

DIAGNOSTIC AND TREATMENT METHODS

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INTERRELATION BETWEEN THE CONCENTRATIONS OF BONE REMODELING MARKERS, OSTEOPOROSIS AND THE RISK OF PATHOLOGICAL BONE FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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The aim of the study: to study the possibility of predicting bone fractures by determining the concentration of bone remodeling markers in patients with rheumatoid arthritis (RA).

Materials and methods. A prospective study was conducted in which 88 female RA patients aged 21 to 81 were under observation. The inclusion criterion was that patients had a reliable diagnosis of RA according to the ACR / EULAR 2010 criteria. When analyzing the age composition, it was found that the majority of patients are aged (from 41 to 55 years).

Results. Patients with RA, suffering from OP, had a significantly higher level of C-terminal type 1 telopeptide ($p = 0.009$), P1NP ($p = 0.001$) serum, urine calcium / creatinine ($p = 0.02$) than patients without OP. Patients with RA suffering from OP were found to have significantly lower levels of 25-OH vitamin D than in patients without OP. Significant changes in the concentration of blood calcium, alkaline phosphatase when comparing these two groups was not observed. A significant increase in the C-terminal telopeptide type 1 ($p = 0.002$), P1NP ($p = 0.002$), urine calcium / creatinine ($p = 0.02$) was also detected, as well as a significant decrease in 25-OH vitamin D ($p = 0.006$) in patients with a history of fractures. When comparing the level of alkaline phosphatase, blood calcium in groups of RA patients with osteoporotic fractures and without fractures in history, no significant change in the concentration of laboratory data was found.

Findings. At RA, complicated by OP, as well as in the presence of pathological bone fractures in patients with RA, an increase in C-telopeptide type I collagen, serum P1NP, urine calcium / creatinine, and a decrease in serum 25-OH vitamin D are observed.

Keywords: rheumatoid arthritis, osteoporosis, markers of bone remodeling.

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Introduction. Rheumatoid arthritis (RA) is an autoimmune rheumatic disease of unknown etiology, characterized by chronic erosive arthritis and a wide range of extraarticular manifestations. The prevalence of this disease in the population reaches 1% [3, 6]. In recent years, the role of markers of bone remodeling in the pathogenesis of rheumatic diseases (RH) has been actively studied [1, 8]. In RA, the study of osteoporosis (OP) is of particular interest [2], which refers to secondary metabolic osteopathies due to a violation of bone remodeling processes, which leads to a progressive decrease in bone mineral density. Until now, the question of the relationship between markers of bone remodeling and the risk of developing bone fractures in patients with RA remains poorly understood [5, 7, 10]. In the process of remodeling, osteoblasts synthesize and secrete a number of compounds, markers of bone formation and bone resorption, into circulating blood [9, 4]. The first include the N-terminal propeptide of type I procollagen (P1NP), alkaline phosphatase, etc., the change in concentration of which reflects the rate of bone formation. The second category includes collagen C-te-

lopeptides of type I collagen, acid phosphatase, etc. It can be assumed that the measurement of all of the above indicators, indicators of phosphorus-calcium metabolism, as well as the serum concentration of vitamin D involved in bone mineralization and in maintaining calcium homeostasis, can be used to assess the activity of osteoblasts and osteoclasts and balance bone remodeling processes. Based on the foregoing, the study of the relationship between concentrations of bone remodeling markers and the state of bone tissue is an urgent task of modern rheumatology, and can be useful for predicting the risk of pathological fractures in patients with RA.

Objective: to study the possibility of predicting bone fractures by determining the concentration of markers of bone remodeling in patients with RA.

Materials and methods. The work was carried out on the basis of the Federal State Budget Scientific Institution Scientific Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Volgograd. A prospective study was conducted, in which 88 female RA patients aged 21 to 81 years were monitored for 3 years. All patients lived in the Volgograd region.

Inclusion criteria:

1. The patient has a reliable diagnosis of RA in accordance with the criteria of ACR / EULAR 2010;

2. Patients who voluntarily gave written informed consent to participate in the study.

When analyzing the age composition, it was revealed that the majority of patients are aged (from 41 to 55 years). Assessment of the activity of the pathological process was determined by calculating the DAS28 index using a visual online calculator. According to the degree of RA activity, the patients were divided as follows: with the activity of 0 (DAS28 <2.6) patients, there were 19 patients in the study (21.59%), with a low degree of activity I (2.6 < DAS28 <3.2) – 10 people (11.36%), with an average degree of activity II (DAS28 ≥ 3.2 - 5.1) – 52 people (59.09%), with a high degree of activity III (DAS28 > 5.1) there were 7 patients (7.96%).

Depending on the presence of osteoporotic fractures identified by collecting medical history data, patients were divided into groups: 1st – RA patients with osteoporotic fractures (n = 11), 2nd – patients with RA without a history of fractures (n = 77).

Also, patients were divided into groups depending on the diagnosis of OP, which was exhibited by measuring BMD during dual-energy x-ray absorptiometry: 1st – patients with RA having OP (n = 22), 2nd – patients with RA who do not have OP (n = 66).

Bone remodeling marker levels were determined in all patients: C-terminal telopeptide of type I collagen, N-terminal pro-peptide of type I collagen, 25-OH vitamin D, alkaline phosphatase, blood calcium, urine calcium / creatinine using commercial kits.

Statistical processing of clinical examination data was carried out using STATISTICA 10.0 for Windows software packages. The significance of differences between the groups was compared using variation statistics (ANOVA) methods. The results were considered statistically significant at $p < 0.05$.

Results and discussion. In order to identify the relationship between the concentrations of bone remodeling markers in patients with RA and the presence of OP, the mean value and standard deviation ($M \pm \sigma$) of bone remodeling markers were calculated in the group of patients suffering from OP and in the group of patients without OP. The results

of the study are presented in Table 1.

From the data presented in the table it can be seen that in patients with RA suffering from OP, a significantly higher level of C-terminal telopeptide type 1 ($p = 0.009$), P1NP ($p = 0.001$) of blood serum, calcium / urine creatinine ($p = 0.02$) than in patients without OP. In patients with RA suffering from OP, a significantly lower level of 25-OH vitamin D was detected than in patients without OP. A significant change in the concentration of blood calcium, alkaline phosphatase when comparing these two groups was not observed.

The relationship between the concentrations of markers of bone remodeling and the presence of pathological bone fractures in patients with RA was also studied. The data are presented in Table 2.

When studying the relationship between the concentrations of the studied parameters and the presence of low-energy bone fractures, a significant increase in the level of the C-terminal telopeptide of type 1 ($p = 0.002$), P1NP ($p = 0.002$), calcium / urine creatinine ($p = 0.02$), and a significant decrease in 25-OH vitamin D ($p = 0.006$) in patients with a history of fractures. When comparing the level of alkaline phosphatase, blood calcium in both groups, no significant change in the concentration of these laboratory parameters was found.

Findings. In RA, complicated by OP, and in the presence of pathological bone fractures patients have an increase in the concentration of type I collagen C-telopeptide, serum P1NP, urine calcium / creatinine, and a decrease in serum 25-OH vitamin D.

Table 1

Biochemical parameters of bone remodeling depending on the presence or absence of OP

Laboratory indicator	The presence of OP, n=22	The absence of OP, n=66	Reliability F, p
C-terminal telopeptide of collagen type 1, ng / ml	0.85±0.54	0.62±0.27	F=6.95. p=0.009
P1NP, ng / ml	88±84.35	49.8±24.29	F=11.02. p=0.001
25-OH Vitamin D, ng / ml	41.47±13.7	52.9±17.77	F=7.58. p=0.007
Urine Calcium / Creatinine, mmol	0.21±0.10	0.15±0.10	F=4.93. p=0.02
Blood Calcium, mmol / L	2.39±0.13	2.45±0.23	F=0.69. p=0.41
Alkaline phosphatase, units / l	85.39±77.58	67.48±27.51	F=1.19. p=0.28

Table 2

Biochemical parameters of bone remodeling depending on the presence or absence of pathological fractures

Laboratory indicator	There are fractures, n=11	No fractures, n=77	Reliability
C-terminal telopeptide of collagen type 1	0.99±0.52	0.63±0.32	F=9.64. p=0.002
P1NP	100.36±108.86	53.49±30.81	F=9.53. p=0.002
25-OH Vitamin D	36.81±16.66	51.93±16.87	F=7.75. p=0.006
Urine Calcium / Creatinine	0.23±0.12	0.15±0.10	F=5.16. p=0.02
Blood Calcium	2.34±0.15	2.45±0.21	F=0.95. p=0.33
Alkaline phosphatase	78.98±78.98	71.46±44.99	F=0.11. p=0.73

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METHOD OF DETERMINING THE DEGREE OF IMPAIRMENT OF THE GASTRIC EVACUATION FUNCTION IN PATIENTS WITH CICATRICAL-ULCERATIVE STENOSIS OF THE DUODENUM

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Aim. To develop the method of determining the degree of impairment of gastric evacuation function in patients with cicatricial-ulcerative stenosis of the duodenum based on the data of standard daily pH-monitoring.

Materials and methods. There were examined 45 patients with with cicatricial-ulcerative stenosis of the duodenum. All patients underwent a comprehensive endoscopic and X-ray examination of the gastric evacuation function. Gastric secretory function was assessed by intragastric daily pH monitoring.

Results. A method for determining the degree of impaired gastric evacuation function is proposed, including intragastric pH monitoring, which determines the number of duodenogastric refluxes and the values of the parameters: "ratio of pH in the body of the stomach to the pH in the antrum of the stomach," "pH range in the cardiac part of the stomach."

Using the obtained data, the formulas are used to determine values of prognostic coefficients d1, d2 и d3, compare their numerical characteristics, which are what is used to evaluate degree of disorder of gastric evacuation function. With the value of d1 is greater than d2 and d3, the I degree is established, with d2 is greater than d1 and d3 - II degree and with d3 greater than d1 and d2, the III degree of impaired gastric evacuation function is established.

Conclusion. The proposed method allows establishing the degree of impaired gastric evacuation function during standard intragastric pH monitoring.

The proposed method can be used for automated computerized, remote, screening diagnostics according to the values of daily intragastric pH monitoring.

Keywords: duodenal ulcerative stenosis, evacuation function of the stomach, intragastric pH monitoring.

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Introduction. Intragastric pH monitoring is a widely accepted standard method for the study of acid and reflux values of the stomach in acid-related diseases, one of which is duodenal (DD) ulcer (UD) [1, 2, 5, 7].

It is known that cicatricial-ulcerative stenosis (CUS) of the duodenum is one of the most frequent complications of ulcer and occurs in 10.0–56.3% of patients [1, 3, 6, 8]. Its main manifestation is a impairment of the gastric evacuation function (GEF), the assessment of the degree of which is crucial for determining indications for surgical treatment, the nature and extent of preoperative preparation [3, 6, 7].

A method has already been proposed for determining GEF impairment according to intragastric pH monitoring after various surgeries for duodenal ulcer [2]. However, a prerequisite for the use of this

method is to restore the patency of the pylorus section of the stomach.

Authors performed a postoperative indirect comparative assessment of the evacuation time from the stomach to restore the initial indices of intragastric pH during evacuation to the duodenum of mixed standard food load. In this case, the degree of its preoperative disorder was not assessed using the claimed method.

The disadvantages of this method are the need to use a mixed standard food load, the patient must be in an upright position for 1.5 hours. In the absence of restoration of the initial value of intragastric pH, the need arises to conduct a repeated study.

The objective of our study was to develop the method of determining the degree of violation of the evacuation function of the stomach in patients with