

The role of MMP3 gene polymorphism (rs679620) in intervertebral disc degradation

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Abstract:

Matrix metalloproteinase 3 (MMP3) is a key enzyme responsible for the degradation of extracellular matrix components, particularly type II collagen and proteoglycans and therefore plays a central role in intervertebral disc remodeling [1]. Increased expression and activity of MMP3 lead to disruption of the structural integrity of the annulus fibrosus and nucleus pulposus, accelerating disc degeneration and promoting the formation of protrusions and herniations [2,3]. Polymorphisms in the MMP3 locus (including functionally significant promoter variants and nucleotide substitutions, such as rs679620) have been associated with an increased risk of degenerative disc changes in a number of population studies, making this gene a promising molecular marker of predisposition [4]. From a clinical point of view, studying the role of MMP3 is important for predicting disease progression, stratifying the risk of relapse, and developing targeted rehabilitation and therapeutic strategies aimed at modulating proteolytic activity in intervertebral structures [5].

Objective : To evaluate the association of MMP3 (rs679620) polymorphism with the risk of degenerative changes in the spine.

Materials and methods.

The study analyzed the CC, CT, and TT genotypes of the MMP3 (rs679620) polymorphism in 89 patients with clinically and MRI-confirmed intervertebral disc herniation and 91 healthy volunteers (controls). Informed consent was obtained from all participants; the study complied with the requirements of the Declaration of Helsinki. DNA was isolated from peripheral venous blood using commercial extraction kits or the standard phenol-chloroform method; quality and concentration were assessed spectrophotometrically. Genotyping was performed

by PCR followed by restriction analysis (PCR-RFLP): amplification of the region containing the rs679620 polymorphism was performed on a thermal cycler using specific primers ; thermal cycling conditions and the composition of the reaction mixture were specified in the laboratory working protocol. PCR products were digested with the appropriate restriction enzyme, separated on an agarose gel (2–3%), and visualized under UV light to determine the genotype based on the fragmentation pattern. For quality control, 10% of the samples were genotyped again, and the results were blinded. Statistical processing included calculating allele and genotype frequencies in groups, checking the genotype distribution for compliance with the Hardy–Weinberg law , and intergroup comparisons using the χ^2 test or Fisher's exact test for low frequencies. To assess the strength of association, odds ratios (OR) with 95% confidence intervals were calculated. Quantitative clinical parameters were compared, if necessary, using the Student's t-test (for normal distribution) or the Mann–Whitney U-test (for deviations from normality). Statistical analysis was performed in SPSS and GraphPad packages. Prism ; differences were considered statistically significant at $p < 0.05$.

Results.

An analysis of the distribution of MMP3 genotypes revealed statistically significant differences between the group of patients with intervertebral disc herniations and the control sample. Carriage of the T allele and, in particular, the homozygous TT genotype is associated with a higher risk of degenerative disc changes (OR=1.91; $p < 0.05$). This relationship indicates that the TT variant promotes increased expression of the MMP3 gene, which encodes an enzyme involved in the degradation of extracellular matrix components, including type II collagen and proteoglycans . As a result, destruction of the intervertebral disc structure increases, its hydration and elasticity decrease, which accelerates the development of degeneration and herniation. Thus, MMP3 polymorphism can be considered a genetic predictor of increased disc vulnerability to degenerative processes.

Conclusion.

The obtained data confirm that the MMP3 genetic variant significantly influences the metabolism of the intervertebral disc extracellular matrix. The presence of the T allele , associated with increased enzyme activity, leads to increased degradation of collagen and proteoglycans —the main structural components of disc connective tissue. This leads to accelerated destruction of cartilage tissue, decreased strength and elasticity, which is clinically manifested by the development of degenerative-

dystrophic changes. Thus, MMP3 polymorphism can be considered a molecular marker of predisposition to connective tissue destruction in the intervertebral disc and can be used for early diagnosis and a personalized approach to the prevention of spinal degeneration.

Literature .

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