

COMPREHENSIVE RADIATION DIAGNOSIS OF OSTEOARTHRISIS OF THE KNEE JOINT IN THE EARLY STAGES

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Abstract

Osteoarthritis (OA) is a chronic joint disease characterized by primary degeneration of articular cartilage, a change in the structure of subchondral bone with the formation of new bone structures (osteophytes), the development of an inflammatory process in the synovial membrane (synovitis) and damage to periarticular soft tissues.

According to modern concepts, OA has a multifactorial genesis, which is based on a violation of the balance of degradation and synthesis within articular cartilage and subchondral bone, which in turn leads to cartilage destruction and characteristic changes in subchondral bone. Among all degenerative joint diseases, OA accounts for 12.3%, i.e. it is slightly inferior to the entire group of inflammatory joint diseases, which currently accounts for 17.7%.

Keywords: osteoarthritis, metabolism of cartilage, T2 relaxometry, multiplex assay.

Introduction

Osteoarthritis (OA) affects 10-20% of the world's population, and in recent decades its prevalence in the population has been steadily increasing [1-5]. At the same time, in the structure of this disease, about 1/3 cases are OA with predominant localization in the knee joints [3]. According to the data of domestic and foreign researchers [6-8], the earliest detection of cartilage degeneration is a promising direction for the development of diagnostic and therapeutic approaches for OA. According to modern concepts, the pathogenesis of OA is based on auto-inflammation [1, 9].

In OA, cellular stress and degradation of the extracellular matrix (ECM) occur, and initially changes occur at the molecular level with subsequent morphological changes in all joint tissues, leading to anatomical and physiological disorders. M. A. Kabalyk and co-authors [9, 10] propose to isolate various molecular endotypes of OA, based on the systemic molecular response to stress: inflammatory, oxidative and mixed, which determines the clinical and structural manifestations of the disease. A number of authors note a strong correlation of inflammation with the severity of pain syndrome and functional disorders of the musculoskeletal system [11]. According to S. Vilá [12], there is also no doubt about the role of the mediator of acute and chronic inflammation IL-1 β



in the processes of apoptosis and cell proliferation in various molecular subtypes of OA. The main non-collagenic protein of the articular cartilage matrix is COMP, which is found not only in the articular cartilage, but also in some other tissues (ligaments, tendons, menisci, synovial membrane) [13]. Its main function in the connective tissue matrix is to stabilize the three-dimensional structure of collagen fibers. Increased amounts of SOMP are released from the cartilaginous matrix in a number of joint diseases of various etiologies and enter the bloodstream. This protein has a long period of circulation in the bloodstream, which makes it possible to use the level of SOMP in the blood as a marker reflecting changes in cartilage metabolism in joint pathology [14, 15].

The purpose of the study

To evaluate the possibilities of magnetic resonance imaging, including T2-relaxometry, in combination with laboratory studies of biological markers, in the diagnosis of hyaline cartilage pathology at the initial stages of knee joint OA.

Materials and methods

37 persons of both sexes aged 35-50 years (9 men and 28 women) were examined. Criteria for inclusion in the study: in the main group of individuals 1) the presence of complaints of periodic pain and discomfort in the knee joints when walking and exercising, 2) the duration of the anamnesis at least two years, 3) absence of any treatment (anti-inflammatory, chondroprotective, metabolic therapy, physio-functional treatment). The control group consisted of 20 people of the same age without clinical manifestations of joint diseases who had not received any medications at the time of the examination. The exclusion criteria were: oncological, cardiovascular, endocrine diseases, systemic connective tissue diseases, immunodeficiency conditions, severe injuries of the musculoskeletal system. All participants gave voluntary informed consent to a comprehensive clinical, laboratory, instrumental examination, which was conducted in compliance with the basic ethical principles of conducting medical research with human participation, set out in the Helsinki Declaration of the World Medical Association.

The intensity of joint pain in the subjects was objectified on a 100 mm visual analog scale. The functional status was assessed according to the Oxford Scale for studying the outcomes of injuries and osteoarthritis of the knee joint KOSS (Knee Injury and Osteoarthritis Outcome Score) by interviewing participants on 100 key questions characterizing the main aspects of life. Radiation diagnostic methods included radiography, ultrasound and magnetic resonance imaging of the knee joints. X-ray examination was performed in a direct projection with the maximum bent position of the knee joint and a lateral projection with flexion in the joint up to 15 ° in the supine position. Ultrasound of soft-tissue structures was performed using a Siemens-2000 device (Germany). Magnetic resonance (MR) examination was performed on a 1.5T magnetic field tomograph by the Echelon device (Hitachi, Japan) using pulse sequences: T1, T2, Pd with saturation of adipose tissue and T2 relaxation with color mapping (T2 Relax Map program).

Results

The gradation of pain on a visual analog scale in patients of the main group ranged from mild to moderate. The KOSS index in the control group was 98-100%, in the experimental group it ranged from 70 to 87%. According to the results of the questionnaire using the KOSS questionnaire, the patients of the main group practically did not experience pronounced discomfort in the knee joints



in everyday life, but noted some signs of functional failure under active loads. When conducting instrumental examination methods in 23 patients of the main group, the X-ray stage of OA was determined as 0-1, in the remaining 14 patients — as 1-2 (according to the classification of J. Lawrence and J. Kellgren). Ultrasound of the knee joints in 11 patients (30%) of the main group revealed the presence of only certain nonspecific changes: the presence of minimal severity of synovitis (thickening of the synovial membrane and a small amount of fluid in the joint cavity), signs of degenerative changes in hyaline cartilage and menisci in the form of heterogeneity of structure, moderate inflammatory changes in paraarticular tissues in the form of ligamentitis of collateral ligaments. In general, the standard instrumental research methods most often used in clinical practice — radiography and ultrasound — showed low information content in the initial degenerative changes of the knee joints.

Intact cartilage, which has normal morphological characteristics, conditionally corresponded to green in the images obtained using T2 Relax Map, while degeneratively altered cartilage corresponded to yellow, orange and red. On the color maps, the areas of the altered cartilage were more clearly visualized, which made it possible to clarify their anatomical and topographic location. In areas with degeneration and thinning of cartilage, chondromalacia, previously identified by the standard protocol of MR examination, changes in the T2 relaxation time were recorded, which may be due to structural changes in the proteoglycan-collagen matrix.

Laboratory studies showed that patients in the main group had an increased content of structural biopolymers of cartilage tissue ECM in biological fluids, as well as an increase in markers of inflammatory activity. Increased values of COMP in blood serum and an increase in daily losses of CTX-II fragments indicated an intensification of catabolic processes in complexly ordered ECM structures.

Based on the obtained laboratory data characterizing the severity of inflammatory manifestations in patients, all persons of the main group were conditionally divided into two subgroups: subgroup No. 1 — with obvious signs of inflammatory activity and subgroup No. 2 — patients with normal values of inflammatory markers. In patients with early manifestations of knee joint OA with signs of increased inflammatory activity, the presence of corresponding changes in the leukocyte formula, an increase in ESR, an increase in the content of IL-1 β , as well as the concentration of highly sensitive CRP were noted. It should be noted that in subgroup No. 1 of the main group there was a tendency to a more pronounced accumulation of the studied extracellular matrix degradation products in biological media. In order to establish significant relationships, a correlation analysis of the links between the indicators of cartilage tissue metabolism and the data of radiation research methods in early manifestations of OA was carried out. As a result, the correlation between the concentration of COMP and the digital data obtained by T2-relaxometry (y. E.), in the main group it was characterized ($p < 0.05$) as a positive strong ($R = 0.83$), between COMP and the thickness of articular hyaline cartilage (in mm) according to ultrasound data — as a negative medium-strength relationship ($R = -0.63$). Correlations of the same orientation, but with a lesser degree of severity, were revealed between the level of daily urinary excretion of CTX-II and the results of morphometry of articular hyaline cartilage according to T2 relaxometry and ultrasound ($R = 0.79$ and $R = -0.59$, respectively).



Discussion

The problem of early detection of OA at the preclinical stage or with minimal manifestations of pathological changes in joints remains relevant research areas, which is facilitated by the development of a wide range of ways to influence the remodeling of articular structures with degenerative and dystrophic changes: chondroprotective therapy, PRP therapy, implantation of autologous chondrocytes, osteochondral transplantation and others, the search for early predictors of occurrence and the progression of OA, which can later be used in the development of effective, pathogenetically based diagnostic and therapeutic algorithms [4, 7, 13–15].

The objectification of existing metabolic disorders in the connective tissue structures of the knee joint system is impossible without the development and introduction into clinical practice of highly sensitive methods of molecular and radiation diagnostics. This area of scientific and practical research includes the study of the levels of entry into biological media of specific collagen and non-collagen proteins, which are structure-forming elements of highly organized ECM of articular hyaline cartilage [3, 7, 13].

It is assumed that the high level of IL-1 β in the inflammatory subtype of OA, although it stimulates the production of proteases by chondrocytes and enhances the proliferation of chondrocytes and synovial fibroblasts, but this proliferative activity occurs imperfectly, which leads to the formation of coarse-fibrous cartilage against the background of chronic inflammation [12]. A distinctive feature of the pathogenesis of OA, including its early manifestations, is a pronounced imbalance of cata- and anabolic processes in articular hyaline cartilage, which results in excessive intake of degradation products of its extracellular matrix into biological media. Considering the fact that the predominant structural units of articular cartilage are type II collagen, which forms a network with aggrecan, sulfated proteoglycans, hyaluronic acid and minor collagens, the study of changes in their concentrations in substrates has a certain prognostic and diagnostic significance [5]. A significant increase in the level of daily excretion of type II collagen fragments, which we detected at the initial stages of knee joint OA, could be a consequence of both the excessive action of a complex of proteolytic enzymes and the disorganization of fibrillar complexes under the simultaneous action of a number of adverse factors. Among them, the main causes destabilizing the extracellular matrix are the synthesis of defective structural macromolecules, a decrease in the resistance of articular cartilage to axial load, and a violation of biomechanical ratios. The COMP glycoprotein plays an important role in maintaining the structural integrity of the collagen network of articular hyaline cartilage.

In patients of the main group, a significant increase in serum levels of the named structural protein was found, which could indicate an intensification of tissue destruction processes. It is this pentamer from the family of thrombospondin proteins that is more associated with damage to the tissues of articular hyaline cartilage, and is a predictor of its destruction even before the appearance of radiological and even MR signs of ECM degradation, also demonstrating a certain dependence of its concentrations on bone mineral density, age of patients, as well as disease activity [14, 15]. The dynamics of changes in type II collagen concentrations is a later marker of destruction of articular hyaline cartilage tissues than COMP, since initially COMP and aggrecan molecules enter the systemic bloodstream, and the destruction of chemical bonds with the release of the C-terminal telopeptide occurs already as a result of these structural changes.



Conclusion

In individuals with initial clinical manifestations of OA, an imbalance of ana- and catabolic processes in articular hyaline cartilage leads to a violation of the composition and structural failure of its extracellular matrix, which can be objectified on the basis of a comprehensive instrumental laboratory examination, including T2 mapping as a non-invasive highly sensitive method for diagnosing morphological changes and determining the content of COMP in biological media and CTX II. The results of the correlation analysis showed that the disorganization of the three-dimensional structure of type II collagen, detected by MRI examination in patients with early manifestations of OA, is associated with an increase in serum COMP levels and the amount of daily urinary excretion of CTX II.

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