggested by previous measurements (13), the interaction between the LAD and the myocardium is minimal in this state. To achieve the RC, we conducted axisymmetric FE simulation (57) using the above-described zero-stress data and validated material parameters described below. A two-layer model (53) was employed for the vessel wall. The radii of the inner, outer, and middle surfaces (Fig. 1B) were 0.78, 1.12, and 0.99 mm, respectively. Although the cross section of a normal LAD artery is not completely symmetrical in the absence of pressure, it distends to nearly a perfect circle when subjected to $>20$ mmHg (53). Although the wall thickness may exhibit some circumferential variation in the LAD artery, the variation is relatively small (3, 4, 22). Therefore, we approximate the vessel as having a circular cross section and uniform wall thickness, consistent with previous studies (5, 12, 15–17, 37–39, 50–53, 57–59).

To simulate the fatty and connective tissues surrounding the LAD artery, a thin layer of soft material, designated “fat,” was added on the outer surface of the adventitia (Fig. 1C). The thickness is 0.06 mm, about half of the adventitia in the RC. The vessel was then embedded into the myocardial tissue, which is co-central with the vessel and has a radius of 5.00 mm. The myocardium was partially removed from the top, so that the vessel was embedded to a depth ($d$) measured from the bottom of the adventitia. For convenience, $d$ was normalized by the outer diameter of the adventitia (2.24 mm) and designated $d'$, with values ranging from 1/4 to 3/2, with increments of 1/8 (Fig. 2, A and B). We also considered a fully constrained (myocardium-intact) vessel ($d' = \infty$) and an untethered (no-myocardium) vessel ($d' = 0$). The myofiber orientation was modeled as parallel to the axis of the vessel, i.e., in the $z$ direction.

**Mechanics Model**

Deformation of the vessel and myocardium requires a finite-strain description of the mechanical properties (see Appendix). The FE method was formulated with a Lagrangian description on the stretched RC (Fig. 1B), whereas the constitutive model or stress-strain relation was based on the ZSC (Fig. 1A). The residual deformation gradient from ZSC to RC was derived in Eqs. A1 and A2. The prestretched vessel is subjected to residual deformation in radial, circumferential, and axial directions (Eqs. A3 and A4). Under the physiological condition, the myocardium is subjected to residual fiber stretch. Near the epicardial surface, the stretch was estimated as 1.1 (42), and the residual deformation gradient is given in Eq. A5. The fat layer was considered free of residual deformation.

The passive mechanical properties of the vessel are described by a hyperelastic and nearly incompressible Fung-type constitutive model (Eqs. A6–A8). The model predicts a uniform stress-strain relation in the circumferential direction. In our previous biaxial test (53), the normal pig LAD vessels remain nearly cylindrical in shape when distended with pressure (as high as 150 mmHg), which implies that the mechanical properties are fairly uniform circumferentially. The constitutive parameters of the intima-media and adventitia layers (Table 1) were obtained by averaging the parameters identified for 10 normal pig LAD vessels (53). The myocardium was also described with an axisymmetric (with respect to myofiber direction) Fung-type constitutive model; parameters of this model (Table 1) were obtained from ex vivo tests of normal pig hearts (8, 12, 44). A classical isotropic two-parameter Mooney-Rivlin model was employed for the soft fat layer (Eq. A9) (26, 41, 56).

**Fig. 1.** Computational model of a vessel partially embedded in the myocardium. A: zero-stress configuration (ZSC). B: reference configuration (RC) subjected to physiological axial stretch. C: vessel surrounded by a thin layer of fatty tissue and embedded in the myocardium with depth ($d$) measured from the lowest point of vessel adventitia to the upper surface of the myocardium. $\Phi$: opening angle; $R_o$, outer radius; $R_i$, inner radius; $R_m$, outer radius of media; $r_{m}^{Ref}$, $r_{o}^{ZSC}$, and $r_{o}^{RC}$, radii of outer, middle, and inner surfaces.

**Fig. 2.** Sample finite-element (FE) mesh. A: vessel embedded in the myocardium with relative depth ($d'$) = 3/4, i.e., 1.68 mm. At the top of the vessel, circumferential stretch ratio ($\lambda_3$) is measured transmurally (arrow) for Fig. 7 and at the top of adventitia (●) for Fig. 8. B: models with $d' = 1/2$, 1, and 9/8.
The FE formulation involved computations of the second Piola-Kirchhoff stress tensor and the tangent stiffness tensor in RC, which are derived in Eqs. A10–A15.

**FE Method**

**FE mesh.** A sample FE mesh is shown in Fig. 2A. A two-dimensional four-node quadrilateral isoparametric element was used. The edge length was 0.02–0.025 mm for the intima-media, adventitia, and fat. The numbers of nodes and elements were in the range 5,000–6,000. In each element, a set of $5 \times 5$ Gaussian quadrature integration points was used. On each integration point, the local $(r, \theta, z)$ coordinates were defined and used for calculating the residual deformation gradient ($F_0$, Eq. A3) and anisotropic stress and tangent stiffness tensors (Eqs. A7–A10).

**Boundary conditions.** On the left boundary of the mesh, no displacement was allowed in the $x$ direction, i.e., $u_x = 0$ (Fig. 2A), reflecting the symmetrical condition. Blood pressure of 80–120 mmHg was applied on the inner surface of the vessel. The rest of the boundary was considered traction free.

**Numerical method.** We developed FORTRAN source codes specifically for the vessel simulations. A standard iterative quasi-Newton method (33) was employed to solve the nonlinear equations involved with use of analytic tangent stiffness matrix. The FE codes have been tested against commercial software (ANSYS) using the same mesh, boundary/loading conditions, and isotropic two-parameter Mooney-Rivlin constitutive model. To ensure convergence, blood pressure was increased gradually by small increments (0.5 mmHg per step initially and 5 mmHg at high pressure). The results were outputted for every 10-mmHg increment.

**RESULTS**

**Vessel Elasticity**

The contours of the local circumferential stretch ratio ($\lambda_{\theta}$) on the deformed vessel at physiological pressures, i.e., 80 and 120 mmHg, are given in Figs. 3 and 4, respectively, with relative embedded depth ($d'$) = 0–3/2 (increased by 1/8), 2, and $\infty$. The undeformed vessel is also shown for reference. The cross section of the vessel remains nearly circular in all the simulations, although the myocardial constraint is not uniform circumferentially. This results from the less stiff myocardium in the $x$-$y$ plane compared with the much stiffer axisymmetric properties of the vessel wall as indicated by Eq. A8 and the material parameters $b_1$, $b_2$, and $b_3$ (Table 1).

The elasticity of the vessel wall is determined from the pressure-radius relation. The deformed diameter was measured by the outer radius in the $y$ direction (Fig. 2A). Figure 5A shows the pressure-outer radius relation with different $d'$. The vessel radius increases quickly at low pressure and then tends to the asymptotic value after ~80 mmHg. The deformed cross sections at 80 and 120 mmHg are very similar (Figs. 3 and 4). This is consistent with previous experiments (13, 27) and the increasing stiffness predicted by Fung-type models. The myocardial constraint significantly reduces the vessel radius when $d'$ is large. Figure 5B shows the relation between $d'$ and vessel radius at normal (80 and 120 mmHg) and hypertensive (160

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**Table 1. Material parameters in Fung-type constitutive model of intima-media, adventitia, and myocardium**

<table>
<thead>
<tr>
<th>Material</th>
<th>$C$, kPa</th>
<th>$b_1$</th>
<th>$b_2$</th>
<th>$b_3$</th>
<th>$b_4$</th>
<th>$b_5$</th>
<th>$b_6$</th>
<th>$b_7$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intima-media</td>
<td>5.11</td>
<td>2.74</td>
<td>3.09</td>
<td>0.95</td>
<td>0.45</td>
<td>0.06</td>
<td>0.10</td>
<td>1.00</td>
</tr>
<tr>
<td>Adventitia</td>
<td>9.05</td>
<td>0.62</td>
<td>2.27</td>
<td>1.67</td>
<td>0.34</td>
<td>0.11</td>
<td>0.07</td>
<td>1.00</td>
</tr>
<tr>
<td>Myocardium</td>
<td>0.383</td>
<td>11.8</td>
<td>40.6</td>
<td>11.8</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>7.10</td>
</tr>
</tbody>
</table>
mmHg) pressures. The results reveal that, for a given pressure, the radius decreases gradually as the vessel goes deeper into the myocardium, from $d'/H_{11032}/H_{11005}$ (free vessel) to slightly less than 1 (Fig. 5). The simulation predicts a quick drop of the radius when $d'$ increases from <1 (partially constrained vessel) to >1 (vessel completely embedded in the myocardium). The drop is significant, inasmuch as it accounts for >25% of the total distension of a free vessel from 0 to 120 mmHg and ~35% of the fully embedded case with $d' = \infty$.

For a completely embedded vessel ($d' > 1$), the myocardial constraint acts approximately as an equivalent pressure on the outer surface of the vessel. By comparing the pressure-radius curves of $d' = \infty$ against the free vessel ($d' = 0$), this effective pressure is >50% of the intravascular pressure, consistent with previous experimental findings (13, 27).

We further investigated the effect of the myofiber stretch ratio on the vessel elasticity. Figure 6 shows the pressure-radius relation of a completely embedded vessel ($d' = \infty$) with myofiber stretch ratios of 1.0, 1.1, 1.2, and 1.3, respectively. A dramatic reduction of elasticity with an increase of myofiber stretch gives rise to a significant increase in stiffness.

**Circumferential Stretch Ratio**

The local $\lambda_n$ was calculated with respect to the ZSC and is shown in Figs. 3 and 4 at 80 and 120 mmHg, respectively. The

![Fig. 4. Deformed vessel wall at 120 mmHg pressure. Undeformed edge of vessel is shown as reference. Contour is plotted for $\lambda_n$. Dotted line, undeformed upper surface of the myocardium.](image)

![Fig. 5. Outer radius of deformed vessel. A: pressure-radius relation for vessels with different $d'$. B: vessel radius-$d'$ relation at 80, 120, and 160 mmHg.](image)
myocardial constraint significantly reduces $\lambda_0$ compared with a free vessel; e.g., in the free vessel at 120 mmHg (Fig. 4A), $\lambda_0 = 1.54–1.59$, and in the embedded vessel with $d' = 9/8$ (Fig. 4E), $\lambda_0 = 1.26–1.37$, indicating a 50% reduction in circumferential Green strain. In completely embedded vessels ($d' > 1$), $\lambda_0$ is nearly uniform circumferentially (i.e., contour is axisymmetric).

For partly embedded vessels ($0 < d' < 1$), the distribution of $\lambda_0$ is no longer axisymmetric (Figs. 3, B–E, and 4, B–E). In the wall region that is tethered to the myocardium, $\lambda_0$ is reduced compared with the free vessel. The untethered region, however, exhibits an increase of $\lambda_0$. Near the location where the vessel enters the myocardium, $\lambda_0$ is highest, apparently due to stress concentration. Figure 7, A and B, shows the transmural stretch ratios at 80 and 120 mmHg, respectively, at the top of the vessel (arrow in Fig. 2A). The relative wall thickness is measured from the inner surface of the vessel in RC. The distribution of $\lambda_0$ does not show large transmural variation, except where $d'$ is close to 1. For all cases, the maximum $\lambda_0$ occurs at the outer surface of the adventitia (Fig. 2A). This maximum value is plotted in Fig. 8A against the internal pressure for various embedded depths and in Fig. 8B as a function of the depth with normal (80 and 120 mmHg) and hypertensive (160 mmHg) pressure. It shows a gradual increase in maximum $\lambda_0$ as the vessel merges deeper and, then, a sudden drop to much lower values after the vessel is completely surrounded by the myocardium ($d' > 1$).

DISCUSSION

This study shows that myocardial constraint is a major factor that affects the passive deformation of the LAD artery. The elasticity of fully embedded vessels is reduced by as much as 25% at physiological loading conditions compared with a free vessel. Correspondingly, the circumferential stretch is significantly reduced, indicating a Green strain that is only ~50% of that in the free vessel. For partially embedded vessels, $\lambda_0$ in the vessel wall tethered to the myocardium is reduced compared with $\lambda_0$ in a free vessel at physiological pressure, whereas that in the untethered region is increased because of the absence of local myocardial constraint. The simulations also suggest that the passive pressure-radius relation of partially embedded vessels can be approximated as free of tethering and that of completely embedded vessels as symmetrically surrounded by thick myocardium.

Vascular Remodeling

It is known that stress and strain are the major stimuli of growth and remodeling in vessels (21, 36). In a previous study (2) of large coronary veins in response to pressure overload (by venous ligation), significant IH was observed in the vessel wall that was not tethered to the myocardium. For vessels that were completely surrounded by myocardium, no IH was observed. In a related study focused on remodeling of coronary venules

![Diagram](image_url)
under elevated pressure (3), the epicardial venules show a stronger tendency of intima-media thickening than subepicardial, midmyocardial, and endocardial vessels. The difference from epicardial to subepicardial is most profound, whereas further transmural variation is smaller, consistent with the present findings (Fig. 8). It has been proposed that the remodeling may be triggered by excessive local circumferential wall strain or stretch ratio. The present simulations support the hypothesis. In a partially embedded vessel, λ₀ is higher in the untethered region and lower in the tethered region than λ₀ in a free vessel without myocardial constraint (Figs. 3, A–E, and 4, A–E). For completely surrounded vessels, λ₀ is nearly uniform and is much lower (Figs. 7 and 8), corresponding to a 50% reduction of circumferential Green strain compared with a free vessel at normal physiological pressure. During hypertension (160 mmHg), the partially embedded vessels are stretched circumferentially to λ₀ > 1.64 in the free wall (Fig. 8B). In comparison, the completely embedded vessels are protected by the surrounding myocardium, with λ₀ < 1.35, which is even lower than that of a free vessel at 40 mmHg (Fig. 8). This suggests that a completely surrounded vessel is less likely than an untethered vessel to remodel at elevated loading.

Vessel Elasticity

The elasticity of coronary vessels has important physiological implications, inasmuch as it affects blood flow pulsatility (10, 32). The vessel elasticity is influenced by several factors, including mechanical properties of the vessel, active wall stress, and constraint by the surrounding tissues. The present simulations demonstrate the central role of myocardial constraint on vessel deformation. For completely surrounded vessels, the myocardial constraint takes up a large portion of the load and causes significant reduction of the elasticity (Figs. 3–5), consistent with our previous in vivo and in vitro experiments (13, 27). For example, the radius increases from 1.12 to 1.60–1.65 mm at 120 mmHg compared with 1.85–1.95 mm for partially embedded and free vessels. In other words, neglecting the myocardial constraint will overestimate the cross-sectional area of a completely embedded coronary vessel by ≥30%.

Therefore, myocardial constraint is an important determinant of blood flow in large epicardial coronary arteries and must be considered in fluid-structure interaction (FSI) simulations (18, 40). For partially constrained vessels, only a small reduction of the elasticity is predicted. The deformed cross section of the vessels, regardless of the circumferentially nonuniform myocardial constraints, remains nearly circular. This is consistent with the previous finding that the “cross talk” or interaction between myocardium and vessels takes place mainly at the level of transmyocardial vessels (54).

A realistic model of the vessel-myocardium interaction requires accurate description of the boundary conditions and adds complexity to FSI study of coronary flow. The most important aspect of FSI is prediction of the motion of the vessel wall at a given pressure and wall shear stress (60). For large epicardial arteries, the blood pressure shows little axial gradient (19), and the shear stress is very low. The present simulation results thus suggest some possible simplification: the wall motion of partially embedded vessels can be simplified as a free vessel (d' = 0) and that of completely surrounded vessels can be approximated with d' = ∞. For either case, the governing equation of vessel deformation is one-dimensional (axisymmetric). The simplification, however, has been validated only when deformation of the myocardium is passive and needs further study with consideration of active contraction and heart motion.

Reference Configuration

The choice of RC is critical for cardiovascular simulations, since the constitutive models are strongly nonlinear and the tangent stiffness increases significantly with the strain. In the present study, the RC of the vessel is subjected to λ₀ = 1.4 and zero intravascular pressure (Fig. 1B), instead of the usual no-load configuration (16, 37–39). This choice reflects an experimental fact that the interaction between the LAD artery and the myocardium is minimal in this state (13). The RC for the myocardium is a physiological stretch ratio of 1.1 in the fiber direction, as found near the epicardial surface (42).
Taking into consideration the residual deformation gradients (see Appendix), we have formulated full FE stress-strain relations in the RC. This FE formulation is difficult to implement using the no-load configuration as RC, since the residual deformation gradients in the vessel, myocardium, and fat are not compatible.

The $\lambda_z$ is known to be a major factor that affects vessel elasticity (53). We increased the myofiber stretch ratio and found dramatic reduction of elasticity of completely surrounded vessels (Fig. 6). The reduction is caused by the myocardium, the stiffness of which increases rapidly with strain. The effect of myofiber stretch on elasticity of the partially embedded vessels, however, was insignificant. This suggests that the RC of myocardial constraint should be formulated accurately as the myofiber stretch ratio varies transmurally (42).

**Limitations**

The present study shows that the boundary conditions (BCs) are critical for accurate simulation of the deformation and strain/stress fields in the vessel. Although the present model has considered the myocardium as the major constraint on vessel deformation, several BCs remain for future refinement. We modeled the connective tissues between the vessel wall and the myocardium with a uniform thin layer of soft material. In reality, the connections have spatial variations. For example, this layer consists of randomly distributed fibers and fatty/connective tissue along the LAD wall in pigs. We conducted simulations with different thicknesses of the connective layer. We have found that the vessel elasticity and $\lambda_z$ in the top region of the LAD artery (Fig. 2A) change very little at physiological pressure. Compared with the strong myocardial constraint, the mechanical details of this layer are not very important.

The myofiber orientation is assumed to be parallel to the LAD axis. If we consider that the myocardium is much stiffer in the myofiber direction than in the sheet and normal directions (Table 1), this approximation underestimates the myocardial constraint. Therefore, a larger reduction of vessel elasticity is expected in more realistic three-dimensional simulations where the LAD is not parallel to the myofiber orientation, especially for completely embedded vessels.

In vivo BCs of the myocardium are difficult to quantify. The present model uses a large volume of myocardium to minimize the far-field effect of BCs. More realistic analysis should take into consideration the motion and active contraction of the myocardium during diastole and systole, the influence of other vessels in the myocardium, and so on. We expect that the elasticity of partially embedded vessels is slightly reduced by these factors. For the completely embedded vessels, however, the elasticity may be strongly affected by the diastolic/systolic stress and strain in the myocardium, inasmuch as they change the stiffness of the myocardium significantly (43).

An additional aspect of the myocardial BC is the pressure in the myocardium, usually referred to as “intramyocardial pressure” (IMP) (54). Although it is well accepted that IMP plays an important role in coronary circulation, there have been debates on the relation to ventricular pressure and local strain and stress in the myocardium (7, 9, 23, 34, 35, 46, 48). For a completely embedded vessel, IMP may cause further reduction of the vessel elasticity, since the effect can be approximated as a perivascular pressure that acts against the intravascular pressure. Similarly, IMP should also reduce the deformation of the tethered portion of partially embedded vessels to a lesser degree, because IMP is very low at the subepicardial surface (1, 14). The untethered region is expected to be insensitive to IMP. Consequently, consideration of IMP may further reinforce the conclusions of the present study.

The pericardium is known as a modulator of heart deformation (20, 24, 25, 30), particularly in diseases such as hypertension. It also restricts the partially embedded epicardial vessels from overstretching at higher pressures. This effect was not considered in the present study. Furthermore, the model did not take into account the effect of muscle tone, which has been found to affect in vivo deformation and residual deformation in arteries (31, 38). These issues remain important topics for future studies.

**Summary and Significance of Study**

An FE model was used to study the effects of myocardial constraint on the passive mechanical behaviors of the LAD vessel wall. The results show that myocardial constraint is a major factor that affects vessel elasticity and wall strain. The constraint significantly reduces the elasticity and strain of vessels that are completely surrounded by the myocardium and, thus, may modulate remodeling at elevated blood pressures. The elasticity and wall strain of partially embedded vessels are found to similar to elasticity and wall strain of the free vessel, with higher local circumferential stretch, indicating a strong tendency of circumferentially nonuniform remodeling, consistent with experimental observations (2). This finding of reduced vessel elasticity, along with experimental observations (13, 27), emphasizes the importance of myocardial constraint in fluid-structure interaction study of coronary circulation. Furthermore, the finding suggests a simplification in the pressure-radius relation of large coronary arteries: 1) a partially embedded vessel can be approximated as free of myocardial constraint, and 2) the completely embedded vessels can be approximated as being axisymmetrically surrounded by the myocardium.

**APPENDIX**

**Residual Deformation**

The FE method was formulated with a Lagrangian description on the stretched RC. Consider a material point $\mathbf{x}_0$ in the zero-stress configuration (ZSC; Fig. 1A), which displaces to $\mathbf{x}_1$ in the RC (Fig. 1B) and then to $\mathbf{x}$ in the deformed configuration (DC). Three deformation gradients are defined as follows

$$
\mathbf{F}_0 = \frac{\partial \mathbf{x}}{\partial \mathbf{x}_0}, \quad \mathbf{F}_1 = \frac{\partial \mathbf{x}}{\partial \mathbf{x}_1}, \quad \text{and} \quad \mathbf{F} = \frac{\partial \mathbf{x}}{\partial \mathbf{x}_0} = \mathbf{F}_1 \cdot \mathbf{F}_0 \quad (A1)
$$

where the dot represents the tensor contraction (or matrix multiplication). The Green strain tensors corresponding to $\mathbf{F}_1$ and $\mathbf{F}$ are defined as

$$
\mathbf{E}_1 = \frac{1}{2}(\mathbf{F}_1^T \cdot \mathbf{F}_1 - \mathbf{I}) \quad \text{and} \quad \mathbf{E} = \frac{1}{2}(\mathbf{F}^T \cdot \mathbf{F} - \mathbf{I}) \quad (A2)
$$

where $\mathbf{I}$ is the second-order identity tensor and $\mathbf{T}$ denotes transpose operation. Although the deformation is described with $\mathbf{F}_1$ and $\mathbf{E}_1$ in FE, computation of the stress must be referred to ZSC through the total Green strain $\mathbf{E}$.

In Eq. A1, $\mathbf{F}_0$ defines the residual deformation gradient from ZSC to RC. For the vessel with principal stretch ratios $\lambda_r$, $\lambda_\theta$, and $\lambda_z$ in the radial, circumferential, and axial directions, $\mathbf{F}_0$ is
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\[ F_0(X_1) = \lambda_0^g e_0 \otimes e_0 + \lambda_0^g e_0 \otimes e_0 + \lambda_0^g e_0 \otimes e_0 \]  \hspace{1cm} (A3)

where \( r, \theta, \) and \( z \) denote entities in radial, circumferential, and axial directions, respectively, in RC; \( e_0, e_0, \) and \( e_0 \) are unit eigenvectors of \( F_0 \) and \( \otimes \) represents dyadic product. In this work, \( \lambda_0^g = 1.4 \) was chosen for the LAD artery (39) as

\[ \lambda_0^g = \lambda_0^g (\lambda_0^g)^{-1/2} = 0.9535 \]  \hspace{1cm} (A5)

For the fat layer, \( F_0 = I \).

Constitutive Models

The passive mechanical properties of the nearly incompressible tissues were modeled as hyperelastic materials with strain energy given by

\[ W(\mathbf{E}) = W(\mathbf{E}, J) = W(\mathbf{E}) + \eta (J - 1)^2 \]  \hspace{1cm} (A6)

where \( J = \det(\mathbf{F}) \) and \( \mathbf{E} = (J^{2/3} \mathbf{F}^T \mathbf{F} - I)/2 \). The parameter \( \eta \) is set large enough to enforce nearly incompressible deformation \((J \approx 1)\) (49). In the simulations, \( \eta = 10,000 \) kPa was employed for all materials, and the maximum volumetric change \((J - 1)\) was <3%.

The Fung-type model (5) was used for the media, adventitia, and myocardium, as

\[ W(\mathbf{E}) = C_2 \exp(\eta Q) - 1 \]  \hspace{1cm} (A7)

where \( \eta Q \) is defined in Eq. (2).

\[ Q = b_1E_{oo}^2 + b_2E_{zz}^2 + b_3E_{xx}^2 + 2b_4E_{oo}E_{zz} + 2b_5E_{oo}E_{xx} + 2b_6E_{zz}E_{xx} + b_7E_{xx}^2 + E_{oo}^2 \]  \hspace{1cm} (A8)

The Fung-type model can also be rewritten as

\[ W(\mathbf{E}) = C_2 \exp(\eta Q) - 1 \]  \hspace{1cm} (A9)

where \( C = 2E_0^2 + C_{10} \) and \( C_{10} = 2.000 \) kPa, and \( C_0 = 1.333 \) kPa (26, 56).

The FE formulation requires computations of the second Piola-Kirchhoff stress tensor \( \mathbf{S}_1 \) and the tangent stiffness tensor \( \mathbf{D}_1 \) in the RC. It can be shown that

\[ \mathbf{S}_1 = \frac{\partial W}{\partial \mathbf{E}_1} = F_0 \cdot \mathbf{S}_0 \cdot F_0^T \]  \hspace{1cm} (A10)

where \( \mathbf{S}_0 = \partial W_0/\partial \mathbf{E}_0 \) and \( \mathbf{D}_1 = \partial \mathbf{S}_1/\partial \mathbf{E}_1 \)

REFERENCES


