Journal homepage: **https://medicinskiglasnik.ba**

Med Glas (Zenica) 2024;21(2)
https://doi.org/10.17392/1728-21-02

Med Glas (Zenica)

ORIGINAL ARTICLE

Association of X-ray disease stage with basic patient data, laboratory values and treatment modalities in patients with seropositive rheumatoid arthritis

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ABSTRACT

Aim To investigate whether the radiographic progression of rheumatoid arthritis (RA) correlates with inflammatory markers and other laboratory values, and its association with treatment modalities.

Methods This observational study included 125 patients with seropositive RA. Data were obtained from patients' medical records from the year of 2022. Inclusion criteria were patients with seropositive RA who had attended follow-up with a rheumatologist. Basic patient data were collected: gender, age, duration of RA, hospital admission, systolic and diastolic blood pressure, and X-ray stage of RA. Stages of RA are defined by the American College of Rheumatology and they ranged from stage 1, which represents no destructive changes on X-ray, up to stage 4 where bony or fibrous ankylosis is present.

Results There were no differences in X-ray stages of RA between genders. Patients with a higher X-ray stage were younger and had a longer duration of illness. Patients in stages III and IV had higher systolic blood pressure (BP), patients in stage IV had higher diastolic BP. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were higher in X-ray stages II-IV compared to stage I. The patients treated with methotrexate had higher radiographic stages.

Conclusion X-ray changes can be associated with CRP and ESR levels, since structural damage is related to RA disease activity and functional disability. The use of newer treatment modalities may be required to stop the radiographic progression of RA.

Keywords: inflammation, radiology, rheumatology

INTRODUCTION

Plain radiography is the mainstay of imaging in the diagnosis and follow-up of rheumatoid arthritis (RA), and plain film radiographs of the hands and feet should be obtained in all patients suspected of having RA (1–3). Radiographic abnormalities are not required for the diagnosis of RA or to initiate therapy, since they are often normal in early disease (1,3). Still, if joint erosions are present, this confirms the diagnosis. Radiographs are most useful for monitoring the progression of joint damage over time (4,5).

The RA has predilection for the proximal interphalangeal and metacarpophalangeal joints, ulnar styloid and triquetrum (2,6). Early changes on radiographs may include soft tissue swelling and periarticular osteopenia. Bone erosions, joint space narrowing, and joint subluxation can be seen later in the disease process (6,7). Radiographic findings mostly have a bilateral and symmetrical distribution (4). An important treatment goal is to prevent these radiographic changes (8).

Erosions are usually a late finding and represent a marker for poor functional outcome in long-standing RA (9).

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 Submitted: 06. Feb. 2024. Revised: 11 Mar. 2024. Accepted: 20 Apr. 2024.

Erosions must erode through the cortex of the bone around the margins of the joint to be detected on radiographs, but they may be present even if there is no pain (1,4).

Monitoring of radiographic changes is important for clinical and scientific research purposes, but its correlation with other patient factors can further enhance the role of X-rays in patients with RA. Previous studies have shown that a radiologic damage correlates well with acute-phase reactants (10–12), although there are interindividual differences in the relationship between disease activity and radiographic progression (13).

The aim of this study is to confirm whether the radiographic progression of RA correlates with inflammatory markers, but also to investigate its relationship with basic patient data, other laboratory values, and treatment modalities, and ultimately to better establish the role of X-rays in monitoring patients with seropositive RA.

PATIENTS AND METHODS

Patients and study design

This observational study included 125 patients from the Public Institution Health Care Centre Visoko. Data was obtained from patients' medical records from the year of 2022. Criteria for inclusion were patients with seropositive RA who had attended follow-up with a rheumatologist. The following basic patient data were collected: patients' gender, age, duration of RA, whether they were admitted to hospital due to RA, systolic and diastolic blood pressure, and X-ray stage of RA.

The study was completed in compliance with the Helsinki Declaration (last revised in 2013).

Methods

The following laboratory data were collected: erythrocyte sedimentation rate (ESR) in the 1st hour, ESR in the 2nd hour, white blood cell (WBC) count, red blood cell (RBC) count, haemoglobin, haematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelets, fasting blood glucose, urea, creatinine, cholesterol, triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP). Also, data on the following treatment modalities were collected: methotrexate, leflunomide, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), topical NSAIDs, protein pump inhibitors (PPIs), vitamin D, glucosamine chondroitin, pomegranate extract supplement, omega-3 fish oil, calcium, and herbal gel.

Stages of RA are defined by the American College of Rheumatology (ACR) (14). Stage 1 represents no destructive changes on X-rays; stage 2 means the presence of X-ray evidence of periarticular osteoporosis and subchondral bone destruction without joint deformity; in stage 3, there is evidence of cartilage and bone destruction in addition to joint deformity and periarticular osteoporosis; stage 4 means the presence of bony or fibrous ankylosis along with stage 3 features.

Statistical analysis

The results of a descriptive analysis were shown in frequencies and percentages. Mann-Whitney U test was used to assess differences in X-ray stages based on gender, hospital admission, and treatment modalities. The effect size was small for r=0.10-0.29, moderate for r=0.30-0.49, large for r=0.5-1.0. To assess differences in X-ray stages based on laboratory values, patient's age, duration of illness, and blood pressure, the Kruskal Wallis test was used. To assess the correlation between duration of illness and age, Spearman's rank correlation was used.

RESULTS

The majority of patients were female, 91 (72.8%). The mean age was 62.3±11.4 years (range 43-100 years). The mean duration of RA was 5.3±1.8 years (range 1-10 years). A total of 44 (35.2%) patients were admitted to the hospital due to RA.

Regarding X-ray stages of RA, results are as follows: stage I 10 patients (8%), stage II 41 (32.8%), stage III 43 (34.4%), and stage IV 31(24.8%) patients.

There were no differences in X-ray stage of RA between genders ($p=0.25$; $r=0.10$). Hospitalized patients had higher X-ray stages ($p<0.001$; $r=0.51$).

The patients with a higher X-ray stage of RA were younger ($p<0.001$) and had a longer duration of illness ($p<0.001$). There was a negative correlation between age and duration of illness ($rs=-0.63$; $p<0.001$), meaning younger patients had a longer duration of RA.

The patients in stages III and IV had higher systolic BP ($p<0.001$), patients in stage IV had higher diastolic BP ($p<0.001$) (Table 1).

The ESR in the first and second hour was significantly higher in patients with X-ray stages II-IV compared to stage I ($p=0.001$ and $p<0.001$, respectively). The CRP was also significantly higher in stages II-IV compared to stage I ($p=0.03$) (Table 1).

Patients treated with methotrexate had a higher X-ray stage of the disease ($p=0.001$; $r=0.29$). No significant differences in X-ray stages were observed for leflunomide, corticosteroids, and supportive pharmacological and non-pharmacological treatment (Table 2).

Table 1. Comparing values between patients based on their X-ray disease stage

Variable (reference value)	**Median value for stage (No of patients)**				p
	Stage I (n=10)	**Stage II** (n=41)	**Stage III** (n=43)	**Stage IV** (n=31)	
Age (years)	74	64	57	53	<0.001
Duration of illness (years)	3	4	6	7	<0.001
Systolic BP (<120 mmHg)	120	120	140	150	<0.001
Diastolic BP (<80) mmHg)	75	80	80	90	<0.001
ESR in the 1st hour (4-12 mm)	5.5	32	31	30	0.001
ESR in the 2nd hour (8-24 mm)	17	62	62	66	<0.001
WBC count (4-11×10^{12}/L)	6.9	6.6	7.1	7.1	0.60
RBC count (4-6×10^{12}/L)	4.8	4.3	4.5	4.6	0.08
Haemoglobin (120-160 g/L)	140	134 g/L	134 g/L	136 g/L	0.43
Haematocrit (0.37-0.53 L/L)	0.41	0.41 L/L	0.39 L/L	0.41 L/L	0.21
MCV (80-100 fL)	88.5	88.5	88.9	89.3	0.72
MCH (27.6- 33.2 pg)	29.5	29.8	29.9	29.9	0.68
MCHC (320-360 g/L)	337	326	336	345	0.09
Platelets (150-450 ×10^{9}/L)	326	266	293	299	0.17
Fasting blood glucose (4.2-5.7 mmol/L)	5.3	5.2	6.2	6	0.21
Urea (3.2-7.1 mmol/L)	5.2	5.4	5.4	5.8	0.77
Creatinine (53-133 µmol/L)	69.5	75	72	72	0.97
Cholesterol (3.6-5.2 mmol/L)	5.05	5.53	5.8	6	0.21
Triglycerides (0.4-2.3 mmol/L)	2	2.8	2.6	2.9	0.18
AST (14-50 U/L)	17	20	22	24	0.79
ALT (14-50 U/L)	19	20	21	22	0.31
CRP (0-5 mg/L)	5.5	10	11	11	0.03

BP, blood pressure; ESR, erythrocyte sedimentation rate; WBC, white blood cell; RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein

Table 2. Association of X-ray stages of rheumatoid arthritis and treatment modalities

Therapy	p	r
Methotrexate	0.001	0.29
Leflunomide	0.95	0.08
Corticosteroids	0.85	0.01
NSAID	0.19	0.11
Topical NSAID	0.66	0.03
PPI	0.89	0.01
Vitamin D	0.51	0.05
GC	0.36	0.08
Pomegranate extract suppl.	0.48	0.06
Omega-3 fish oil	0.96	0.003
Calcium	0.41	0.07
Herbal gel	0.37	0.07

NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor; GC, glucosamine chondroitin

DISCUSSION

Evidence suggests that higher disease activity in RA leads to more rapid joint destruction (15). Disease activity is reflected by elevated inflammatory parameters. ESR and CRP levels were correlated with X-ray stages of RA in our study. Previous studies have also shown that elevated ESR and CRP correlate with radiographic progression of RA (10,11). A stronger association was reported for ESR, which was also confirmed in our study (11) There is a much greater difference in median values of ESR in both first and second hour, for X-ray stage II versus stage I. Median CRP levels were higher in stage II comparing to stage I. Since stage II is the first stage where destructive changes are present, this is consistent with previous reports where high ESR and CRP predicted structural damage in patients with RA (16,17).

As expected, patients with a longer duration of illness had a higher X-ray stage of the disease, but so did younger patients. Subsequent analysis showed that younger patients in our study had a longer duration of RA. It is possible that a small patient sample contributed to this result. Previous studies have conflicting results regarding difference in joint damage based on age (18–20). Mangnus et al. reported that older patients with RA are expected to have more severe joint damage, one of the explanations is more severe local inflammation at higher age (21).

Blood pressure was higher in patients with a higher X-ray stage. This favours the possibility that good control of RA disease activity can improve blood pressure control. Systemic inflammation has its role in the pathogenesis of hypertension, but other factors like anti-rheumatic medications and physical inactivity also contribute to the development or progression of hypertension in RA. More studies are required to better understand the relationship between hypertension and RA (22,23).

Prior to the introduction of biologic disease-modifying antirheumatic drugs (DMARDs), joint erosions were identified on radiographs in 15-30% of patients in the

first year of the disease. That number rose to 90% by the end of the second year of the disease in patients who did not respond to treatment (1). With newer treatment options, joint erosions are becoming less common, as are characteristic deformities such as ulnar deviation, boutonniere and swan neck deformities of the hands, and subchondral cyst formation (2,3). Patients in our study were not treated with biologic DMARDs, rather with conventional DMARDs, and we observed a high proportion of the patients in stages III-IV of the disease on X-ray. The patients treated with methotrexate had a higher X-ray stage of the disease, and since we did not collect data on the length of the treatment with methotrexate and baseline radiographs, we can assume that the treatment started in advanced stages of the disease.

The main limitation of our study is a lack of baseline radiographs to demonstrate the progression of structural damage with the treatment. Also, previous laboratory values would allow monitoring changes in relation to radiologic abnormalities.

In conclusion, radiographic changes can be associated with CRP and ESR levels, since structural damage is related to RA disease activity and functional disability. Higher blood pressure can be expected in patients with higher X-ray stages of RA. The use of newer treatment modalities, such as biologic DMARDs, may be required to stop the radiographic progression of RA.

FUNDING

No specific funding was received for this study

TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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