THE VALUE OF DETERMINING THE ROLE OF CARTILADIC OLIGOMERIC MATRIX PROTEIN (COMP) IN THE EARLY DIAGNOSIS OF OSTEOARTHRITIS

Sagdiyana. N. Buranova
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

Khalmurad. S. Akhmedov
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

Davron. M. Kholmurodov
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

ABSTRACT

60 patients with radiologically determined 0-II stages of knee joint osteoarthritis aged 50.3±4.4 years old with average duration 5.4±3.6 years were involved in the study. At the same time 10 healthy individuals (average age 47.5±7.1years old) of the age and gender compatible with the patients of OA group were also enrolled in the study.

According to the results of the study radiological stage of osteoarthritis, progression and duration are characterized by certain structural changes. Within pre-radiological stage rise of cartilage oligomeric matrix protein (COMP) in blood serum indicates early destruction of cartilage.

Keywords: osteoarthritis, cartilage oligomeric matrix protein, X-ray, joint

Currently, the problems of the pathology of the musculoskeletal system are relevant in many medical fields [4]. In particular, osteoarthritis (OA), which is based on the destruction of cartilage tissue, remodeling of the bone structure, osteophytosis and inflammatory processes, is distinguished by a peculiar clinical picture and features that depend on articular anatomical and physiological disorders that lead to disability, especially in middle-aged patients, which determined its social significance and relevance [1,3]. Currently, many experts have noted that OA is considered a multifactorial disease. Thus, the pathogenesis of OA development is based on such important risk factors as age, obesity, hereditary factors, defects in the development of the musculoskeletal system, including joint hypermobility, hormonal disruptions in the body, adverse effects of drugs, injuries, comorbid pathologies. [2,13]. The negative socio-economic impact of diseases of the skeletal system, especially OA, are of great

importance. For example, according to W.Felts and E.Yelin (2013), in the USA alone, 5% of all patients in clinics, 10% of diagnostics and therapy, and 5% of visits to doctors are rheumatological patients. For example, in Canada, the economic burden of skeletal pathologies can be compared with the cost of treating cancer patients. In this regard, modern biomarkers are of great scientific interest in medicine, which would allow early diagnosis of OA and control of ongoing therapy due to the high prevalence of OA, an increase in the level of limitation of the working-age population and a deterioration in the quality of life. The National Institutes of Health Foundation's (FNIH) Biomarkers in OA Special Science Project found that biomarkers provide urgent indications for certain interventions and facilitate the development of new therapeutics. Recent references [11,14] contain important information about the metabolic changes in the cartilage oligomeric matrix protein (COMP) that occur under the influence of the aforementioned enzymes in the cartilage matrix. Some scientific papers [9,10] report that there is a correlation between serum COMP and the clinical stage of OA and certain histological changes. According to the data in other references [7, 12], osteoarthritis develops within initial stages of RA, and rise of cartilage oligomeric matrix protein (COMP) indicates early destruction of cartilage. Rise or drop of serum COMP, actually, indicate exacerbation or remission of the pathology. That is why, for coordination of cytokines, collagenase, and matrix metalloproteinases in the development of pathologic process it is correct to decrease COMP. It is known, that many rheumatic diseases differ by clinical presentation and articulate syndrome, with certain morphological alterations and specific inflammatory process. Certainly, differences in the development of rheumatic diseases and variety of underlying factors leads to specific alterations in joints. In compliance with various opinions, it can be explained by several factors from negative influence of environmental factors [8], to aggressive impact of cytokine profile (TNF-α, IL-1 and IL-6) on joints [5, 6]. Accordingly, OA is considered to be a disease with different progression, in other words with various clinical, radiological and functional changes. In its turn, it serves the basis for intensification of structural alterations in joints and causes deterioration of patients' life quality. That is why, definition of early destruction in cartilage has a practical significance.

THE OBJECTIVE

was assessment of cartilage oligomeric matrix protein (COMP) definition method in diagnosis of cartilage early destruction in patients with OA.

MATERIALS AND RESEARCH METHODS

60 patients with radiologically determined 0-II stages of knee joint osteoarthritis aged from 42 to 57 years old (average 50.3±4.4 years old) with average duration 5.4±3.6 years were enrolled in the study. At the same time 10 healthy individuals

(average age 47.5±7.1years old) of the age and gender approximately compatible with the patients of OA group were also enrolled in the study.

Classification of the patients enrolled in the study

Groups		Gender		Mean age of the patients
		Male	Female	
I group (n =18)	abs	7	11	47.3±6.3
	%	38.9	61.1	
II group (n=22)	abs	9	13	49.2±5.1
	%	40.9	59.1	
III group (n=20)	abs	8	12	52.4±3.9
	%	40	60	

The study included pain visual analogue scale (VAS), Lequesne index of joint activity assessment, and common clinical and biochemical blood analysis.

Cartilage oligomeric matrix protein (COMP) and female sexual hormones were identified using immunoassay (ELISA, Russia).

Exclusion criteria for the study were the following:

1) patients with no OA diagnosed according to EULAR/ACR criteria;
2) no surgical treatment of OA before or during the study;
3) severe concomitant pathology (renal, hepatic, cardiac failure, uncontrollable high AH, decompensated diabetes mellitus, etc), traumas;
4) malignant tumors, consumption of alcohol, psychic diseases, including dementia and cognitive impairments;
5) secondary OA.

Statistical processing of the obtained results was done using Microsoft Office Excel 2013 software and standard statistical methods.

The greater part of the patients enrolled in the study were women (60%) (Table 1). According to the results of history analysis, mean age of the patients at the time of appearance of OA initial symptoms was 47.2±2.1. Average time period from the appearance of initial symptoms till the diagnosis was 1.9 months.

Table

Clinical laboratory values of the patients with OS enrolled in the study

Parameters	I group (n =18)	II group (n =22)	III group (n =20)
Duration of the disease, years	1.9±1.1	2.8±1.8	3.2±1.4
Pain VAS, mm	35.4±4.7	55.4±5.9*	69.4±8.7$^{\&}$
Duration of morning stiffness, minutes	4.1±1.9	8.6±1.8*	10.9±2.5$^{\&}$
Synovitis, %	5.6	59.1*	75$^{\&\nabla}$
Lequesne index	7.1±1.8	7.9±1.6	9.3±2.1$^{\nabla}$
Functional failure of joints			
I class	83.3	18.2*	10$^{\&\nabla}$
II class	11.1	54.5	30$^{\&\nabla}$
III class	5.6	27.3	60$^{\&\nabla}$
Laboratory results			
C-reactive protein, mg/L	6.5±1.2	8.2±1.4	9.9±1.6$^{\&}$
Erythrocyte sedimentation rate (Westegren) mm/s	16.2±3.8	18.2±4.3	17.9±3.2
BMI			
18-24.9 (%)	11.1	4.5	5
25-29.9 (%)	16.7	36.4	10
30-34.9 (%)	22.2	13.6	45
35-39.9 (%)	27.8	27.3	30
Above 40 (%)	22.2	18.2	10

According to the results clinical presentation of the disease was different in three groups (table 2). Dysfunctions in joints can be linked to dynamic changes in typical x-ray images of degenerative process in cartilage. In the Table 2 it is seen, that indicators of articulate functional failures were reliably ($p<0.05$) different; in other words, the greater were radiological differences the more limited functionally the joint became.

At the same time, comparison of the groups showed, that structural alterations in joints were based on pain syndrome. Pain VAS and morning stiffness indicators were

The data in table 2 show, that most part of the patients were those with overweight and 1-3 stages of obesity.

It is known, that in arthritis joint structure undergoes some changes. For example, progression of OA with alterations on different levels cause bone erosion and incongruence of the joint surface. That process, in its turn, is linked with the change in

characteristics of cartilage morphologic substrate. Thus, the results show, that rise of serum COMP indicate metabolic changes in the cartilage [9]. It should be noted, that COMP varied greatly among the patients enrolled in the study. As it is depicted in figure 1, in compison to the control group patients of all three groups had reliable total COMP rise ($p<0.05$).

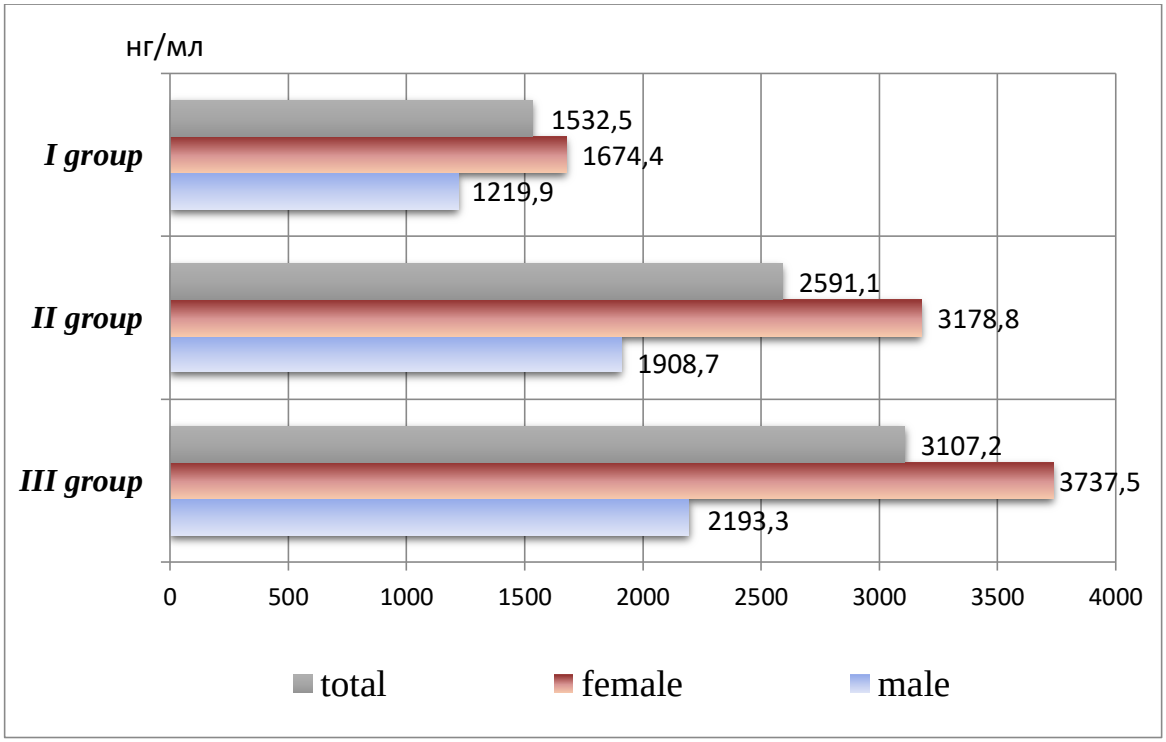

Figure 2. COMP change according to OA radiologic stage.

At the same time, analysis of COMP in the groups showed reliable differences therein ($p<0.05$), and as figure 2 illustrates, the total value in the I group was 1532.5±113.1ng/mL, in the II group it was 2591.1±96.5 ng/mL, and in the II group it was 3107.2±102.6 ng/mL. So, in patients with OA intensification of cartilage destruction in joint is accompanied by rise of COMP.

Moreover, according to our results, there are definite differences in roentgenologic stages and duration of disease between the genders. Particularly, compared to men it was more expressed in the women ($p<0.05$). Surely, that confirms the link between the way of disease progression and the gender and probability that hormonal disorders serve the basis for its genesis.

Table 3

Change in COMP according to radiologic stage of OA

Groups

Control group (n=10)		836.5±62.4	
Duration	I group (n=18)	II group (n=22)	III group (n=20)
0-12 months	1354±91.3*	1909.6±117.1*	2789.1±96.8*
12-24 months	1695±119.2*	2240.3±109.25*	3290.6±129.4*
24-36 months	1860,1±95.8*	2955.8±102.1*	3969.2±182.4*

*Note: * - $p<0.05$ reliability in comparison with the control group.*

The study of serum COMP in the patients with OA showed specific dynamics with the progression of the disease. Table 3 shows, that in the I group within initial stage of the disease that value reliably increased ($p<0.05$) and continued growing with progression of the disease.

It is known, that cartilage destruction in OA can be linked with specific alterations in case of joint inflammation. In this case irreversible bone erosions appearing as an immune response to aggressive impact of pro-inflammatory cytokines such as IL-1, IL-6 and TNF-α maintain degenerative alterations in cartilage [3]. The study of COMP changes related to inflammation process in OA was based on the analysis of correlation between the values.

The analysis showed negative feedback between COMP and CRP and ESR and positive correlation with Lequesne index in the control group. In its turn, in patients with OA, particularly in the III group, rise of serum COMP conditioned negative feedback. Figure 2 illustrates, that the graph based on the results of correlation of the parameters of acute stage of inflammation and VAS with COMP in the control group is horizontal pentagon, while in the I, II, and III groups i8t is vertical. Correlation between IL-6 and COMP in the control group had positive r=0.44, but intensification of radiological changes led to formation of negative feedback (I group r=-0.58, II group r=-0.7 and III group r=-0.61; $p<0.05$).

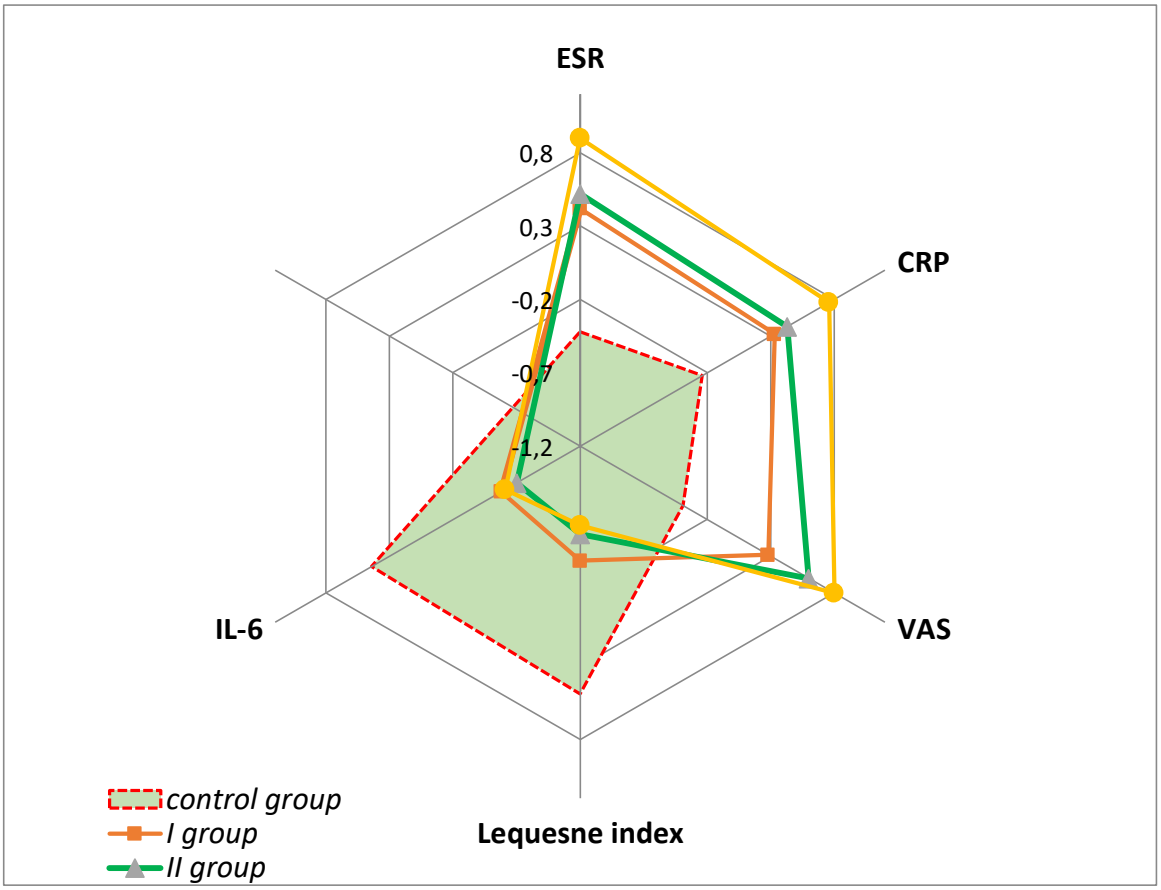

Figure 3. Correlation of COMP with inflammation process.

Thus, immune inflammatory process in OA, or pro-inflammatory cytokine IL-6 aggression is linked with the rise of COMP.

According to the obtained results, we can say that on the basis of OA of knee joint inflammatory markers and COMP amount indicating destruction of cartilage structures, and taking into account clinical radiological stage of OA, its progression can be classified into three variants (table 5):

1. variant with no clear clinical manifestations and relatively low COMP in blood (1500<2000 ng/mL) and normal ESR and CRP (A variant).
2. Low expression of CRP and ESR, clinical manifestations and high COMP (<2000 ng/mL) (B variant).
3. Simultaneous rise of CRP, ESR and COMP (<2000 ng/mL) with expressed destruction of cartilage (C variant).

Table 5

Variants of OA clinical presentation based on the obtained results

	A variant	B variant	C variant
I group (n=18)	4	8	6
II group (n=22)	2	10	10
III group (n=20)	2	7	11
% of clinical variants	13.3%	41.7%	45%

According to the results of the study prevalence of knee synovitis in cases of OA C variant was higher than in A and B variants. Thus, among the patients enrolled in the study there were 47 cases with synovitis, and 30 out of them corresponded to C variants of OA clinical form.

CONCLUSION

Radiological stage of OA, progression and duration are characterized by certain specific structural alterations in joints. Rise of serum cartilage oligomeric matrix protein (COMP) within pre-roentgenologic stage of OA indicates early destruction of cartilage.

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