Evolution of structure-function properties in human aortic and pulmonary valves

Evolution of Structure-Function Properties in Human Aortic and Pulmonary Valves

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Introduction

Although valvulogenesis and tissue morphogenesis of semilunar heart valves have been extensively studied (Fig 1), the evolution of structure-function properties with maturation remains largely unexplored in human valves.

Therefore, the **objective** of this study is to quantify tissue mechanical properties, extracellular matrix (ECM) composition, architecture and maturation of human aortic and pulmonary valves in different age groups to study valve remodeling with time and to provide target values for future therapies like tissue engineering.

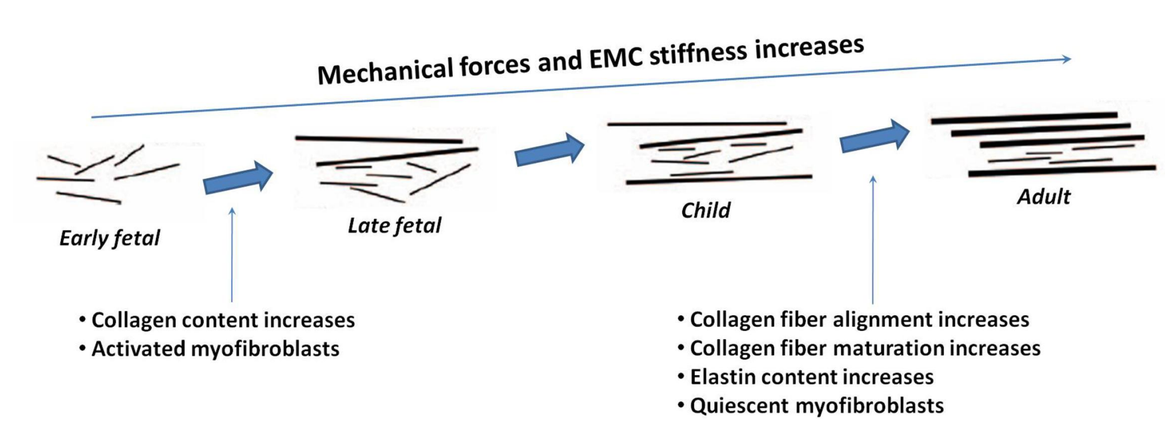

Figure 1. *Adapted from Aikawa et al, 2006 [1] and Merryman, 2009 [2]. During the fetal development the myofibroblasts have an acitivated phenotype to remodel the tissue in a functioning valve. After birth, the cells become more quiescent and are accompanied by maturation of the collagen (by fiber thickness and alignment) and increasing ECM stiffness.*

Methods

Up to now, 7 sets of structurally and mechanically unaffected human aortic and pulmonary valves, rejected for transplantation purposes, were obtained from Dutch donors, who gave permission for research. The valves were assigned into 3 groups (*child* [4 yr], *adolescent* [17–23 yr], and *adult* [40-55 yr]) to study valve maturation. ECM composition and organization were analyzed quantitatively from biochemical assays, and qualitatively by histology, immunofluorescence, and vital collagen staining. Mechanical properties were obtained from biaxial tensile tests and indentation tests to mechanically probe specific areas of the valve leaflets.

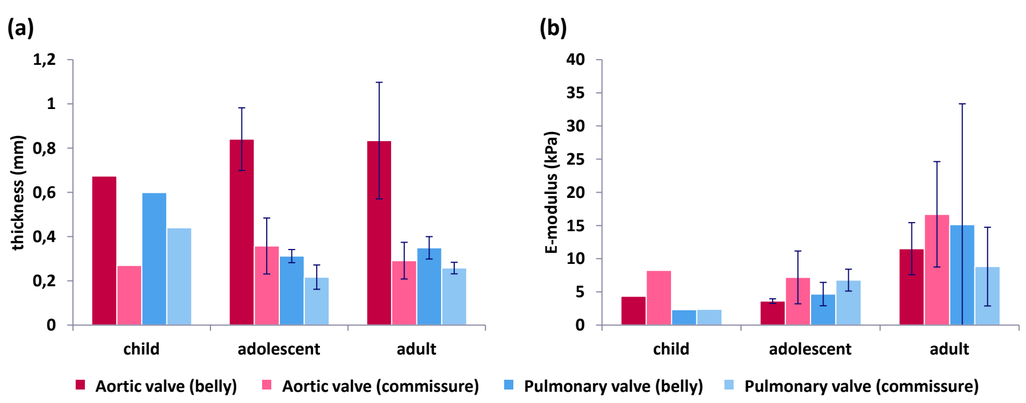

Figure 2. *Thickness (a) and Elastic modulus (b) as measured by indentation.*

Results

This data set shows variations between aortic and pulmonary valves, but also within the valves. The aortic valve belly is thicker than the commissure (Fig 2a). The Elastic modulus increases with age, with notably more variation in the adult valves (Fig 2b). With respect to the ECM properties, a trend of age-related changes was observed (Fig 3 and 4), including a decreasing GAG content and increasing collagen content with age. These changes were more apparent for aortic valves then for pulmonary valves.

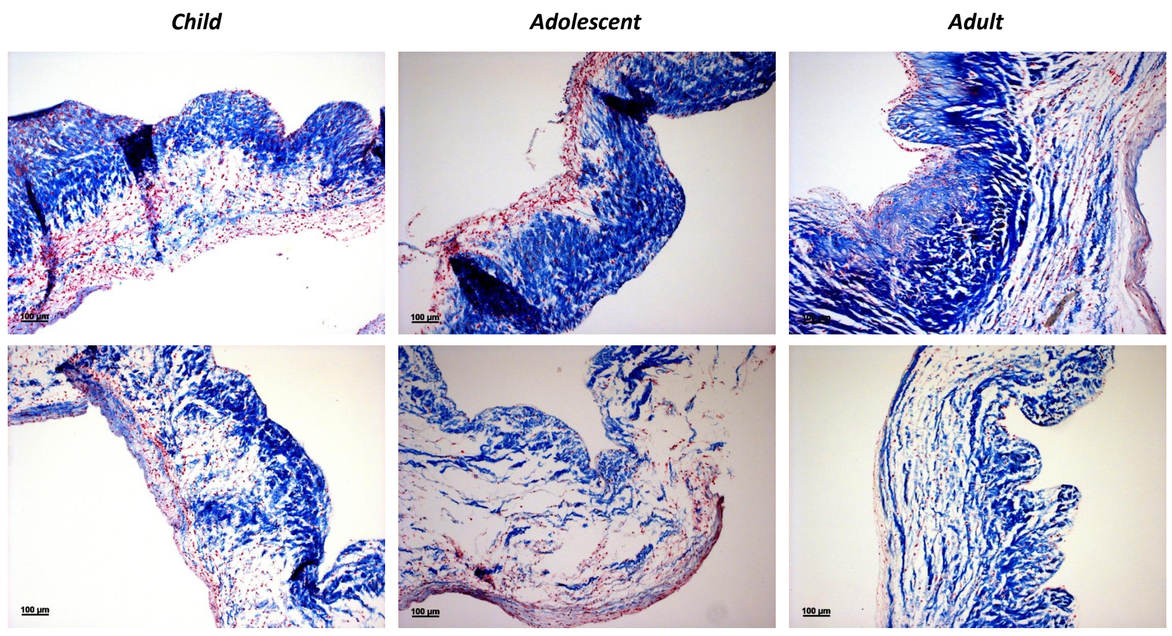

Figure 3. *Masson trichrome straining of aortic (top) and pulmonary valves (bottom). The layered structure is observed in all age groups. Collagen content and maturity are increasing with age, while cell number is decreasing.*

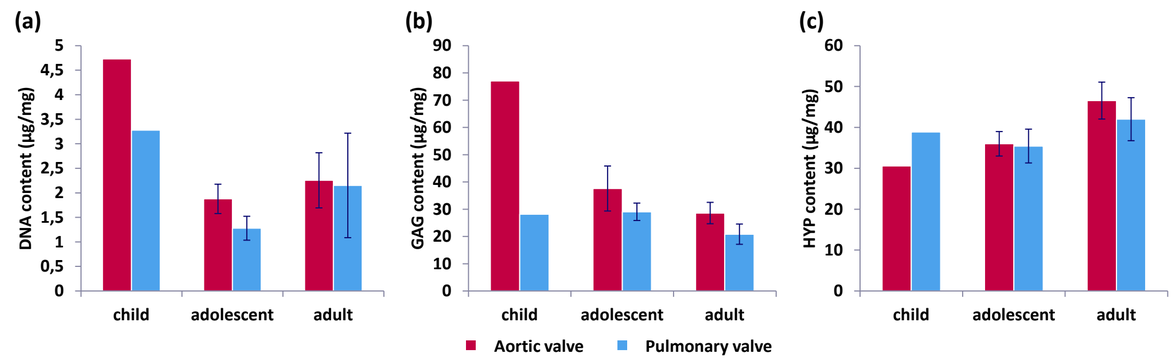

Figure 4. *ECM composition of the aortic and pulmonary valves is analyzed by measuring DNA -(a), glycosaminoglycan- (b), and hydroxyproline content (c).*

Conclusion

The ECM of the aortic valve remodels with age with a decreasing GAG content and increasing collagen content. In addition to this remodeling, an inter-subject variation in valve properties was observed within age groups. The latter variation is also observed in tissue engineered heart valves prepared in our group using cells from different donors [3]. The obtained results might be used to identify target properties for tissue engineered heart valves and to optimize these protocols.

/ Soft Tissue Biomechanics & Engineering

References
[1] Aikawa E. et al. Circulation 2006;113:1344-1352
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