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Research paper

Mechanics of the pulmonary valve in the aortic position

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ABSTRACT

Mathematical models can provide valuable information to assess and evaluate the mechanical behavior and remodeling of native tissue. A relevant example when studying collagen remodeling is the Ross procedure because it involves placing the pulmonary autograft in the more demanding aortic valve mechanical environment. The objective of this study was therefore to assess and evaluate the mechanical differences between the aortic valve and pulmonary valve and the remodeling that may occur in the pulmonary valve when placed in the aortic position. The results from biaxial tensile tests of pairs of human aortic and pulmonary valves were compared and used to determine the parameters of a structurally based constitutive model. Finite element analyzes were then performed to simulate the mechanical response of both valves to the aortic diastolic load. Additionally, remodeling laws were applied to assess the remodeling of the pulmonary valve leaflet to the new environment. The pulmonary valve showed to be more extensible and less anisotropic than the aortic valve. When exposed to aortic pressure, the pulmonary leaflet appeared to remodel by increasing its thickness and reorganizing its collagen fibers, rotating them toward the circumferential direction.

1. Introduction

The mechanical function of cardiovascular tissue is mainly determined by the extracellular matrix (ECM) composition and structure. The matrix defines the response of the tissue to mechanical load and can also remodel in response to changes in its environment. Thus, an improved understanding of the adaptation capabilities of cardiac valve ECM is essential for understanding both valve pathology and physiology and for designing materials for valve repair or replacement. Yet, the events and mechanisms by which the matrix remodels and adapts are largely unknown since the collagen architecture and the local mechanical loading condition within the tissue are highly coupled. Mathematical models can give insight in this interaction and in predicting the tissue's response and adaptation.

One particular case of a tissue undergoing a strong change in mechanical environment is the so called Ross procedure. The operation consists of replacing the aortic valve (AV) by the pulmonary autograft and the use of a homograft valve instead

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of the pulmonary valve (PV) (Ross, 1967). This procedure is particularly attractive for children, athletes and women of childbearing age because it eliminates the need for anticoagulation therapy and has the potential for somatic growth.

Usage of a pulmonary autograft has several advantages, in particular its ability to grow and its improved hemodynamics and durability (Elkins et al., 1994; Chambers et al., 1997; Santini et al., 1997). There are, however, potential disadvantages. In adults, the AV and PV are known to differ in morphology and structure, (Stradins et al., 2004; Vesely et al., 2000; Azadani et al., 2012; Hokken et al., 1997) and after pulmonary autograft replacement of the AV, the autograft is subjected to higher pressures. This mechanically more demanding environment may cause remodeling of the autograft. The valve explants show thickened leaflets and severe aneurysmal degeneration of the wall, which was characterized by intimal thickening, medial elastin fragmentation, and adventitial fibrosis (Schoof et al., 2006; Mookhoek et al., 2010). Concern exists, that these structural and functional changes in the implanted autograft lead to progressive aortic root dilatation and neoaortic regurgitation.

Another limitation of the technique is the lack of long term results (Phillips, 2003; Kouchoukos, 2011). Some midterm studies however, reported freedom from autograft reoperation between 93% and 98.6% at 10 years (Rabkin-Aikawa et al., 2004; Favaloro et al., 2008; Elkins et al., 2008; Takkenberg et al., 2009). This range of values may be dependent on the technique employed, the surgeon and the patient group selected. Therefore uncertainty remains regarding the suitability of the autograft to potentially become a viable permanent replacement.

The objective of this study was therefore to assess and evaluate the mechanical differences between the AV and PV leaflets and the remodeling that may occur in the PV leaflets when placed in the aortic position. The mechanical properties of sets of PVs and AVs leaflets from the same donor were assessed and evaluated. Next, a structurally based model for collagenous cardiovascular tissues (Driessen et al., 2005) was applied to describe the mechanical behavior of the leaflets. Finite element analyzes (FEA) were performed to simulate the mechanical response of both leaflets to a transvalvular aortic pressure load. Last, the previous model extended with remodeling equations for the collagen angular fiber distribution (Driessen et al., 2008) was applied to study the remodeling of the PV leaflets when subjected to the aortic valve diastolic load.

2. Materials and methods

2.1. *Tissue preparation*

Five sets of human aortic and pulmonary heart valves from patients 11 to 51 years (mean 31.8±16.1 years) of age were obtained from Dutch postmortem donors, giving permission for research. The valves, which were assessed to be unfit for implantation, were obtained from the Heart Valve Bank (Erasmus University Medical Center, Rotterdam, The Netherlands). All valves were structurally and mechanically unaffected. Previous studies suggest that the study of tissue (mechanical) properties can be done in cryopreserved heart valves since the structural integrity of collagen and elastin (Gerson et al., 2009) and mechanical properties (Virues Delgadillo et al., 2010) are not affected by the applied cryopreservation protocol. Furthermore, valvular disease or conditions known to precede valvular disease were not related to the cause of dead of the donors.

The cryopreserved valves were stored at −80 °C. Prior to the ECM analysis and mechanical testing, the valves were thawed according to the guidelines of the Dutch Heart Valve Bank. Briefly, the package containing the cryopreserved homograft was gently agitated in warm saline (±40 °C) to dissolve ice-crystals and soften the graft. After thawing, the package containing the valve was opened and deposited in phosphate buffered saline (PBS; Sigma-Aldrich, St. Louis, USA) to allow dimethyl sulfoxide (DMSO) to dilute from the tissue into the solution. Immediately after thawing, the cusps were carefully excised from the intact heart valves, using a scalpel. The specimens were cut in a square shape, using parallel razor blades ($n=21$ for the AV leaflets and $n=26$ for the PV leaflets, with n being the sample size). Each specimen had a dimension of 6×6 mm and its edges were aligned with the circumferential and radial axes. Mechanical testing was performed within 48 h after thawing. The leaflet specimen thickness distribution was obtained using a SensoFar PLμ 2300 optical imaging profiler (SensoFar-Tech, Barcelona, Spain) and the average thickness of each sample was measured.

2.2. *Experimental protocol*

The specimens were placed in aluminium foil and kept hydrated. The specimens were then mounted in a Bio-Tester 5000 test device (CellScale, Canada) using a BioRakes mounting system with pins with 0.7 mm tine space. These BioRakes had neglecting values of force due to pin deflection for stretches lower than 200%. To produce visual surface texture, the tissue was sprinkled with graphite particles. The samples were then tested while submersed in phosphate buffered saline (PBS) to mimic natural conditions.

The samples were biaxially tested to peak values ϵ_{CC} and ϵ_{RR}, where subscripts C and R correspond to the circumferential and radial directions, respectively. The complete biaxial testing regime consisted of 6 groups of 5 protocols. The first group of protocols of strain ratios was defined as $\epsilon_{CC}:\epsilon_{RR}=0:60, 11.5:55, 23:23, 24:11.5, 25:0(\%)$. The strains were then sequentially increased during the next 5 group of protocols in steps of 5% or 10% until the last group $\epsilon_{CC}:\epsilon_{RR}=0:110, 49:105, 78:78, 79:49, 80:0(\%)$ was performed. Preliminary studies showed that this particular biaxial stretch ratio could capture the nonlinear mechanical behavior of the heart valve leaflets without damaging the tissue and taking into account inter patient variability. The samples were left to recover for 1 min between protocols. Due to their viscoelastic properties (Lee et al., 1984), the specimens were preconditioned, before each group of protocols, for 10 contiguous cycles first to the maximum ϵ_{CC} and then to the maximum ϵ_{RR} of the group. The strain rate in the radial and circumferential direction was defined as l_0/min, with l_0 being the sample edge length. As the specimens were stretched, images were captured using a 1280×960 pixel charge-coupled device (CCD) camera at a sampling frequency of 5 Hz. The group of protocols that more closely achieved the valve working tension