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Collagen and Elastin Changes in Degenerative Diseases of Heart Valves

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Abstract: Degenerative diseases of heart valves (aortic stenosis, mitral valve prolapse and degenerative regurgitation) are widespread among the pathologies of the cardiovascular system, especially in elderly patients. The main morphological substrate of these diseases is the structural and functional changes in collagen and elastin fibers contained in the extracellular matrix of heart valves. Under normal conditions, collagen provides mechanical strength of the valve, while elastin maintains its elasticity and adaptability to hemodynamic loads. During the degenerative process, disorganization, hyperproduction and redistribution of collagen fibers, as well as fragmentation and degradation of elastic fibers are observed. These changes are closely related to the transition of fibroblasts to the myofibroblast phenotype, impaired activity of matrix metalloproteinases and activation of TGF-β signaling pathways. As a result, fibrosis, matrix remodeling and gradual calcification develop. Osteoblast-like differentiation of interstitial cells enhances the mineralization process. This article analyzes the normal histological structure of heart valves, the mechanisms of changes in collagen and elastin at the molecular level, and their hemodynamic consequences. The stages and clinical significance of the degenerative process are also highlighted from a morphological point of view. The results of the study provide a scientific basis for a deeper understanding of the pathogenesis of degenerative valvular diseases and the development of new therapeutic approaches.

Keywords: Heart Valve, Degenerative Disease, Collagen, Elastin, Extracellular Matrix, Fibrosis, Calcification, Valvular Stenosis, Microscopic Changes

Relevance of the Topic

Degenerative diseases of heart valves (especially aortic stenosis and mitral valve degeneration) are one of the most common structural pathologies in cardiology today. The frequency of these diseases is increasing with the aging of the population. The degenerative process can be subclinical for a long time, but progressive fibrosis and calcification lead to severe hemodynamic disturbances, heart failure, and the need for surgical intervention.

In recent years, it has been proven that degenerative valvular diseases are not a simple “aging process”, but a pathological remodeling that develops on the basis of active cellular and molecular mechanisms. In particular, structural remodeling of extracellular matrix components - collagen and elastin, impaired activity of matrix metalloproteinases (MMP), activation of TGF-β signaling pathways and osteoblast-like differentiation of interstitial cells are at the heart of the process. While disorganization of collagen fibers changes the mechanical strength of the valve, elastin fragmentation reduces its elastic properties. This disrupts the biomechanics of valve opening and closing. As a result, stenosis or regurgitation develops. Therefore, a deep study of the histological and molecular basis of degenerative valve diseases is of not only theoretical but also practical importance. Identifying matrix changes at early stages can serve to develop pharmacological targets in the future. This direction is scientifically promising, especially for specialists like you who are interested in cardiology and surgery.

Objective

The main goal of this study is to conduct a comprehensive analysis of histological, ultrastructural and molecular changes in collagen and elastin fibers in degenerative diseases of heart valves and to determine their role in pathogenesis.

To achieve this goal, the following tasks were set:

- ✓ Characterize the normal histological structure of heart valves and extracellular matrix components.

- ✓ Determine the change in the ratio of collagen types (I and III) in the degenerative process.
- ✓ Study the mechanisms of fragmentation and degradation of elastin fibers.
- ✓ Analyze the role of matrix metalloproteinases and TGF-β signaling pathways.
- ✓ Determine the step-by-step development of fibrosis and calcification processes.
- ✓ Assess the relationship between histological changes and clinical hemodynamic disorders. Also, the long-term goal of the study is to create a scientific basis for the development of new therapeutic strategies aimed at matrix remodeling in degenerative valvular diseases.

Main part

Degenerative diseases of heart valves are a complex and multi-stage pathomorphological process, the focus of which is a deep remodeling of the components of the extracellular matrix. Structural and functional changes in collagen and elastin fibers play a leading role in this process. Under normal conditions, heart valves operate under constant hemodynamic pressure, and adaptation to this pressure is ensured by a well-established histological structure of the valve tissue. At the initial stage of the degenerative process, microdamages occur in the endothelial layer covering the valve surface. These damages develop under the influence of mechanical stress, oxidative stress, and metabolic factors. As a result of the disruption of the endothelial barrier, inflammatory mediators are activated and valve interstitial cells are involved in the pathological process. At the next stage, valve interstitial cells switch to the fibroblast and myofibroblast phenotype. Collagen synthesis by these cells increases sharply. In particular, an increase in type I collagen leads to stiffening of the valve tissue. Collagen fibers are arranged irregularly, and their normal parallel orientation is disrupted. As a result, the fibrosis process develops in the valve tissue and the mechanical flexibility decreases. In elastin fibers, the degenerative process proceeds in the opposite direction. Fragmentation, disruption and disintegration of elastic fibers are observed. The decrease in elastin sharply reduces the elastic properties of the valves. This disrupts the mechanism of valve opening and closing, creating the basis for the development of regurgitation or stenosis. Elastin degradation, especially in the aortic valve, leads to severe hemodynamic consequences. An imbalance between matrix metalloproteinases and their inhibitors plays an important role in the reconstruction of the extracellular matrix. Although metalloproteinases control the breakdown of collagen and elastin, their excessive activity causes pathological remodeling. At the same time, the activation of TGF-β signaling pathways further enhances the fibrosis process. At the next stage of the degenerative process, calcification develops in the valve tissue. Valve interstitial cells switch to an osteoblast-like phenotype and increase the deposition of calcium salts. Calcification increases the stiffness of the valve and sharply limits its mobility. As a result, hemodynamic flow is seriously impaired and heart failure develops. Thus, increased collagen synthesis, elastin degradation, fibrosis and calcification processes develop in close interrelation and constitute the main pathomorphological basis of degenerative diseases of the heart valves.

Conclusion

Degenerative diseases of heart valves are a multi-stage, active pathomorphological process, which is based on the structural and functional reconstruction of extracellular matrix components - collagen and elastin fibers. Studies show that this pathology is not a result of simple "age-related wear", but a complex biological process associated with cellular activation, inflammatory mediators, signaling pathways and matrix remodeling.

In the degenerative process, excessive synthesis and disorganization of collagen fibers leads to stiffening of the valve tissue. Fragmentation of elastin fibers weakens the elastic and reversible properties of the valves. These changes disrupt the biomechanical function of the valve, resulting in the development of stenosis or regurgitation. At the next stage of the process, osteogenic differentiation of interstitial cells increases calcification, which sharply limits valve mobility.

Also, the interaction of matrix metalloproteinases, TGF-β signaling pathways and inflammatory mediators deepens the degenerative process. The imbalance between collagen and elastin disrupts the structural integrity of the valve tissue and leads to clinically severe hemodynamic consequences. Thus, the main pathogenetic mechanism in degenerative heart valve diseases is pathological remodeling of the extracellular matrix. A thorough study of these mechanisms will provide an important scientific basis

for early detection of the disease, development of pharmacological targets, and optimization of surgical interventions. In the future, molecular and immunohistochemical studies may serve to develop new treatment strategies in this direction.

REFERENCES

Robbins and Cotran Pathologic Basis of Disease. Kumar V., Abbas A.K., Aster J.C. Elsevier.
Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Zipes D.P., Libby P., Bonow R.O., Mann D.L., Tomaselli G.F. Elsevier.
Valvular Heart Disease. Otto C.M., Bonow R.O. Elsevier.
Textbook of Medical Physiology. Hall J.E. Elsevier.
Pathologic Physiology of Heart Disease. Lilly L.S. Wolters Kluwer.
Circulation Research — valvulyar kaltsifikatsiya va matriks remodelirovkasi bo'yicha maqolalar.
Journal of the American College of Cardiology — degenerativ klapan kasalliklari patogenezi bo'yicha ilmiy maqolalar.