THE AORTIC ROOT-VALVE DYNAMIC FIBROSTRUCTURAL INTERRELATIONS

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Rezumat

Obiectiv: Studiu imunohistochimic al complexului interjoncțional ventriculo-aorto-valvar și relevanța dinamică a acestora.

Material și metodă: Secțiuni seriate obținute din teritoriul cardiac investigat au fost prelucrate de rutină, fiind colorate cu metoda tricrom pentru evidențierea fibrelor colagene și elastice. Celulele interstițiale valvare au fost marcate imunohistochimic folosind markerii SMA-ab1 și vimentină. Reacția a fost detectată cu ajutorul UltraVision Labeled Polymer System.

Rezultate: Joncțiunea ventriculo-aortică are o constituție musculo-fibroasă circulară în jurul anulusului clinic. Fasciculele de ancorare ale rădăcinii aortei la ventricul sunt benzi conjunctive dense și triunghiurile intervalvulare. Valvulele sunt atașate de media peretelui aortic prin fibrospongioasa acestuia, având un traiect recurbat cu arhitectură tipică.

Concluzii: Legăturile dintre rădăcina aortei și valvă reflectă transferarea forțelor tensionale și stresurilor valvulare la peretele compliant al aortei. Celulele interstițiale valvare, miofibroblastele, au rol mechanosenzitiv, sunt activate de către semnalele factorilor de creștere, adaptând fibrele conjunctive pentru remodelare mechanostructurală.

Cuvinte cheie: aorto-valvar, fibrostructură

The aortic root valve dynamic fibrostructural interrelations

Abstract

Objective: Immunohistochemical study of the left ventricle-aortic root and valvar junction complex and its relevant dynamics.

Material and method: Serial sections of cardiac samples have been performed using usual histological procedures and stained with trichrome technique in order to evaluate collagen and elastic fibers. The valvar interstitial cells were immunohistochemically marked using SMA and vimentin antibodies, visualized by UltraVision Labeled Polymer System.

Results: The ventriculo-aortic junction is a musculo-fibrous circle surrounding the clinical annulus. The interposed dense connective bundles and interfoliate triangles anchor the aortic root to the outflow tract of the aortic ostium. The valvular leaflets

have a fibro-spongious core turning into the middle layer of the aortic root. The structure of the fibrous layer support has a typical mechanical architecture.
Conclusions: The bindings between the aortic root and valve reflect the valvular loads and tensile forces to the compliant aortic root. The valvar interstitial cells, mechanoreceptive myofibroblasts, are activated by transforming growth factor signals in the process of adaptation of fiber orientation during junction remodeling.

Keywords: aorto-valvar, fibrostructure,

Introduction

The aortic root is a clinical definition and demarcation of the left ventricular outflow tract and the aortic bulbo-sinus continuity. The components of the aortic root form a complex unit and frame the ventricular aortic ostium, the trifoliate valve and its supporting structures, and the controversial "mythic anulus". (1)

The aortic valve joins the root in a crown-like fashion and not in a ring-shaped fibrous structure. The components of the valvar support system are positioned spatially between two main hinge lines or virtual circles: (2)

• The apex of the leaflets (the top of the crown) is attached to commissures which suspend them and with their fibrous core they join the media of the aortic root's wall. Above the commissures there are the aortic ridge and the sino-tubular junction (STJ).

• The basal attachment of leaflets are semilunar sleeves borders crossing the ventriculo-aortic junction (VAJ) and surrounding the ventricular aortic orifice constituting the clinical anulus (annulus).

The aortic anulus and its components are dynamic structures in aspects of circulatory correlations, the cardiac cycle, transvalvular hemodynamic forces and tensile stresses.

As part of the cardiac cycle, the aortic valve guarding the anulus performs about 3 billion openings and closures during an expected lifetime. (3, 4) At end-diastole the leaflets are exposed to considerable mechanical pressure, to bending forces, with highest loading at their basal attachment. The valvular sinuses reduce the stresses of the leaflets by fluid dynamics. (18)

The key structure of the aortic root and valvar functions is the ventriculo-aorto-valvar junctional complex, an interposed fibrous connective territory with important clinical connotations.

Aim of the study

To investigate the fibrostructure of the subvalvular junction using immunohistochemistry, and to make correlations with dynamics of the area.

Material and methods

The connecting left ventricular-proximal aortic parts were excised from dissected normal hearts, and after routine histological processing 5 µm thick sections were obtained. The sections were dewaxed and rehydrated using routine processing (xylene, alcohol).

Histological stains were performed using the trichrome technique for collagen (Masson) and elastin (orcein). Immunohistochemical markers were used for labeling of smooth muscle cells and myofibroblasts (SMA-ab1), and mesenchymal cells (vimentin). Endogenous peroxidase blocking was performed, followed by antigen retrieval by pressurized steam cooking (citrate solution, pH=6). Monoclonal mouse antibodies were used (IA4, V9), the reaction was developed by diaminobenzidine, and this was followed by counterstaining with hematoxylin. For detection of primary antibodies UltraVision Labeled Polymer System (LabVision, Fremont, CA, USA) was used. The investigations were performed at the Department of Anatomy (UMPh Targu-Mures). (8)

Results

The structure of the interconnecting ensemble of the subaortic area should be approached in two regions: the ventriculo-aortic and the aorto-valvar joints. (Figure 1)

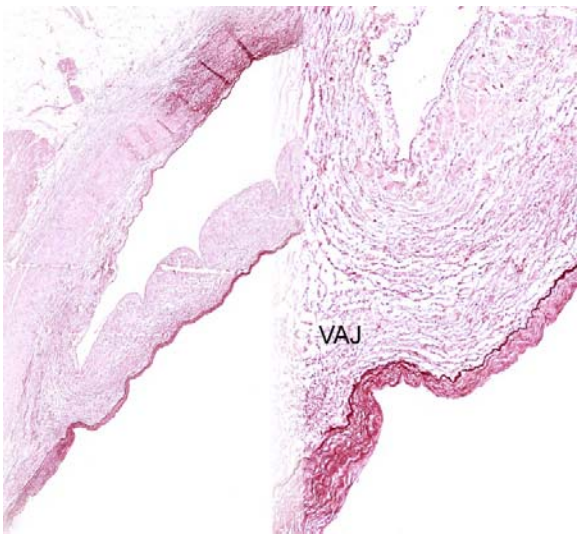

Figure 1 Ventriculo-aortio-valvar junctions

The VAJ is a circular musculo-fibrous junctional component surrounding the anulus. The medial quadrant is of interventricular septal origin, and the anterior quadrant is made up by lateral margin of risen intermyocardial fibrous fascicles of the left ventricle. The posterior parts are extensive fibrous body prolongations. (6)

The interposed fasteners are dense convergent fibrous tissue bundles in continuation of the intermyocardial connective tissue fascicles, guided to the aortic root medial wall layer, and in the proximal part they are smooth muscle rows – collagen fibrous structures intermingled with each other. The bundles join the aortic root to the ventricle in an anchoring wire aspect. (Figure 2)

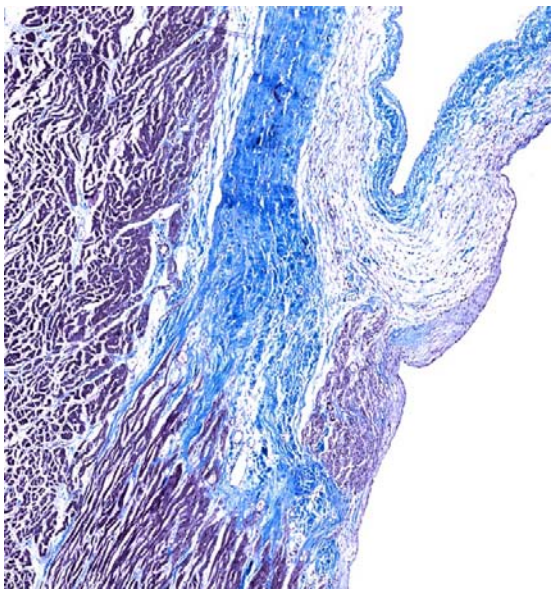

Figure 2 Ventriculo-aortic fibrostructure

The intervalvular triangles are three extensions of the basal ventricular attachment of leaflets, and tend to the commissures. The subcommissural collagen and elastic fibers are part of the medial aortic wall (ventriculus in aorta) with a binding role and a role in the swinging movement of the valvulae in diastole. As part of the valvar crown are upholding pillars for consolidation of the anulo-commissural distane. (7)

The attachment of arotic valve to VAJ is a peculiar junction. The leaflets enveloped by endothelium have an interposed trilaminar fibrosspongious core with arteriosa, spongiosa and ventricularis layers. (9)

The fibrosa of the aortic aspect is constituted of thick, large, undulated collagen fibers, lined up parallel to each other. These advancing to the aortic root form an infrasinusal hollow, and turn as radiating collagen fibers into the medial layer of it.

The spongiosa is loose connective tissue with thin and loose collagen fibers oriented to the aortic root, similar to arteriosa. This contains a rich extracellular matrix and valvar interstitial cells, labeled immunohistochemically as fibroblasts and myofibroblasts. (Figure 4)

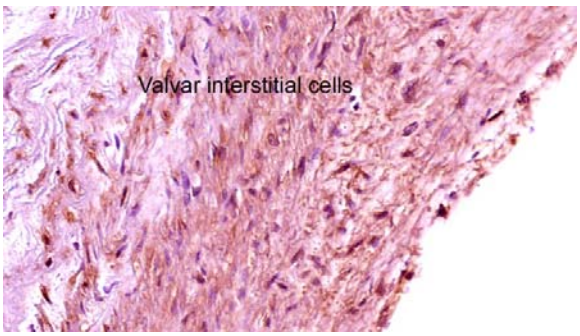

Figure 4 Valve interstitial cells

The ventricularis is a thinner layer with circumferential collagen and wavelike elastic fibers. The elastic fibers are detached from the spongiosa and progress to the muscular part of VAJ.
The nadir of the leaflets (aorta in ventriculus) are the hinge lines located below the VAJ. The collagen and elastic fiber constituents attached to myocardial fascicles ascend embossing as "culmen". (8, 10) (Figure 3)

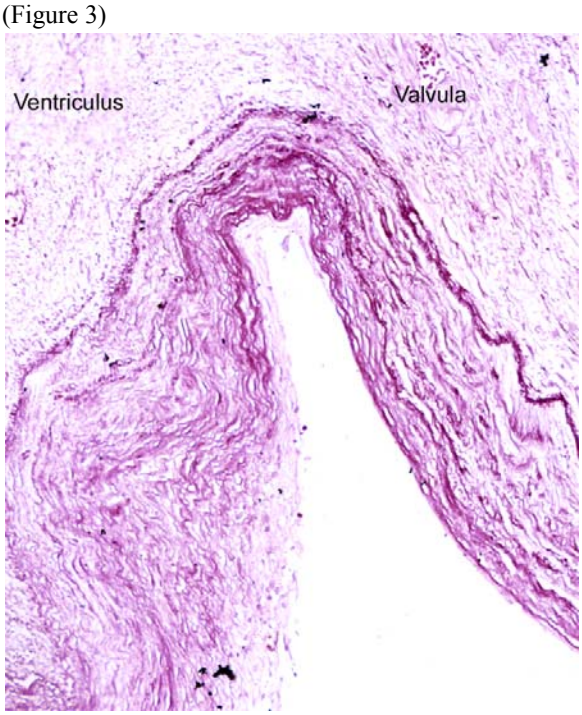

Figure 3 Valvular nadir, elastic culmen

Between the organized junctional connective structures there is an interposed loose cushion-like connective tissue atmosphere, allowing for adaptive motions of the aortic root, according to the cardiac cycle.

Comments

The ventricular ejection tract and aortic root have intricate conjunctival joining components related to the ventriculo-aortico-valvar junctions and the clinically defined anulus.
The binding of the aortic root to the left ventricle provide the connective tissue components originating from the aortic root, the anchoring bundles and subcommissural triangles in axial arrangement, with dynamic characteristics, imposing the geometrical change of shape and motions in accordance to the cardiac cycle and hemodynamics.
The junction between the VAJ and basal ring of the aortic valve has a characteristic mechanoadaptative fibrostructure, reflecting the valvar pressure and load transfer to the compliant aortic wall, for including these in their potential energy storage. (8, 11)
The spongious layer has mechanostructurally arranged collagen fibers. The gelatinous loose connective tissue and extracellular matrix act as shock absorbers and facilitate the adaptation of the leaflets during movement.
The elastic fibers of the ventriculosa of the leaflets and nadir head towards and attach to the myocardial segment of VAJ. The expansion and recoil of leaflets upon opening and closing movements are coherent with the ventricular cycle.
The extracellular matrix of the aortic valve has two types of resident cells, named commonly valvar interstitial cells (VIC), with fundamental role in fibroarchitectural mechanostructuralization and homeostasis of the leaflets.
The fibroblasts synthesize biomolecules of structural proteins, specialized anchor proteins and store growth factors.
The myofibroblasts (MFB) differentiated from fibroblast-like precursors, induced consecutively by valvar mechanical tension doe to hemodynamic strength forces, possess contractile capacity, mechanoresponsive features as mechanosensitive receptor and mechanotransductor, mechanical properties to regulate tissue remodeling and homeostasis. The rich expansions of MFBs called "stress fibers" extend between collagen bundles aligning them cytomechanically according to mechanical forces into an architectural assembly.
The signaling activator of MFBs is TGF-beta1 stored in the extracellular matrix, and released in response to mechanical stimuli and transducer pathways. (12, 13, 14)

The clinical importance of the valvulo-anular morphology in pathology is crucial. The imaging evaluation of anular diameters, the aortic size indices, and valve orifice areas (15) support the diagnose and establishment of surgical strategy. (16, 17)

Conclusions

1. The aortic root-valvar complex is a dynamic fibrostructure, interrelated with the ventriculo-aorto-valvar connective junctions and the clinical aortic anulus.
2. The arrangement of elastic and collagen fibers forms a mechanostrcuture that is aligned to the tensional and loading stresses and operating forces of the leaflets, supporting structures of valves and the aortic wall.
3. The adaptive mechanisms of the constituents are determined by the cardiac cycle and hemodynamics.
4. The mechanoreceptor and responsiveness properties are supported by valvar interstitial cells and signaled through transforming growth factor pathways.
5. The clinical importance of the valvo-anular unity and junctional complexes impose the morphometric imaging and surgical strategies.

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