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EVOLVING BIAXIAL MECHANICAL PROPERTIES OF MOUSE CAROTID ARTERIES IN HYPERTENSION

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Abstract

Quantifying the time course of load-induced changes in arterial wall geometry, microstructure, and properties is fundamental to developing mathematical models of growth and remodeling. Arteries adapt to altered pressure and flow by modifying wall thickness, inner diameter, and axial length via marked cell and matrix turnover. To estimate particular biomaterial implications of such adaptations, we used a 4-fiber family constitutive relation to quantify passive biaxial mechanical behaviors of mouse carotid arteries 0 (control), 7–10, 10–14, or 35–56 days after an aortic arch banding surgery that increased pulse pressure and pulsatile flow in the right carotid artery. In vivo circumferential and axial stretches at mean arterial pressure were, for example, 11% and 26% lower in hypertensive carotids 35–56 days after banding than in normotensive controls; this finding is consistent with observations that hypertension decreases distensibility. Interestingly, the strain energy W stored in the carotids at individual in vivo conditions was also less in hypertensive compared with normotensive carotids. For example, at 35–56 days after banding, W was 24%, 39%, and 47% of normal values at diastolic, mean, and systolic pressures, respectively. The energy stored during the cardiac cycle, $W_{\text{sys}} - W_{\text{dias}}$, also tended to be less, but this reduction did not reach significance. When computed at normal in vivo values of biaxial stretch, however, W was well above normal for the hypertensive carotids. This net increase resulted from an overall increase in the collagen-related anisotropic contribution to W despite a decrease in the elastin-related isotropic contribution. The latter was consistent with observed decreases in the mass fraction of elastin.

Keywords

pulse pressure; stiffness; wall stress; distensibility; remodeling

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1. Introduction

Altered blood pressure and flow induce changes in arterial wall geometry, microstructure, and mechanics. For example, increased mean pressure and flow typically correlate with increased wall thickness and inner diameter, respectively (Dajnowiec and Langille 2007; Hayashi and Naiki 2009). In addition, however, the pulsatile character of hemodynamic loading also has a strong impact on the evolving histo-mechanics of the wall (Boutouyrie et al. 1999; Eberth et al. 2010; Guyton and Hartley 1985). Of particular note, otherwise stable elastin can be fragmented by the heightened cyclic loading that results from increased pulse pressure in hypertension (Arribas et al. 2006; Avolio et al. 1998; Greenwald 2007); such changes are often accompanied by a significant cyclic stretch-induced synthesis of collagen, particularly in the adventitia (Li et al. 1998; Sasamura et al. 2005; Strauss and Rabinovitch 2000).

In this work, we sought to identify possible relations between overall changes in mechanical properties and alterations in the composition of the arterial wall that occur in response to increased pulse pressure. Toward this end, we used a 4-fiber constitutive relation to re-analyze data from a prior study of the time course of biomechanical and histological changes in the carotid artery of the mouse due to a transverse aortic arch banding procedure that increased pulsatile hemodynamics (Eberth et al. 2010). Only passive biaxial data were used to estimate the parameters in the constitutive relation so as to focus on the primary load bearing constituents within the wall, mainly elastin and fibrillar collagens. Moreover, to simplify comparisons of altered mechanical properties, we quantified overall changes in terms of the strain energy stored in the arterial wall at appropriate states of biaxial stretch. The results suggested that the material stiffness is lower under *in vivo* conditions in hypertension compared with normotension, which appeared to be due in part to a diminished load carrying capability of elastin. We submit that this approach to quantification will provide additional guidance for the continued development of growth and remodeling (G&R) models of hypertension.

2. Methods

Experimental Data

Details on the experimental methods and data collection can be found elsewhere (Eberth et al. 2010; Rockman et al. 1993). Briefly, cyclic pressure-diameter and axial force-length tests were performed on right common carotid arteries excised from mature male wild-type C57BL/6J-129Sv mice at 0 ($n=6$), 7–10 ($n=9$), 10–14 ($n=8$), or 35–56 ($n=6$) days following transverse aortic arch banding surgery. This procedure results in a marked increase in both pulse pressure and pulsatile flow in the right carotid artery while leaving mean values close to normal. The pressure-diameter tests (0 – 140 mmHg) were performed at the individual *in vivo* axial stretch (λ_z^{iv}) as well as at 5% above and below this stretch, with all values of stretch computed relative to the individual unloaded (evolving) configurations. Although our prior report did not include the data from passive tests, all data used herein were collected under passive conditions (10^{-5} M sodium nitroprusside and 2×10^{-3} M EGTA) to isolate contributions by the primary extracellular matrix proteins.

Constitutive Relations and Parameter Estimation

Mechanical properties were quantified using a 4-fiber family constitutive relation that describes biaxial data well for mouse carotid arteries (Eberth et al. 2009b; Gleason et al. 2008; Wan et al. 2010). Briefly, this relation is motivated by the assumption that the primary load bearing constituents include an isotropic, elastin-dominated amorphous matrix, 4 families of oriented collagen fibers (axial, circumferential, and symmetric diagonal), and

passive smooth muscle (circumferential). The associated strain energy function takes the form $W=W_{iso}+W_{anis}$, where

$$W_{iso}=\frac{c}{2}(\lambda_\theta^2+\lambda_z^2+\lambda_r^2-3), \quad (1)$$

$$W_{anis}=\frac{C_z^1}{4C_z^2}\left\{e^{c_z^2((\lambda_z)^2-1)^2}-1\right\}+\frac{C_\theta^1}{4C_\theta^2}\left\{e^{c_\theta^2((\lambda_\theta)^2-1)^2}-1\right\}+2\frac{C_d^1}{4C_d^2}\left\{e^{c_d^2((\lambda_d)^2-1)^2}-1\right\}. \quad (2)$$

The circumferential (λ_θ) and axial (λ_z) stretches were measured whereas the radial stretch (λ_r) was computed assuming incompressibility; the stretch experienced by diagonal fibers was computed as

$$\lambda_d=\sqrt{\lambda_\theta^2 \sin^2 \alpha_d^0 + \lambda_z^2 \cos^2 \alpha_d^0}. \quad (3)$$

Finally, $c, c_z^1, c_z^2, c_\theta^1, c_\theta^2, c_d^1, c_d^2$ are material parameters and α_d^0 is the angle between the symmetrically oriented diagonal collagen fibers and the axial direction in the unloaded configuration. Assuming plane stress (i.e., $\sigma_r \ll \sigma_\theta$ and $\sigma_r \ll \sigma_z$), the non-zero components of the Cauchy stress can be computed in circumferential and axial directions as

$$\sigma_\theta^{mod}=\lambda_\theta \frac{\partial W}{\partial \lambda_\theta} - \lambda_r \frac{\partial W}{\partial \lambda_r}, \quad (4)$$

$$\sigma_z^{mod}=\lambda_z \frac{\partial W}{\partial \lambda_z} - \lambda_r \frac{\partial W}{\partial \lambda_r}. \quad (5)$$

The 8 unknown model parameters within equations 1–2 were estimated by minimizing the sum of the squares of the differences between experimentally measured (exp) and theoretically modeled (mod) pressure and forces, namely by minimizing the error e

$$e=\sqrt{\frac{\sum_{i=1}^N (P^{exp} - P^{mod})^2}{\sum_{i=1}^N (P^{exp})^2}} + \sqrt{\frac{\sum_{i=1}^N (F^{exp} - F^{mod})^2}{\sum_{i=1}^N (F^{exp})^2}}$$

where N is the number of data points, with data from the multiple biaxial protocols combined for each specimen separately. This minimization was accomplished using the simplex method. Note, too, that the theoretical (or, model) pressure and axial force were computed from the constitutively determined mean Cauchy stresses and geometry using standard relations,

$$\sigma_\theta=\frac{Pr_i}{r_a - r_i}, \quad (7)$$

$$\sigma_z = \frac{f_r + P\pi r_i^2}{\pi(r_a^2 - r_i^2)}, \quad (8)$$

where P is the transmural pressure, f_T is the axial force measured by the in-line transducer, and subscripts i and a denote intimal and adventitial, respectively. The total force is a combination of the value measured by the force transducer and the contribution of the static pressure, namely $F = f_T + P\pi r_i^2$.

Because of the difficulty of assessing specimen-to-specimen differences based on 8 best-fit material parameters in a highly nonlinear model, or similarly based on the 3 non-trivial components of the nonlinear stiffness tensor (e.g., $K_{\theta\theta\theta\theta}$, K_{zzzz} , and $K_{\theta\theta zz} = K_{zz\theta\theta}$ where $\mathbf{K} = \partial^2 W / \partial \mathbf{E} \mathbf{E}^2$ and $\mathbf{E}$ is the Green strain), all assessments of overall stiffness were based primarily on the strain energy stored in each artery in response to appropriate deformations.

Microstructural Analysis and Statistics

Standard Verhoeff-Van Gieson (VVG) staining was used to quantify elastin content as described in Eberth et al. (2010). Briefly, fixed cross-sections were stained, imaged at 20 $\times$, and analyzed using a thresholding algorithm to quantify the ratio of elastin (black) to other tissue. Representative figures can be found in Eberth et al. (2010). Comparisons between groups were performed using a Student's t-distribution with $n-2$ degrees of freedom and two tails; values are listed as mean $\pm$ standard error of the mean. Finally, potential correlations were determined using the Pearson coefficient (r^*) and significance was assumed at a level $p < 0.1$.

3. Results

Table 1 lists measured values of geometry, axial force, and biaxial stretch that correspond to the passive state at mean arterial pressure. Table 2 lists mean values of the best-fit model parameters. Of particular note was the consistent decrease in the isotropic material parameter (c), which was only 38% of its baseline value after 35–56 days of remodeling due to hypertension. The anisotropic parameter (c_z^1) also decreased in the axial direction, but its corresponding exponential parameter (c_z^2) increased. These anisotropic coefficients (equations 1–2) must be considered as pairs when inferring changes in stiffness, which emphasizes one utility of stored energy considerations. Together, the anisotropic circumferential coefficients (c_θ^1, c_θ^2) suggested a possible stiffening in this direction at 35–56 days despite the exponential term decreasing for a short period from 7–14 days. Similar tendencies toward possible stiffening were also suggested by the anisotropic diagonal coefficients (c_d^1, c_d^2). The mean angle α_o^d for the diagonal collagen fibers increased marginally in the hypertensive vessels (i.e., tended toward circumferential). Finally, variations in all model parameters suggested marked differences in remodeling amongst the individual mice subjected to hypertension, which resulted in part from variability in the banding procedure as noted previously. For this reason, all subsequent interpretations are based on group means.

Values of strain energy W , averaged separately for each group at each time-point, also suggested a possible overall stiffer behavior in hypertension when evaluated at stretches experienced in vivo during normotension, but they further suggested an overall less stiff

behavior in hypertension when evaluated at the actual in vivo stretches (Figure 1). Note, therefore, that W is plotted as a function of the biaxial state of stretch, with values within the dashed lines indicating those achieved during in vitro experiments. In addition, however, W was computed over the range of stretches appropriate to the control normotensive arteries ($\lambda_\theta = 1-2.00$; $\lambda_z = 1-1.85$); these values are shown beyond the dashed line for purposes of comparison. Finally, the downward pointing white triangle in each plot indicates the individual in vivo condition for the control and hypertensive vessels, meaning biaxial stretches corresponding to the group mean arterial pressure (MAP) and in vivo axial stretch λ_z^{iv} . The λ_θ^{MAP} for the 7–10, 10–14, and 35–56 day groups were 9.1%, 9.9%, and 11% lower than those for the controls. Similarly, λ_z^{iv} for these same groups were 14%, 19%, and 26% lower (Table 1). Both of these decreases in the in vivo stretch are consistent with the in vivo observation of decreased distensibility in hypertension.

The isotropic contribution to the strain energy W_{iso} is shown in Figure 2, with λ_θ and λ_z again ranging over both the individual stretches that were achieved experimentally and those experienced by the control arteries. Note the marked progressive decrease in W_{iso} over the period 0 to 56 days following aortic banding; note, too, that this finding appeared consistent with the aforementioned decrease in the isotropic material parameter c . Because these findings suggested a possible loss in stiffness associated with elastin, consistent with many reports of fragmentation or degradation of elastin in hypertension (Arribas et al. 2006; Avolio et al. 1998; Greenwald 2007), we plotted the value of c versus the histologically measured mass fraction of elastin (Figure 3), which also decreased progressively with the duration of hypertension (Eberth et al. 2010). As it can be seen, there was a strong, significant correlation between changes in the elastin parameter and its mass fraction. Also shown in Figure 3 are plots of circumferential Cauchy stress versus stretch that delineate contributions due to the isotropic (primarily elastin) and anisotropic (primarily collagen, but possibly passive smooth muscle) constituents. A diminished contribution in hypertension due to elastin is evident once again.

Plots of net Cauchy stress versus stretch in both circumferential and axial directions are shown in Figure 4 (using mean parameters from Table 2) for ranges of stretch consistent with the in vitro experiments. Note again the apparent stiffening due to hypertension when evaluated at the same stretches, with greater stiffening in the axial direction. Given the apparent loss of stiffness due to elastin, this finding also suggests an increased stiffness due to collagen and/or passive smooth muscle. Anisotropic contributions to the strain energy comparable to those in Figure 3 are not shown simply because they can be inferred via the subtraction $W - W_{iso}$. Nevertheless, such plots consistently confirmed that increases in strain energy for hypertensive arteries, when evaluated at normotensive stretches, was likely due to an increased deposition of collagen, consistent with histological findings reported by Eberth et al. (2010).

Because of the significant increase in pulse pressure following banding (Eberth et al. 2010), we also computed the in vivo strain energy stored at diastolic, mean, and systolic pressures (Figure 5). For example, the 35–56 day hypertensive vessels stored only 24%, 39%, and 47% of the normotensive values of W at diastolic, mean, and systolic pressures, respectively. These values were not statistically different from the 10–14 day time group. Furthermore, the change in strain energy across the cardiac cycle ($\Delta W = W_{sys} - W_{dias}$) was 22.04, 19.56, 14.61, 14.74 (kPa) respectively for 0, 7–10, 10–14, and 35–56 days following aortic arch banding surgery, with no significant differences between the groups.

4. Discussion

Tremendous advances in arterial mechanics were achieved from the mid-1960s through the mid-1990s using purely phenomenological constitutive relations, which led for example to our appreciation of the role of residual stress in homogenizing the transmural stress field in arterial homeostasis. Nevertheless, there has been a move toward structurally-motivated constitutive relations that can provide increased insight into contributions of individual structurally significant constituents to overall wall mechanics. In most cases (e.g., Gasser et al. 2006; Gleason et al. 2008; Holzapfel et al. 2000; Ogden and Saccomandi 2007; Stylianopoulos and Barocas 2007; Zulliger and Stergiopoulos 2007), there is a separation of elastin-dominated and collagen-dominated contributions to the net strain energy function in these structurally motivated models. A notable exception is the “eight chain” model, based on advances in polymer mechanics, which does not attempt to delineate contributions by particular constituents (e.g., Ning et al. 2010). Of the various models available, we adopted a 4-fiber family model that is an extension of the popular model of Holzapfel et al. (2000). This model has been shown to describe well the biaxial behavior of mouse carotid arteries (e.g., Gleason et al. 2008; Wan et al. 2010), to reflect underlying changes in matrix in diverse cases of growth and remodeling (e.g., Eberth et al. 2009a; Ferruzzi et al. 2011), and to not be over-parameterized (Zeinali-Davarani et al. 2009).

The 4-fiber family constitutive relation captured well the biaxial mechanical behavior of mouse carotid arteries at 0, 7–10, 10–14, and 35–56 days following the sudden onset of hypertension, which was induced primarily by an increase in systolic (and thus pulse) pressure following transverse aortic arch banding. When evaluated near individual *in vivo* stretches, that is, at group-specific mean arterial pressures and *in vivo* axial stretches (λ_{θ}^{MAP} , λ_z^H), the net strain energy W was lower in hypertensive arteries at all times compared with that for normotensive controls (cf. Figures 1 and 5). This finding appeared to be due, in part, to the higher values of biaxial stretch under normotensive conditions (cf. Table 1). Indeed, when evaluated at the original values of stretch, the hypertensive arteries were predicted to store more strain energy than their normotensive counterparts, hence implying an overall stiffer behavior at higher stretches.

Nonetheless, it appeared that another contributor to the lower values of strain energy stored in the hypertensive arteries at individual *in vivo* stretches was a progressive decrease in the parameter c (Table 2, Figure 2), which is thought to model the elastin-dominated contribution to wall mechanics. Because of the use of nonlinear regression to determine best-fit values of the material parameters, this finding need not imply that elastin was necessarily less stiff in hypertension; rather, it could simply reflect that there was a greater contribution to the overall strain energy by the anisotropic terms, which are motivated by the collagen. Figure 3 suggested, however, that there was a strong correlation between the diminished contribution of the elastin-dominated term to the strain energy and a real decrease in the contribution of elastin to the mechanics. Related to this, Eberth et al. (2009b) previously showed that the parameter c was also less for fibrillin-1 deficient mice than for wild-type controls. This finding was expected because fibrillin-1 plays a crucial role in elastin maintenance. Similarly, Ferruzzi et al. (2011) reported a progressive decrease in the parameter c based on fits to data for aging human abdominal aorta and abdominal aortic aneurysms, each of which are known to have diminished elastin. Indeed, using elastase to selectively remove the contribution of elastin to overall wall mechanics, Fonck et al. (2007) reported a marked decrease in a similar elastin-related material parameter. It seems, therefore, that loss of elastin effectiveness contributed to the material behavior in hypertension, as expected based on prior histologically based studies (Arribas et al. 2006;

Avolio et al. 1998; Greenwald 2007), and that the 4-fiber family model was able to delineate this effect.

Best-fit material parameters in hypertension also suggested a possible increase in both the circumferential stiffness, which could be due to either the collagen or passive smooth muscle, and that associated with the diagonal fibers (Table 2). The interpretation of differences in best-fit parameters associated with the axial direction was less clear because one parameter increased and one decreased (Table 2). Yet, this change appeared to be consistent with both the observed greater axial stiffening and loss of axial extensibility in hypertension and a prior interpretation (Ferruzzi et al. 2011) that relative magnitudes of the paired exponential parameters reflect how rapid the stress – stretch curve stiffens. This interpretation is also very similar to the suggestion that the collagen “recruitment stretch” decreases with a loss of elastin (Fonck et al. 2007). Finally, the small change in fiber angle α_d^o (Table 2) due to hypertension was even more difficult to interpret.

Indeed, it was because of the difficulty of interpreting possible changes in stiffness based on changes in the many best-fit regression parameters (8 in the 4-fiber family model) and the similar difficulty of interpreting changes in the different components (3 in this case) of the nonlinear stiffness tensor that we used total stored strain energy as a metric of overall stiffness. This scalar is particularly convenient given the aforementioned common assumption of additive elastin-dominated and collagen-dominated contributions to the material behavior. That values of strain energy, like those of components of the stiffness tensor itself, depend explicitly on deformation in nonlinear materials is a good reminder that we should compare material behaviors relative to appropriate reference configurations and over appropriate ranges of deformation or loading. We used the evolving unloaded configurations for the hypertensive vessels because these are experimentally available and most relevant. When contrasting the present results to those based on growth and remodeling simulations (cf., Cardamone et al. 2010; Driessen et al. 2004; Tsamis et al. 2009), it is important to note that the latter often employ a single, rather than evolving, reference configuration(s). Regardless, our data suggest that evolution of the unloaded configuration was fundamentally important: unloaded outer radius was 201 ± 4.3 , 225 ± 25.4 , 304 ± 145 , and 313 ± 6.5 μm , respectively, and unloaded wall thickness was 79.3 ± 0.94 , 98.9 ± 19.3 , 125 ± 34.6 , 152 ± 7.59 μm at 0, 7–10, 10–14, and 35–56 days post banding.

More importantly, however, comparisons amongst material behaviors should account for any differences in the in vivo conditions rather than, as often is the case, simply compare results at the same distending pressure (e.g., 100 mmHg). As seen in Figure 1, when based on individual in vivo deformations, the overall material stiffness was found to be lower in hypertension. In addition, we compared the energy stored at individual diastolic, mean, and systolic pressures (Figure 5). Comparisons at mean arterial pressure were particularly revealing herein for this pressure changed little in the transverse aortic banding model; it was systolic (and pulse) pressure that changes most (Eberth et al. 2010). Again, the hypertensive arteries stored less strain energy at mean arterial pressure than did the normotensive controls. Although this finding was likely influenced by the higher in vivo stretches in normotension (i.e., greater distensibility), it appears that a diminished load carrying capability of elastin also played a key role. Here we emphasize that the parameter c necessarily models the combined effects of elastin mass fraction, structural integrity, and intrinsic stiffness (cf. Figure 3). Because hypertension is often thought to reflect an associated accelerated aging, note that Wuyts et al. (1995) reported a similar progressive decrease in an elastin related parameter in aging whereas Zullinger and Stergiopulos (2007) reported a progressive decrease in the elastin mass fraction and a less marked progressive increase in an elastin elastic modulus. Taken together, these reports support our finding of a diminished value of c (Table 2), the associated decreased contribution of the elastin-

dominated strain energy to the overall energy stored (Figure 2), and the strong correlation between c and the elastin mass fraction (Figure 3).

In closing, we emphasize that our model, like all others, is structurally-motivated yet primarily phenomenological; material and most structural parameters are determined primarily via fits to data. In other words, no current biomechanical model accounts for the full microstructural complexity of the arterial wall. There is a need, for example, to account for the separate mechanical contributions of types I and III collagen, the microfibrils (e.g., fibrillins and fibulins) that support the elastin, the proteoglycans, and the many other proteins, such as type V collagen, that contribute to the structural integrity of the wall. Similarly, there is a need to account for cross-links, physical entanglements, and secondary bonds, not to mention cell-cell and cell-matrix interactions. For these and similar reasons, we must not over-interpret results from microstructurally motivated constitutive relations. We suggested previously, for example, that the extreme thickening of the carotid artery following aortic banding may have resulted in part from an increased deposition of proteoglycans or non-fibrillar collagens (Eberth et al. 2010). Such components could dampen effects of the increased pulse pressure and thereby protect intramural cells. Non-tensile bearing constituents could also result in an overestimation of wall thickness and underestimation of wall stress and thereby lead to lower stresses predicted by the model. These and similar complexities were not considered herein. Nevertheless, we submit that, like other current models, the 4-fiber family model continues to capture salient features of arterial behavior during growth and remodeling and thus continues to serve as a useful foundation for such studies.

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Figure 1.

Contour plots of total strain energy W (in kPa, which is equivalent to kJ/m^3) as a function of biaxial stretch, in circumferential (λ_θ) and axial (λ_z) directions, for carotid arteries before (0 days – top) and 7–10, 10–14, or 35–56 days following banding surgery. Data are described by equations 1–8 and Table 2. The in vitro tested range of stretches is enclosed by (–). The downward pointing triangle indicates the strain energy at mean arterial pressure and the group-specific in vivo axial stretch.

Figure 2.

Contour plots of the isotropic part of the strain energy W_{iso} (kPa) as a function of biaxial stretch, in circumferential (λ_θ) and axial (λ_z) directions, for carotid arteries before (0 days – top) and 7–10, 10–14, or 36–52 days following banding surgery. Data are described by equations 1–8 and Table 2. The in vitro tested range of stretches is enclosed by (–). The downward pointing triangle indicates the strain energy at mean arterial pressure and the group-specific in vivo axial stretch.

Figure 3.

(a) Plot of the isotropic model parameter c (kPa) versus the mass fraction of elastin ϕ^e measured from standard microscopy. Note that c correlated strongly with elastin mass fraction ($r^*=0.842$; $p<0.001$). Panels (b) and (c) show typical circumferential stress-stretch behaviors over physiological ranges for data sets with high (0 days) and low (35–56 days) values of ϕ^e . The solid curve (—) represents the total stress whereas the dashed-dot (— · —) and dot-dot (····) curves represent the isotropic (largely elastin) and anisotropic (largely collagen) portions, respectively. Total stress is a summation of isotropic and anisotropic contributions.

Figure 4.

Mean Cauchy stress-stretch responses, in (a) circumferential (σ_θ - λ_θ) and (b) axial (σ_z - λ_z) directions, for mouse common carotid arteries predicted by the 4-fiber constitutive relation (equations 1–8 and Table 2). Curves are before (0 days – $\times$) and 7–10 ($\circ$), 10–14 (Δ), and 35–56 ($\square$) days following banding surgery. Data shown in panel (a) correspond to in vivo axial stretches (λ_z^{iv} = 1.70, 1.46, 1.37, 1.25 at 0, 7–10, 10–14, and 35–56 days, respectively) and a range of circumferential stretches (λ_θ) while data shown in panel (b) correspond to mean arterial circumferential stretches (λ_θ^{MAP} = 1.61, 1.48, 1.45, 1.44 at 0, 7–10, 10–14, and 35–56 days, respectively) and a range of axial stretches (λ_z) used during in vitro mechanical testing. Modeling errors are noted in Table 2.

Figure 5.

Total strain energy W (kPa) at physiologic operating points, including in vivo axial stretch and circumferential stretches corresponding to diastolic, mean, or systolic pressures. Data are shown for each group before (0 days: $\lambda_{\theta}^{MAP}=1.61$, $\lambda_z^{iv}=1.70$ ■) and 7–10 ($\lambda_{\theta}^{MAP}=1.48$, $\lambda_z^{iv}=1.46$ ▨), 10–14 ($\lambda_{\theta}^{MAP}=1.45$, $\lambda_z^{iv}=1.37$ □), and 35–56 ($\lambda_{\theta}^{MAP}=1.44$, $\lambda_z^{iv}=1.25$ ▩) days following banding surgery. All results are mean $\pm$ standard error, with (*) indicating statistical significance ($p < 0.1$) between the control group (0 days) and hypertensive sets (7–10, 10–14, or 35–56 days) and (**) indicating a significant difference from the chronologically preceding data point. Note that there was a trend for the change in strain energy over the cardiac cycle ($\Delta W = W_{sys} - W_{dias}$) to decrease with increasing duration of hypertension, but this did not reach significance for any remodeling time-point ($p < 0.1$).

Table 1

Post-Surgery Time [days]	Inner Diameter [μ m]	Wall Thickness [μ m]	Axial Force [mN]	λ_0	λ_z
<i>Control</i>					
0	531 $\pm$ 23.92	23.1 $\pm$ 2.44	3.55 $\pm$ 0.19	1.61 $\pm$ 0.10	1.70 $\pm$ 0.01
<i>Hypertension</i>					
7–10	612 $\pm$ */** 25.9	40.5 $\pm$ */** 4.12	0.86 $\pm$ */** 0.52	1.48 $\pm$ *0.05	1.46 $\pm$ *0.09
10–14	664 $\pm$ */** 73.9	64.3 $\pm$ */** 30.2	1.27 $\pm$ */** 0.11	1.45 $\pm$ *0.22	1.37 $\pm$ *0.19
35–56	592 $\pm$ */** 55.4	85.7 $\pm$ */** 11.5	1.20 $\pm$ *0.42	1.44 $\pm$ *0.11	1.25 $\pm$ */** 0.02

Table 2

Post-Surgery Time [days]	c [kPa]	c_z^1 [kPa]	c_z^2	c_θ^1 [kPa]	c_θ^2	c_d^1 [kPa]	c_d^2	α_d^o [deg]	e
<i>Control</i>									
0	16.14±3.13	0.94±0.54	0.69±0.154	6.18±2.26	0.110±0.370	0.372±0.09	0.184±0.104	43.9±2.17	0.04±0.007
<i>Hypertension</i>									
7 – 10	9.71±2.15	0.20±0.10	1.09±0.548	15.5±7.88	0.005±*0.001	7.09±*2.13	0.658±*0.151	45.6±*1.72	0.05±0.003
10 – 14	6.51±*/*2.22	0.20±0.14	1.35±0.680	16.6±10.10	0.064±0.063	5.81±*1.76	0.799±*0.185	45.7±1.54	0.04±0.009
35 – 56	6.09±*2.56	0.06±*0.06	1.54±1.02	11.7±5.24	1.06±*1.06	10.9±*3.94	1.34±*/*0.071	46.4±1.77	0.04±0.008