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Predictive biomechanical analysis of ascending aortic aneurysm rupture potential

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ABSTRACT

Aortic aneurysm is a leading cause of death in adults, often taking lives without any premonitory signs or symptoms. Adverse clinical outcomes of aortic aneurysm are preventable by elective surgical repair; however, identifying at-risk individuals is difficult. The objective of this study was to perform a predictive biomechanical analysis of ascending aortic aneurysm (AsAA) tissue to assess rupture risk on a patient-specific level. AsAA tissues, obtained intra-operatively from 50 patients, were subjected to biaxial mechanical and uniaxial failure tests to obtain their passive elastic mechanical properties. A novel analytical method was developed to predict the AsAA pressure-diameter response as well as the aortic wall yield and failure responses. Our results indicated that the mean predicted AsAA diameter at rupture was 5.6 ± 0.7 cm, and the associated blood pressure to induce rupture was 579.4 ± 214.8 mmHg. Statistical analysis showed significant positive correlation between aneurysm tissue compliance and predicted risk of rupture, where patients with a pressure-strain modulus $\geqslant$100 kPa may be nearly twice as likely to experience rupture than patients with more compliant aortic tissue. The mechanical analysis of pre-dissection patient tissue properties established in this study could predict the "future" onset of yielding and rupture in AsAA patients. The analysis results implicate decreased tissue compliance as a risk factor for AsAA rupture. The presented methods may serve as a basis for the development of a pre-operative planning tool for AsAA evaluation, a tool currently unavailable.

1. Introduction

Aortic aneurysm is a leading cause of death of adults [1], often claiming lives without any premonitory signs or symptoms. Adverse clinical outcomes of aortic aneurysm are preventable by elective surgical repair; however, identifying at-risk individuals is difficult [2]. Currently the decision to repair an ascending aortic aneurysm (AsAA) lies predominantly on the aneurysm diameter: namely, patients with an AsAA dilated to 5.5 cm or greater are recommended for surgery [3,4]. However, the reliability of the diameter criterion to predict aneurysm rupture and dissection has been largely debated in the literature [3,5,6]. Ruptured AsAAs at diameters less than 4.5 cm have been documented [3].

Recent studies have shown that the peak vessel wall stress in abdominal aortic aneurysms may be a more reliable rupture criterion than the overall diameter, as the peak wall stress for ruptured aneurysms is about 60% higher than for non-ruptured [7,8]. In a study by Koullias et al. [4] the ascending aortic wall stress was estimated *in vivo*. They found that the aneurismal wall stress in a hypertensive patient with an AsAA 6 cm in diameter may exceed the strength of the tissue [4]. However, this conclusion may not be sufficient to assess rupture risk on a patient-specific level, because the AsAA tissue elastic properties and failure strength are different for each individual. The aortic tissue strength may be compromised by underlying microstructural changes brought on by aging [9,10], disease progression [11], or other factors [12,13]. Therefore, the patient-specific tissue strength and the aortic wall stress are both critical for assessing AsAA rupture potential.

In this study, we performed a biomechanical analysis of the passive AsAA tissue elastic properties and failure strength. A total of 50 AsAA patients were studied among 3 sub-groups: AsAA – patients without a bicuspid aortic valve (BAV) or bovine aortic arch (BAA) (n = 20), ASAA-BAV – patients with a BAV (n = 17), and ASAA-BAA – patients with BAA and without a BAV (n = 13). We developed a novel analytical method to characterize the experimental data and predict the *in vivo* failure criteria (aneurysm diameter and blood pressure) on a patient specific level. We focus on AsAA patients with concomitant BAV and BAA in this study, because BAV has long since been known as a risk factor of AsAA and dissection [14], and a recent study by the Yale Aortic Institute [15]

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suggests a link between BAA and dissection. The failure criteria for each patient group were compared to determine whether the presence of BAV or BAA elevates rupture risk in patients with AsAA.

The details of the experimental methods, data and results are presented in part 1 [16] of this study, while the focus of this paper (part 2) is the analytical methods and results to predict AsAA rupture risk in different patient groups.

2. Methods

2.1. Patient selection

AsAA tissue specimens were collected perioperative from 50 patients undergoing elective AsAA repair at Yale – New Haven hospital between December 2008 and September 2010 and stored fresh at −80 °C. Once the fresh frozen specimens were transported to our lab, the samples were cryopreserved [17] and stored at −80 °C until they could be tested (refer to Fig. 1 in [16]). The use of human tissues in this study was approved by the Research Compliance Office of the University of Connecticut. The 50 AsAA patients studied were divided among 3 sub-groups: AsAA – patients without a BAV or BAA ($n = 20$), AsAA-BAV – patients with a BAV ($n = 17$), and AsAA-BAA – patients with BAA and without a BAV ($n = 13$). The mean patient age was 58.2 ± 11.6 years and the ratio of male to female patients was 38:12. The following clinical data were provided for each patient: the systolic/diastolic blood pressure, age, gender, height, weight, aneurysm diameter, and presence of a BAV or a BAA. The AsAA diameter provided by the Yale Aortic Institute for each patient was assumed to correspond to the systolic condition, because the clinical practice is to record the largest diameter observed. The patient characteristics are summarized in Table 1.

2.2. Biomechanical testing

2.2.1. Planar biaxial mechanical test

The tissue specimens were defrosted via the published method [17] and inspected for the presence of calcification and evidence of prior dissection before undergoing mechanical testing. The biaxial tests were performed [16] according to the methods of Sacks and Sun [18]. Briefly, specimens were submerged in a bath of Ca^{2+}-free and glucose-free Tyrode solution (mM: NaCl 136.9, KCl 2.7, $MgCl_2$ 1.05, $NaHCO_3$ 11.9, $NaHPO_4$ 0.47, EGTA 2.0, and 0.1 M papaverine) at 37 °C for the duration of each test, which consisted of preconditioning for at least 40 continuous cycles followed by tension-controlled loading protocols at the following first Piola Kirchhoff tension, $\boldsymbol{\tau}$, ratios: $\tau_{11}:\tau_{22} = 0.75{:}1$, 0.5:1, 0.3:1, 0.1:1, 1:1, 1:0.75, 1:0.5, 1:0.3, and 1:0.1 (see Fig. 1a). An illustrative set of biaxial data is given in Fig. 1b–c for one specimen. For a more complete description of the biaxial mechanical testing, please refer to part 1 of this study [16].

2.2.2. Uniaxial tensile failure test

The uniaxial failure properties of the tissue specimens were also quantified in part 1 of this study [16]. Briefly, thin strips of tissue approximately 15 × 5 mm in size were cut along both the circumferential and longitudinal directions of the biaxial test specimens. Each strip of tissue was loaded to failure with a Tinius Olsen uniaxial test device (Horsham, PA). From the uniaxial test data, the yield (YT) and ultimate tension (UT) were determined for each specimen in each anatomical direction. The **YT** represents the points in the tension-strain curves where the slope decreases marking the elastic limits of the tissue, while the **UT** represents the highest tension values in each direction. Representative failure test data is presented for one AsAA patient in Fig. 2. Further details on the uniaxial tensile failure test can be found in [16].

2.3. Predictive modeling

2.3.1. Constitutive modeling of biaxial testing data

The AsAA tissue specimens were assumed to be anisotropic, incompressible, nonlinear hyperelastic materials. Therefore, the second Piola Kirchhoff stress ($\boldsymbol{S}$) can be expressed as

$$\boldsymbol{S} = \frac{\partial W}{\partial \boldsymbol{E}} \tag{1}$$

where $\boldsymbol{E}$ represents the Green-Lagrangian strain tensor and W is a strain energy function. The experimental data was fitted with the generalized Fung-type strain energy function [19] for the planar biaxial responses of soft biological tissues given by the following equations:

$$W = \frac{c}{2}(e^{Q} - 1), \tag{2}$$

$$Q = A_1E_{11}^2 + A_2E_{22}^2 + 2A_3E_{11}E_{22} + A_4E_{12}^2 + 2A_5E_{11}E_{12} + 2A_6E_{22}E_{12}, \tag{3}$$

where c and A_{1-6} are the material constants. The Cauchy stress tensor, $\boldsymbol{\sigma}$, can then be calculated by

$$\boldsymbol{\sigma} = J^{-1}\boldsymbol{F}\boldsymbol{S}\boldsymbol{F}^{T}, \tag{4}$$

where $\boldsymbol{F}$ is the deformation gradient and J is the determinant of $\boldsymbol{F}$. The tension tensor in the spatial description, $\boldsymbol{t}$, can be obtained by

$$\boldsymbol{t} = h\boldsymbol{\sigma}, \tag{5}$$

where h is the deformed tissue thickness.

To fit and extrapolate the 1:0.5 protocol biaxial testing data to higher loads, $\boldsymbol{F}$ was incremented, and $\boldsymbol{t}$ was determined for each increment through Eqs. (1)–(5).

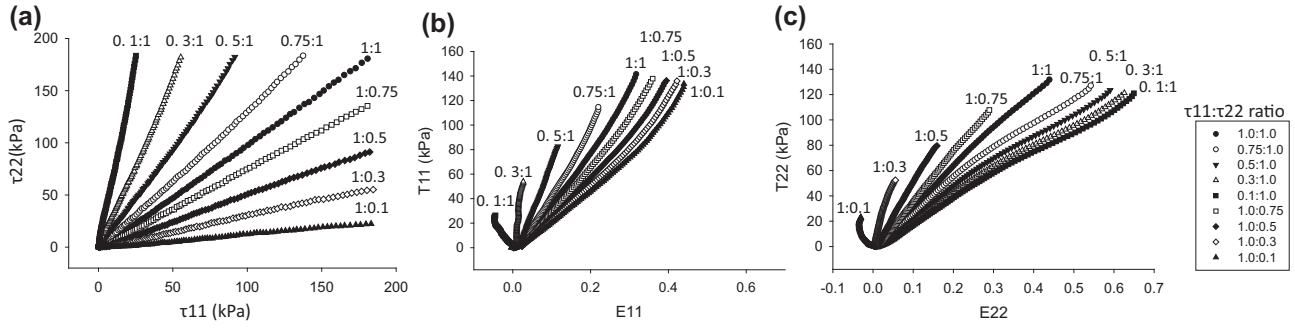

Fig. 1. (a) τ_{11} vs. τ_{22} plot, (b) τ_{11} vs. E11 plot, and (c) τ_{22} vs. E_{22} plot with all biaxial test protocols.

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