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Quantification of regional differences in aortic stiffness in the aging human

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ABSTRACT

There has been a growing awareness over the past decade that stiffening of the aorta, and its attendant effects on hemodynamics, is both an indicator and initiator of diverse cardiovascular, neurovascular, and renovascular diseases. Although different clinical metrics of arterial stiffness have been proposed and found useful in particular situations, there remains a need to understand better the complex interactions between evolving aortic stiffness and the hemodynamics. Computational fluid–solid-interaction (FSI) models are amongst the most promising means to understand such interactions for one can parametrically examine effects of regional variations in material properties and arterial geometry on local and systemic blood pressure and flow. Such models will not only increase our understanding, they will also serve as important steps towards the development of fluid–solid-growth (FSG) models that can further examine interactions between the evolving wall mechanics and hemodynamics that lead to arterial adaptations or disease progression over long periods. In this paper, we present a consistent quantification and comparison of regional nonlinear biaxial mechanical properties of the human aorta based on 19 data sets available in the literature and we calculate associated values of linearized stiffness over the cardiac cycle that are useful for initial large-scale FSI and FSG simulations. It is shown, however, that there is considerable variability amongst the available data and consequently that there is a pressing need for more standardized biaxial testing of the human aorta to collect data as a function of both location and age, particularly for young healthy individuals who serve as essential controls.

1. Introduction

A healthy aorta augments left ventricular function by distending during systole and recoiling elastically during diastole. That is, a distensible aorta reduces systolic pressure, and thus workload on the heart, and it enhances diastolic pressure, and thus coronary perfusion (e.g., O'Rourke and Hashimoto, 2007; Boutouyrie et al., 2008). In contrast, a stiffened aorta propagates the pulse pressure wave faster and farther, which adversely affects the heart, because reflected waves return earlier in the cardiac cycle and increase central artery pulse pressure, and likewise the brain and kidneys, because of increased pulsatility within

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the cerebral and renal microvasculatures (e.g., Adji et al., 2010). Given the importance of quantifying aortic stiffness and its attendant effects on the hemodynamics, it should not be surprising that diverse clinically inferable quantities have been identified, including the pressure–strain modulus (E_p), distensibility (D), central pulse pressure (cPP), augmentation index (AI_x), pulse wave velocity (PWV), and the amplitude of the backward traveling pressure wave (P_b)—see, for example, Agabiti-Rosei et al. (2007), Najjar et al. (2008), Avolio et al. (2009), Adji et al. (2010), McEniery et al. (2007), Redheuil et al. (2010), and Wang et al. (2010).

Notwithstanding arguments that particular metrics are better than others, especially for certain age groups (cf. Barodka et al., 2011), the carotid-to-femoral pulse wave velocity (CF-PWV) has tended to find the most favor clinically; indeed, it is sometimes referred to as the "gold standard" for measurement of arterial stiffness (Lacolley et al., 2009; Boutouyrie et al., 2010). Although CF-PWV is simply an empirical metric, the Moens–Korteweg equation ($c=\sqrt{Eh/2\rho a}$, where c is wave speed, E the Young's modulus of isotropic linear elasticity, ρ the mass density of the blood, and a and h the inner radius and thickness of the wall) is often cited to appropriately emphasize the fundamental importance of both arterial geometry (radius and thickness) and intrinsic physical properties (material stiffness and density) on wave propagation. Nevertheless, this simple equation is based on many assumptions that do not apply over the aorta and iliac artery that span the distance from the carotid to the femoral arteries. Namely, one cannot assume a uniform radius and wall thickness or a uniform, isotropic, linear material behavior under small strains. There is, therefore, a pressing need to understand more rigorously the roles of spatial and temporal changes in arterial geometry and material properties on pulse wave propagation as well as other postulated clinical metrics of arterial stiffening. Because of the associated geometric and material complexities, one must resort to computational models for such understanding and use appropriate methods from nonlinear mechanics.

Fortunately, advances in medical imaging and computational mechanics now enable patient-specific anatomical models for simulating the hemodynamics within large segments of a deformable vasculature tree (cf. Coogan et al., 2012; Xiao et al., 2013). These models remain limited, however, due to the continuing lack of information on potential regional variations in anisotropic wall properties and changes therein due to genetic mutations, exercise, aging, disease, and so forth. The goals of this paper, therefore, are twofold: first, to mine and compare information from the literature on the material properties of non-atherosclerotic human aorta as a function of location and age, and second, to present a consistent representation of these data via an appropriate linearization of a single nonlinear, anisotropic constitutive descriptor of the aortic wall. Finally, we also calculate the associated distensibility for comparison to data that have been reported based on clinical measurements. We conclude that, although considerable information is available, much more consistently and rigorously collected biaxial data are needed, particularly for young, healthy aortas that serve as important controls in most modeling efforts.

2. Methods

2.1. Constitutive relation

The aortic wall exhibits a nonlinear mechanical behavior over finite strains, hence one must employ an appropriate theoretical framework (Humphrey, 2002). Amongst the many constitutive relations that have been proposed to describe the passive mechanical properties of the aorta, we employed a "four-fiber family" model that has been shown to describe well an extensive set of biaxial data for both human abdominal aortic aneurysms and aging of the human abdominal aorta (Ferruzzi et al., 2011a). Moreover, this four-fiber family model motivates relations that have been found useful in simulations of aneurysmal development from an initial non-aneurysmal abdominal aorta (cf. Wilson et al., 2012). This particular functional form is motivated by the assumption that the primary constituents that bear load under tension are an elastin-dominated amorphous matrix and multiple embedded families of locally parallel collagen fibers. Notwithstanding increasingly better data on site-specific collagen fiber orientations (Schriefl et al., 2012), the four-fiber family model can phenomenologically capture stress–stretch data that may be influenced by yet unquantified lateral cross-links, physical entanglements, and even passive smooth muscle contributions. It can be written in terms of a (pseudo) strain energy function W of the form

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

where c, c_1^k, and c_2^k are material parameters, I_c is the first invariant of the right Cauchy–Green tensor $\mathbf{C}$ (i.e., tr$\mathbf{C}$), and λ^k is the stretch experienced by the kth fiber family, which is oriented in direction $\mathbf{M}^k=[0,\ \sin\alpha_0^k,\cos\alpha_0^k]$ in an appropriate reference configuration (i.e., $\lambda^k=\sqrt{\mathbf{M}^k\cdot\mathbf{C}\mathbf{M}^k}$). We let $\alpha_0^1=0^\circ$ (axial family), $\alpha_0^2=90^\circ$ (circumferential family), and $\alpha_0^{3,4}=\pm\alpha_0$ (symmetric diagonal families), the last of which is thus a free parameter. It should be noted that families 3 and 4 are typically assumed to be mechanically equivalent, which in combination with the assumption of their symmetric orientations about the axial direction disallows twisting of the vessel due to pressurization.

2.2. Simulated biaxial data

Best-fit values of the eight model parameters (c, c_1^1, c_2^1, c_1^2, c_2^2, $c_1^{3,4}$, $c_2^{3,4}$, α_0) within Eq. (1) can be estimated using nonlinear regression, and such estimates are best found from data obtained via multiple biaxial stretching protocols (Humphrey, 2002). Moreover, when comparing results for different vessels or ages thereof, it is best to use data from the same protocols. Because data in the literature have been collected using different types of tests (e.g., uniaxial, equibiaxial, and non-equibiaxial stretching tests on excised strips or slabs of aorta as well as extension–distension tests on cylindrical specimens), we re-analyzed results from diverse studies wherein a nonlinear constitutive relation was reported with associated best-fit values of the material parameters. Specifically, based

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