Journal of Biomechanics 45 (2012) 805–814

Contents lists available at SciVerse ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Review

Mechanics, mechanobiology, and modeling of human abdominal aorta and aneurysms

J.D. Humphrey [a,*], G.A. Holzapfel [b,c]

[a] Department of Biomedical Engineering and Vascular Biology and Therapeutics Program, Malone Engineering Center, Yale University, New Haven, CT 06520-8260, USA
[b] Institute of Biomechanics, Graz University of Technology, Graz, Austria
[c] Department of Solid Mechanics, Royal Institute of Technology (KTH), Stockholm, Sweden

ARTICLE INFO

Article history:
Accepted 10 July 2011

Keywords:
Wall stress
Growth
Remodeling
Finite elements
Hemodynamics

ABSTRACT

Biomechanical factors play fundamental roles in the natural history of abdominal aortic aneurysms (AAAs) and their responses to treatment. Advances during the past two decades have increased our understanding of the mechanics and biology of the human abdominal aorta and AAAs, yet there remains a pressing need for considerable new data and resulting patient-specific computational models that can better describe the current status of a lesion and better predict the evolution of lesion geometry, composition, and material properties and thereby improve interventional planning. In this paper, we briefly review data on the structure and function of the human abdominal aorta and aneurysmal wall, past models of the mechanics, and recent growth and remodeling models. We conclude by identifying open problems that we hope will motivate studies to improve our computational modeling and thus general understanding of AAAs.

Contents

* Corresponding author. Tel.: +1 203 432 6428; fax: +1 203 432 0030.
E-mail address: jay.humphrey@yale.edu (J.D. Humphrey).

0021-9290/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2011.11.021

1. Introduction

Abdominal aortic aneurysms (AAAs) are focal, asymmetric dilatations of the infrarenal aortic wall. These lesions rupture when intramural mechanical stress exceeds strength and they are increasingly responsible for morbidity and mortality in our aging society. Wall stress is dictated by the evolving geometry, wall properties, and hemodynamic loads/perivascular boundary conditions, but clinical estimates of rupture potential, and thus interventional planning, continue to be based primarily on geometry. That is, intervention is typically advocated if the maximum diameter of the lesion reaches 5.0 cm in women or 5.5 cm in men, or if the maximal diameter increases more than 0.5–1 cm in one year (Lederle et al., 2002; Hans et al., 2005; Grootenboer et al., 2009). Yet, many smaller lesions rupture (e.g., 13% of those less than 5 cm) while larger lesions may not rupture over long periods (e.g., 54% of those over 7 cm)—see Vorp (2007). There is clearly a need for increased understanding (cf. Wassef et al., 2007).

Although wall stress has been shown to predict rupture better than does maximum diameter (Fillinger et al., 2002, 2007), we must develop computational models that exploit our increasing understanding of the underlying mechanobiology and pathophysiology. That is, most models have employed classical continuum mechanics and have only used advances in medical imaging to define patient-specific lesion geometries. Without accounting for the biochemomechanics, such models cannot be expected to predict either the time course of enlargement or the likelihood of rupture. The goal of this paper is to review our current understanding of AAA mechanics and mechanobiology and to identify specific needs for improving patient-specific modeling.

2. Background

2.1. Risk factors

Primary risk factors associated with AAAs are male gender, aging, cigarette smoking, and hypertension, but other factors can include atherosclerosis, prior surgery (e.g., lower limb amputation), spinal cord injury, and genetics (Choke et al., 2005; Sakalihasan et al., 2005). Noting that amputation and spinal cord injury alter the hemodynamics within the infrarenal aorta and tend to increase the incidence of AAAs suggests further the importance of the mechanics and mechanobiology (Dua and Dalman, 2010).

Reasons for gender-related differences remain unclear, but older (over 65) men are $\sim 6\times$ more likely than older women to have an AAA while older women having an AAA are ~ 3–$4\times$ more likely to experience a rupture (Grootenboer et al., 2009). There is a similar dearth of information on the effects of cigarette smoking on the aortic wall (Enevoldsen et al., 2011), yet smoking is perhaps the most potent controllable risk factor (increasing risk up to $7\times$). Like aging (Table 1), hypertension tends to increase the caliber and stiffness of the aorta (O'Rourke and Hashimoto, 2007; Lakatta et al., 2009). It is thus important to remember when modeling AAAs that these lesions typically arise from aged vessels in the presence of co-morbidities that alter wall properties and thereby can affect subsequent aneurysmal dilatation (Watton et al., 2009a; Wilson et al., submitted for publication). See Humphrey (2002) and Holzapfel and Ogden (2010a) for reviews of constitutive relations for arterial behavior in health and disease.

2.2. Abdominal aorta

AAAs occur primarily in the infrarenal aorta, which is delimited by the renal arteries and the aorto-iliac bifurcation. The normal human infrarenal aorta is approximately 12 cm long, 2 cm in diameter, and 0.2 cm in thickness (Table 2). Because the renal arteries take $\sim$19% of total cardiac output (cf. 13% by cerebral arteries and 4% by coronary arteries; Milnor, 1990), volumetric blood flow is less in the infrarenal than in the suprarenal aorta—this explains, in part, its smaller diameter and thinner wall (cf. Collins et al., 2011). Hemodynamic studies suggest that the infrarenal aorta experiences reversed flow (and thus oscillatory wall shear stress), which may contribute to its susceptibility to aneurysmal dilatation (Amirbekian et al., 2009). Classified as an elastic artery, the young healthy infrarenal aorta consists of a thin intima, layered media containing abundant smooth muscle cells, proteoglycans, and collagen organized within $\sim$30 concentric elastic lamellae, and collagen-rich adventitia. The lower number of elastic lamellae than expected of a vessel of its size may also contribute to its susceptibility to aneurysmal dilatation (Wolinsky and Glagov, 1969). Likely because of perivascular support from the spine and adjacent tissue, the normal aorta is thinner along its posterior aspect than its anterior aspect. Nevertheless, cyclic wall strain is greater along the anterior surface, which, along with the presence of the posterior support, may contribute further to the susceptibility of the antero-lateral surface to dilatation (Goergen et al., 2007).

By dry weight, the normal infrarenal aorta consists of $\sim$40% collagen, 25% elastin, 20% vascular smooth muscle, and 15% ground substance (Table 2; He and Roach, 1994). Residual stresses, which are associated with marked three-dimensional deformations best quantified in terms of stretch and curvature (Holzapfel et al., 2007; Holzapfel and Ogden, 2010b), and axial pre-stresses, which associate with significant axial pre-stretches (Humphrey et al., 2009), arise during development and are important determinants of wall mechanics; both change with aging and aneurysmal dilatation and must be accounted for in computational models. Although such modeling can be difficult for geometries other than cylindrical (cf. Humphrey, 2002), rule-of-mixture models may allow these stresses to be included naturally (Cardamone et al., 2009). Possible thickening and stiffening of the intima with age or disease, eventually occupying

Table 1
Clinical data showing effects of aging on the abdominal aorta. Noting that aneurysms develop in aged, diseased aorta, these effects likely influence greatly any subsequent response to injury or insult that leads to the development of an aneurysm. It appears that the diameter strain was defined as $(d_s-d_d)/d_d$, where d denotes luminal diameter and indices s and d denote systolic and diastolic. The metric of stiffness is the so-called in vivo pressure–strain modulus: $(P_s-P_d)d_d/(d_s-d_d)$, where P is luminal pressure.

Mean age (years)	Heart rate	Systolic pressure	Diastolic pressure	Systolic diameter	Diastolic diameter	Diameter strain	Stiffness (kPa)
25/25	62	117	70	17.0	15.6	0.094	69/40
46/–	62	134	79	18.0	17.4	0.056	144/–
60/55	61	133	80	20.2	19.5	0.030	220/104
71/71	62	143	77	21.1	20.6	0.028	337/140

Note: Age (years) and pressure–strain modulus (i.e., stiffness in kPa) are taken from two reports: Länne et al. (1992)/MacSweeney et al. (1992). All other data are from Länne et al. (1992). Note, too, that MacSweeney et al. report a stiffness of 313 kPa for AAAs, which is not very different from the stiffness reported by Länne et al. for the oldest group of aortas. Heart rate in bpm, pressure in mmHg, and diameter in mm.