Biomechanical characterization of ascending aortic aneurysm with concomitant bicuspid aortic valve and bovine aortic arch

T. Pham\textsuperscript{a}, C. Martin\textsuperscript{a}, J. Elefteriades\textsuperscript{b}, W. Sun\textsuperscript{a,\ast}

Tissue Mechanics Laboratory, Biomedical Engineering Program and Mechanical Engineering Department, 207 Bronwell Building, University of Connecticut, Storrs, CT 06269-3139, USA

\textsuperscript{a} Aortic Institute at Yale-New Haven, Yale University, New Haven, CT 06510, USA

1. Introduction

Thoracic aorta aneurysms represent the 18th most common cause of death in adults [1]. Approximately 6–9% of people age 65 and older in the Western world have an aortic aneurysm [2]. There are a number of conditions that have been linked to aortic dilation, including Marfan syndrome, Loeys–Dietz syndrome, Ehlers–Danlos syndrome type IV, arterial tortuosity syndrome, autosomal dominant polycystic kidney disease and autosomal recessive cutis laxa type 1 [3]. In addition to these disorders, there appears to be a strong genetic link associated with aortic aneurysms, as up to 20% of patients referred for thoracic aortic aneurysm or dissection have family members with the same condition [1].

The development of ascending aortic aneurysms (AsAA) may also be linked to anatomical anomalies. It is well known that patients with a bicuspid aortic valve (BAV; a condition in which two of the three aortic leaflets fuse together) are more likely to develop AsAA than patients with a normal, tricuspid aortic valve. In the US, approximately four million people harbor a BAV, making BAV the most common congenital malformation [4]. Approximately 50% of BAV patients will develop an AsAA, and 5% will experience aortic dissection in their lifetime [5]. There is some debate on whether the high prevalence of AsAA in BAV patients is due to abnormal aortic hemodynamic stresses or intrinsic material property differences rendering the aortic wall weaker than in normal patients [6–8].

More recently, a link between “bovine aortic arch” (BAA) anatomy and thoracic aortic aneurysms has also been suggested [9]. In the majority of patients (74%), there are three great vessels branching from the aortic arch: the innominate artery, the left carotid
artery and the left subclavian artery [10]. However, there are many other possible anatomic configurations of the aortic arch, the most common being the BAA configuration, in which the innominate and the left carotid arteries originate from a common stem off the aortic arch [10]. Although BAA is generally thought to be a benign anatomic difference, recent research shows the incidence of BAA dissection is significantly higher among patients with AsAA than among the general population [9]. Again, it is unclear why BAA patients may be more susceptible to AsAA formation. This may be due to altered hemodynamics or possible innate aortic tissue property differences in these patients.

Rupture of the aortic wall is generally accepted as mechanical failure of the vessel due to a combination of excessive hemodynamic forces [3,11–13] and degeneration of the medial wall [6,8,14–17]. The microstructural components, mainly elastin, collagen fibers and smooth muscle cells (SMC) play an important role in maintaining proper structure and function of the aortic wall. Damage to the elastic fibers and aortic dilation might cause increased wall stiffness and stress. Eventually, acute aortic dissection and rupture can occur in response to certain dramatic events such as a spike in blood pressure during intense physical or emotional exertion [1]. Therefore, an understanding of the elastic properties and the microstructure of the vessel wall is important in predicting the risk of wall rupture.

Studies have shown that patients harboring BAV or BAA are more likely to develop AsAA than the general population, but a thorough quantification and comparison of the AsAA tissue properties for these patient groups, to the present authors’ knowledge, have not been reported in the literature. Such information may offer insight into the underlying mechanisms of AsAA development in these patients. Thus, the objective of this study was to investigate and compare the mechanical and microstructural properties of aortic tissues from AsAA patients with and without concomitant BAV or BAA.

2. Materials and methods

2.1. Clinical data and aortic specimens

Aortic specimens were obtained from a total of 55 patients who underwent elective AsAA surgery at Yale–New Haven Hospital between December 2008 and September 2010. Patients who experienced aortic dissection prior to surgery were excluded from the study. Upon perioperative harvest, the specimens were fresh frozen and stored in a −80 °C freezer. Once the tissue specimens were transported to the lab, they were cryopreserved [18] at −80 °C prior to mechanical testing. The use of human tissues in this study was approved by the Research Compliance Office of the University of Connecticut. The patients were divided into three groups: AsAA (patients without BAV or BAA (n = 20)); BAV (AsAA patients with BAV but without BAA (n = 20)); and BAA (AsAA patients without BAV but with BAA (n = 15)). The dilated aortic section from the patients was excised during surgery, from which a small sample size was removed and preserved in a −80 °C freezer, see Fig. 1. All samples were then transported to the laboratory and cryopreserved [18] at −80 °C until mechanical testing.

2.2. Mechanical tests

2.2.1. Planar biaxial mechanical test

Frozen samples were submerged in a 37 °C water bath until totally defrosted, following the two-stage slow thawing method to remove the cryopreserving agent [18]. The tissue thickness was measured at six regions with a thickness gauge (Mitutoyo, Model 7301), and the average value was recorded. Each specimen was then biaxially tested according to the methods previously presented [19]. Briefly, all specimens were trimmed into square specimens with a side length of ~20–25 mm and mounted in a trampoline fashion, with the specimen circumferential (CIRC) and longitudinal (LONG) directions aligned with the primary axes of the biaxial test fixture. All specimens were tested in a Ca²⁺-free and glucose-free Tyrode solution (mM: NaCl 136.9, KCl 2.7, MgCl₂ 1.05, NaHCO₃ 11.9, NaHPO₄ 0.47, EGTA 2.0 and papaverine 100.0) at 37 °C. A tension-controlled test protocol was used [20] and converted to the first Piola–Kirchhoff tension P, wherein the ratio of CIRC (11) to LONG (22), that is P₁₁:P₂₂ was kept constant with the shear terms P₁₂ = P₂₁ = 0. All specimens were stretched to a maximum membrane tension value of 120 N m⁻¹ (~300 g) [21], above which samples might be torn in biaxial testing experiments. Preconditioning was performed to minimize tissue hysteresis. Each tissue specimen was preconditioned for at least 40 continuous cycles with P₁₁:P₂₂ = 1:1. Seven successive protocols were performed using ratios P₁₁:P₂₂ = 1:0.3, 1:0.5, 1:0.75, 1:1, 1:0.75:1, 0.5:1 and 0.3:1. This range was chosen for extensive coverage of the in-plane stress state [20]. The in-plane Green strain tensor E was calculated from the deformation gradient F, using

\[ E = \frac{1}{2}(F^T F - I) \]

The extensibility of the samples was quantified by means of the secant modulus at both low (60 N m⁻¹) and high (120 N m⁻¹) membrane tension regions under the equibiaxial loading protocol (P₁₁:P₂₂ = 1:1). The extensibility of the samples was calculated via the areal strain equation, e = λ₁₁,maxλ₂₂,max−1, where λ₁₁,max and λ₂₂,max are the circumferential and longitudinal peak stretch values from the equibiaxial protocol, respectively. The degree of anisotropy (DA) was analyzed using the ratio of peak Green strains: DA = E₁₁,max/E₂₂,max. A DA value of 1 indicates an isotropic tissue response, whereas other values represent various degrees of anisotropy.

2.2.2. Uniaxial failure test

Following the biaxial test, each specimen was cut into strips ~15 × 5 mm in both the circumferential and longitudinal directions. In some cases, only one uniaxial specimen was prepared in either the circumferential or the longitudinal direction, because of limited tissue size. The specimens were tested using a Tinius Olsen uniaxial machine (Horsham, PA). The force and deformation in terms of stretch were measured continuously as the specimen was loaded to failure. The ultimate tensile strain (UTS) and strength (UTS) were determined from the maximum tension, which correlated with the complete rupture of the specimen.