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Technical note

Stress–strain behavior of the passive basilar artery in normotension and hypertension

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Abstract

Vascular cells are very responsive to even subtle changes in their local mechanical environment, thus there is a pressing need to quantify normal states of stress and strain as well as any perturbations from these normal states. Toward this end, we must quantify constitutive behaviors for both normal and adapted (maladapted) arteries. In this note, we report the first quantification of changes in the biaxial mechanical behavior of the passive basilar artery due to hypertension.

Keywords: Stress; Strain; Stiffness; Cerebral artery; Hypertension; Biomechanics

1. Introduction

Hypertension (HT) is a significant risk factor for many diseases, including those of the cerebrovascular system: stroke, aneurysms and arteriovenous malformations. Although it is well known that HT induces marked changes in the structure, function, and material behavior of cerebral arteries (Hajdu and Baumbach, 1994; Lee, 1995), there has been surprisingly little attempt to quantify such changes in terms of appropriate biomechanical constitutive relations. Quantification is essential if we wish to understand better the mechanobiological processes by which growth and remodeling occur in hypertension as well as in the other types of cerebrovascular disease progression or responses to injury. The goal of this note is to evaluate the utility of three different nonlinear stress–strain relations to fit published biaxial data on porcine basilar arteries under normotensive (NT) and HT conditions.

2. Methods

We recently reported pressure-diameter data at the in situ length on the passive biomechanical behavior of porcine basilar arteries 2, 4, 6, and 8 weeks after inducing a hypertension defined by a mean arterial pressure greater than 150 mmHg (Hu et al., 2006). Because there was no statistically significant difference in behavior from 2 to 8 weeks, however, data were pooled to compare NT versus HT. That the associated growth and remodeling appeared to be largely completed by 2 weeks of HT suggested that the transmural distribution of stress was likely restored back toward normal, which in turn is thought to be a uniform distribution (Fung, 1990; Humphrey, 2002). Hence, finite inflation and extension data (in the absence of shear) were quantified via mean values of the Cauchy stress,

$$\sigma_\theta = \frac{Pa}{h}, \quad \sigma_z = \frac{L + \pi a^2 P}{\pi h(2a+h)}, \tag{1}$$

where P is the applied transmural pressure, L is the axial load imposed by extending the vessel, a and h are the deformed inner radius and wall thickness, respectively, and $\sigma_\theta \gg \sigma_r$ and $\sigma_z \gg \sigma_r$. Consistent with a "2-D" analysis, and if we restrict our attention to pseudoelastic behavior (cf. Monson et al., 2003) under cyclic loading, the mean Cauchy stresses can also be determined constitutively using a strain energy function W, namely

$$\sigma_\theta = \lambda_\theta^2 \frac{\partial W}{\partial E_{\theta\theta}}, \quad \sigma_z = \lambda_z^2 \frac{\partial W}{\partial E_{zz}}, \tag{2}$$

where λ_θ and λ_z are circumferential and axial stretches, respectively, and $E_{\theta\theta}(= (\lambda_\theta^2 - 1)/2)$ and $E_{zz}(= (\lambda_z^2 - 1)/2)$ are components of the 2-D Green strain tensor in the circumferential and axial directions; or alternatively

$$\sigma_\theta = \lambda_\theta \frac{\partial W}{\partial \lambda_\theta}, \quad \sigma_z = \lambda_z \frac{\partial W}{\partial \lambda_z}. \tag{3}$$

Although there are no prior reports on the biaxial mechanical properties of intracranial arteries, characteristic behaviors in the circumferential (Hayashi et al., 1980; Hajdu and Baumbach, 1994) and the axial (Monson et al., 2003) directions are qualitatively similar to, albeit stiffer than the

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behaviors of extracranial arteries. Hence, consider two forms of W that were useful in modeling extracranial arteries. First, a Fung-exponential model (Fung, 1990)

$$W = c(e^{Q} - 1), \quad Q = c_1 E_{\theta\theta}^2 + c_2 E_{zz}^2 + 2c_3 E_{\theta\theta} E_{zz}, \tag{4}$$

where c,c_1,c_2, and c_3 are material parameters. Note, to satisfy physical and mathematical (convexity) constraints, $c>0, c_1>0, c_2>0, c_3>0$ and $c_1 c_2 > c_3^2$ (Humphrey, 1999; Holzapfel et al., 2000). Second, a Holzapfel model (Holzapfel et al., 2000)

$$W = \frac{c}{2}(I_1 - 2) + \sum_{k=1,2} \frac{c_1^k}{4c_2^k}\left\{\exp\left[c_2^k\left(\left(\lambda^k\right)^2 - 1\right)^2\right] - 1\right\}, \tag{5}$$

where the superscript k denotes the kth fiber family, c, c_1^k, c_2^k are material parameters (typically with $c_1^1 = c_1^2$ and $c_2^1 = c_2^2$). I_1 is the first invariant of the 2-D right Cauchy–Green tensor, $\lambda^k = \sqrt{\lambda_\theta^2 \sin^2\alpha^k + \lambda_z^2 \cos^2\alpha^k}$ is the stretch of the kth fiber family, and α^k is the angle between the fiber direction and the axial direction, with $\alpha^1 = -\alpha^2$. Physical and mathematical constraints are satisfied with all four material parameters positive (Holzapfel et al., 2000). Whereas the Fung model is purely phenomenological, the Holzapfel model was motivated by the assumptions that the non-collagenous matrix (e.g., elastin) contributes isotropically to overall load bearing, which can be accounted for by a neo-Hookean-type term, and that collagen fibers are arranged helically and can be accounted for by exponential functions in terms of fiber stretch. Note that the two fiber families considered in this model arrange in symmetrical helices; moreover, Holzapfel and colleagues presented this 2-fiber family model within the context of modeling separately the media and adventitia, thus requiring six material parameters plus two structural parameters (angles) for the arterial wall.

In addition, consider a straightforward extension of the Holzapfel model, which will be referred herein as the 4-fiber family model,

$$W = \frac{c}{2}(I_1 - 2) + \sum_{k=1,2,3,4} \frac{c_1^k}{4c_2^k}\left\{\exp\left[c_2^k\left(\left(\lambda^k\right)^2 - 1\right)^2\right] - 1\right\}. \tag{6}$$

In contrast to the original model, this model also accounts directly for axially ($\alpha^3 = 0$) and circumferentially ($\alpha^4 = 90°$) oriented fibers, which can be assumed to have the same mechanical properties ($c_1^3 = c_1^4$ and $c_2^3 = c_2^4$). For example, for this 4-fiber family model,

$$\sigma_\theta = c\lambda_\theta^2 + \lambda_\theta^2 \sum_{k=1,2,3,4}\left\{c_1^k\left(\left(\lambda^k\right)^2 - 1\right) \times \exp\left[c_2^k\left(\left(\lambda^k\right)^2 - 1\right)^2\right]\sin^2\alpha^k\right\}, \tag{7}$$

$$\sigma_z = c\lambda_z^2 + \lambda_z^2 \sum_{k=1,2,3,4}\left\{c_1^k\left(\left(\lambda^k\right)^2 - 1\right) \times \exp\left[c_2^k\left(\left(\lambda^k\right)^2 - 1\right)^2\right]\cos^2\alpha^k\right\}. \tag{8}$$

Best-fit values of the material parameters were determined separately for each of these three constitutive models using a nonlinear regression (Nelder–Mead simplex method; in numerical recipes in *C*) of biaxial data from eight NT and nine HT specimens. This was accomplished using a modified fminsearch function (Matlab) to minimize the objective function (fitting error):

$$e = \sum_{i=1}^{N}\left[\left(\sigma_\theta^{\mathrm{Theory}} - \sigma_\theta^{\mathrm{Exp}}\right)_i^2 + \left(\sigma_z^{\mathrm{Theory}} - \sigma_z^{\mathrm{Exp}}\right)_i^2\right], \tag{9}$$

where N is the number of data points, and superscripts Theory and Exp denote theoretically calculated Eqs. (2 or 3) and experimentally determined Eq. (1) values, respectively. To contrast the goodness-of-fit by models having different numbers of material parameters, we computed two metrics: one is an error measure defined by Schulze-Bauer et al. (2003),

$$\varepsilon = \frac{1}{\sigma_{\mathrm{ref}}}\sqrt{\frac{e}{N-q}}, \tag{10}$$

where q is the number of material parameters and σ_{ref} is the average of the mean circumferential and axial Cauchy stresses at a selected physiological condition (e.g., $\lambda_\theta = 1.1$ and $\lambda_z = \lambda_{\mathrm{in\ situ}}$), and the other is the Akaike information criterion, or AIC (Akaike, 1974),

$$\mathrm{AIC} = N \ln\left(\frac{e}{N}\right) + 2q. \tag{11}$$

Smaller values of each of these two metrics indicate an overall better fit to data.

3. Results

All three models—Fung, Holzapfel, and 4-fiber family—fit the biaxial stress-stretch data (Table 1) well for both NT and HT. Nevertheless, the best overall fit was obtained using the 6-parameter, 4-fiber family relation ($\varepsilon = 104.13 \pm 85.92$, AIC $= 304.5 \pm 78.6$), while fits by the Fung ($\varepsilon = 221.55 \pm 184.27$, AIC $= 319.4 \pm 76.0$) and Holzapfel ($\varepsilon = 412.91 \pm 346.99$, AIC $= 339.8 \pm 85.4$) models were similar. For purposes of comparison, therefore, consider in detail the results for the Fung and the 4-fiber family models. The Fung model tended to overestimate slightly the circumferential stress and to underestimate slightly the axial stress whereas the 4-fiber family model tended to fit the data well in both directions (Fig. 1). Values of the material parameters and goodness-of-fit metrics are listed in Tables 2 and 3, respectively, for the Fung and 4-fiber family models. Based on the values of the

Table 1
Geometrical and structural data for each specimen (1–8 are NT and 9–17 HT)

Specimen	Treatment	$\bar{\lambda}_z$	A (μm)	a (μm)	h (μm)*	a/h**	Collagen (%)*
1	SC	1.16	242	352	36	9.65	20.4
2	SC	1.15	224	305	35	8.67	31.9
3	SC	1.14	264	329	32	10.25	21.7
4	2NT	1.13	246	324	34	9.64	23.1
5	2NT	1.19	296	396	37	10.79	22.6
6	4NT	1.22	238	320	31	10.44	17.1
7	4NT	1.15	288	379	36	10.58	31.2
8	6NT	1.22	250	333	26	12.99	25.5
Mean	NT	1.17	256	342	34	10.38	24.2
9	2HT	1.17	284	330	44	7.47	26.4
10	2HT	1.24	242	321	29	10.96	28.7
11	2HT	1.15	306	349	63	5.53	31.7
12	2HT	1.16	274	306	43	7.12	29.8
13	4HT	1.18	256	284	41	6.94	34.1
14	6HT	1.11	244	306	40	7.58	35.5
15	6HT	1.25	278	315	41	7.69	43.1
16	8HT	1.21	312	370	55	6.69	36.1
17	8HT	1.17	300	343	53	6.49	33.7
Mean	HT	1.18	277	324	45	7.39	33.2

Note: a, h, and a/h were calculated at 80 mmHg for NT and 120 mmHg for HT based on the unloaded dimensions and their mechanical properties. The associated values of the mean circumferential stress (~110–120 kPa) are comparable to those reported in Walmsely et al. (1983). A is the unloaded inner radius. SC denotes surgical control, 2NT 2-week normotension, 2HT 2-week hypertension, and so forth. Finally, the * and ** indicate that NT and HT groups were significantly different (Student's t-test) with p-values <0.01 and <0.001, respectively.