Impact of osteoporosis on the quality of life in patients with rheumatoid arthritis

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ABSTRACT

Introduction. Rheumatoid arthritis (RA) patients have poor quality of life due to inflammation and joint destruction that characterizes the disease. Osteoporosis, through the fragile osteoporotic fractures as a complication, also associates an important decrease in the quality of life. Knowledge of the impact of osteoporosis on quality of life in patients with RA is currently required.

Objectives. The main objective of the study is to evaluate the impact that osteoporosis has on the quality of life in patients with RA. The secondary objective of the study is to identify correlations that the quality of life quantified by health assessment questionnaire (HAQ) has with nonspecific inflammatory syndrome (erythrocyte sedimentation rate – ESR, C-reactive protein – CRP, fibrinogen – FI), rheumatoid autoimmunity (rheumatoid factor – RF and anti-citrullinated protein antibodies – ACPA) and osteoporosis assessment elements (T score and bone mineral density – BMD of the lumbar spine and hip, FRAX algorithm).

Material and methods. This is a descriptive, retrospective, observational clinical study based on the observation sheets found in the database of the "Sf. Maria" Clinical Hospital, Department of Internal Medicine and Rheumatology, Bucharest, Romania which included patients with RA hospitalized during the period November 2018-December 2019. The patients studied were divided into two groups according to the presence or not of osteoporosis: group A patients with RA without osteoporosis and group B patients with RA and osteoporosis. Multiple paraclinical variables related to biological investigations (hemoglobin, hematocrit, alkaline phosphatase – AP, TSH), nonspecific inflammatory syndrome (ESR, FI, CRP), RA evaluation items (RF, ACPA, disease activity score 28 – DAS28 and HAQ) and evaluation elements of osteoporosis (T score and BMD at lumbar spine and hip, FRAX algorithm) were followed in the studied group.

Results. The study included 85 patients diagnosed with RA with an average age of 67.64 years (95% CI 65.7885 to 69.5018) and SD of 9.01 years. There were no statistically significant differences between the 2 groups of paraclinical variables used. Significant statistical differences were established between the 2 groups regarding ESR and CRP in favor of lot B, which seems to have high values of FB, but without statistical significance; in addition, there were statistically significant differences between the 2 groups in favor of group B regarding all the elements of evaluation of osteoporosis except the FRAX algorithm (risk of major osteoporotic fractures and hip fracture within 10 years) which were higher in the group B compared to group A but without statistical significance, confirming there is osteoporosis in this group. By analyzing the correlation relation on the whole group of patients between the activity of the disease objectified by DAS28 and the quality of life quantified by HAQ, a directly proportional and highly statistically significant relation is obtained ($r = 0.64$, $p < 0.0001$).

Discussion. Although in "real life", patients with RA and osteoporosis have a lower quality of life than patients with RA without osteoporosis as established by the current study, there is only a relationship between the quality of life of patients evaluated by HAQ and the activity of the disease evaluated by DAS28. But, there is no relationship between HAQ and osteoporosis assessment elements.

Conclusions. The quality of life of patients with RA is related to the activity of inflammatory disease (DAS28), and the overlap of osteoporosis does not lead to a statistically significant decrease in quality of life, which makes us conclude that osteoporosis per se does not lead to decreased quality of life.

Keywords: osteoporosis, rheumatoid arthritis, quality of life

INTRODUCTION

Rheumatoid arthritis (RA) is a connective tissue disease of unknown etiology and totally unspecified pathogenesis, characterized by symmetrical erosive

chronic synovitis that generates severe joint injuries responsible for physical disability and sometimes lower quality of life. In general, patients have a chronic evolution with disease fluctuations, which

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untreated leads to progressive joint dysfunction with permanent joint deformities accompanied by motor deficits involving joint functionality and reduced life expectancy (1).

Osteoporosis is defined as a systemic disease characterized by decreased bone mass and deterioration of the bone tissue microarchitecture, which increases the fragility and the possibility of fractures. Currently, osteoporosis is defined as a skeletal disorder characterized by low bone resistance that predisposes to an increased risk of fragility fracture. By this definition focusing on bone strength, two main characteristics are integrated: bone mineral density (BMD) and bone quality (2).

Osteoporosis is one of the most common comorbidities associated with RA, its importance being so high that osteoporosis is now considered an extra-articular manifestation of RA (3). By inducing osteoporotic fractures at known sites (vertebral, hip, non-vertebral) osteoporosis brings an important supplement to lower quality of life of RA patients, with significant morbidity and mortality (4). It is noteworthy that, despite the efforts of the rheumatologists to treat RA correctly, the incidence of fragility fractures remains high in patients with RA and osteoporosis, which opens the way for new methods of screening, prevention and treatment of osteoporosis from this rheumatic disease.

OBJECTIVE

The main objective of the study is to evaluate the impact that osteoporosis has on the quality of life in patients with RA. The secondary objective of the study is to identify correlations that the quality of life quantified by HAQ has with nonspecific inflammatory syndrome (ESR, CRP, FI), rheumatoid autoimmunity (RF and ACPA) and osteoporosis assessment elements (T score and DMO at the lumbar spine and hip, FRAX algorithm).

MATERIAL AND METHODS

Patients

The study included patients diagnosed with RA by their attending rheumatologists, who also met the 2010 American College of Rheumatology and European League Against Rheumatism (ACR/EULAR) classification criteria (5), and who came to the rheumatology department in a random order of presentation between November 2018 and December 2019.

The following exclusion criteria were applied: age under 18 years; overlap syndromes of RA; secondary causes of osteoporosis; lack of data regarding osteoporosis status. Each patient gave written informed consent for the use of clinical data and the study was approved by the local ethics committee.

Variables

Demographic data (age, gender, dwelling, education level, smoking), RA-specific data (disease activity score – DAS28, health assessment questionnaire – HAQ (6)), serology (rheumatoid factor – RF, anti-citrullinated protein antibodies – ACPA), acute phase reactants (erythrocyte sedimentation rate – ESR, C-reactive protein – CRP, fibrinogen – FI), hematology tests (hemoglobin, hematocrit), osteoporosis data (diagnosis, T score at lumbar spine and hip as well as bone mineral density (DMO)), alkaline phosphatase (AP), thyroid stimulation hormone (TSH) and the FRAX score (7). DAS28 was calculated using four variables: number of tender joints, number of swollen joints, patient global assessment on a visual analogue scale and CRP. Based on DAS28 values, the following disease activity categories were defined: remission ($\text{DAS28} < 2.6$); low disease activity ($2.6 \leq \text{DAS28} < 3.2$); moderate disease activity ($3.2 \leq \text{DAS28} < 5.1$) and high disease activity ($\text{DAS28} \geq 5.1$) (8). The health assessment questionnaire (HAQ) was applied and based on the values the following categories were defined: 0-1 minor affection, 1-2 moderate affection, 2-3 severe affection. Inflammation was defined with the acute phase reactants (ESR – normal < 20 mm/h, Westergren method, CRP- normal < 5 mg/l turbidimetry method; FI – normal < 490 mg/dl, enzyme-linked immunoabsorbant assay). Positive serology was defined if RF and ACPA were above the laboratory's upper limit of normal (ULN): 15 U/ml (turbidimetry method) and respectively 20 U/ml (enzyme-linked immunoabsorbant assay method). The presence of osteoporosis was defined according to the WHO criteria, dependent on the BMD value: T score ≥ -1 = normal BMD; $-2.5 < \text{T score} < -1$ = osteopenia and T score ≤ -2.5 = osteoporosis (9). Hemoglobin was defined normal from 12 to 16 gm/dl and hematocrit was defined normal from 38% to 46%. TSH was defined normal between 0.45 and 4.12 mU/l. For the 10 year probability of a major fracture (vertebral, hip, humerus, or wrist fracture) was used the computer-based algorithm FRAX (7). This algo-

rhythm includes several clinical risk factors, including, among others, age, smoking, previous fractures, parental history of hip fracture, use of GC, diagnosis of RA and it was adapted for the population in Romania (10).

Statistics

For the statistical analysis of the data we used the program MedCalc 14.1 as follows: the t test for independent variables to compare the differences between means and the Pearson or Spearman correlation coefficient depending on the observance of the Gaussian distribution of the data. For all analyzes the confidence interval is 95%, so that a p value less than 0.05 is considered to be statistically significant.

RESULTS

This descriptive, retrospective, observational study includes 85 patients with RA who will be divided into two groups using osteoporosis diagnostic criteria.

In order to answer the main end point (quality of life), we will use the HAQ score. Also, paraclinical data were considered: hemoglobin, hematocrit, AF, TSH, nonspecific inflammatory syndrome: ESR, FI, C-reactive protein and osteoporosis scores: T score, BMD and FRAX algorithm. The disease activity will be quantified with the DAS28.

The two groups of patients: group A of patients with RA who do not suffer from osteoporosis (n = 33 pts. of which 31 women and 2 men) and group B of patients suffering from RA and osteoporosis (n = 52 pts. of which 48 women and 4 men), a total of 85 patients with an average age of 67.64 years, with the

confidence interval (CI) 65.7885 to 69.5018 and a standard deviation (ST) of 9.01 years.

Regarding the description of the total group (85 patients), there are several demographic characteristics: the vast majority of the group were women – 79 patients (92.94%) with a level of training being secondary education (high school) – 51 patients (60%), with a disease duration of 9.17 years, with the most of patients of urban areas – 62 patients (72.94%). It is important to note that most patients were non-smokers -72 patients (84.01%) and only 13 patients (15.99%) were smokers. Regarding the presence of comorbidities 73 patients (85.88%) had cardiovascular diseases, 34 patients (40%) had lung diseases, 32 patients (37.64%) had gastrointestinal diseases and 50 patients (58.82%) had metabolic disorders; degenerative osteoarticular diseases were present in more than half of the patients, 54 patients (63.52%).

For the comparative analysis of the paraclinical data between the two groups we used the t test for the independent variables and as can be seen in table 1, there is no statistically significant difference between the studied data.

The t test for independent variables was also used to search for differences between the means for non-specific inflammatory syndrome. As can be seen in table 2, there are statistically significant differences in the value of ESR and FI, in favor of patients with RA and osteoporosis. Group B of RA patients and osteoporosis appears to have higher levels of CRP compared to group A of RA patients without osteoporosis, but the difference is not statistically significant (table 2).

TABLE 1. Comparative analysis of the paraclinical data

Paraclinical data	Mean group A	Mean group B	95% CI group A	95% CI group B	Standard error of difference	p value
Hemoglobin	12.1469	12.3050	11.5457 to 12.7481	11.9236 to 12.6864	0.33	0.64
Hematocrit	36.2875	36.8167	34.5027 to 38.0723	35.7916 to 37.8417	0.9482	0.57
AF	73.9181	73.3224	66.9120 to 80.9243	68.0735 to 78.5713	4.3551	0.89
TSH	2.5777	2.2682	1.2485 to 3.9069	1.6586 to 2.8777	0.6485	0.63
ACPA	247.03	137.24	105.33 to 388.73	80.38 to 194.10	64.1333	0.09

TABLE 2. Comparative analysis of non-specific inflammatory syndrome data

Paraclinical data	Mean group A	Mean group B	95% CI group A	95% CI group B	Standard error of difference	p value
ESR	39.3000	54.6562	32.5851 to 46.0149	42.6274 to 66.6851	6.2925	0.01
CRP	26.2002	36.4794	9.6071 to 42.7932	22.1270 to 50.8318	12.4802	0.41
FI	361.2472	432.7313	335.1223 to 387.3722	380.4707 to 484.9918	25.8466	0.0069

TABLE 3. Comparative analysis of specific osteoporosis quantification items

Paraclinical data	Mean group A	Mean group B	95% CI group A	95% CI group B	Standard error of difference	p value
T score hip	-1.3656	-2.3317	-1.6669 to -1.0643	-2.5415 to -2.1218	0.1796	< 0.0001
T score LS	-0.9594	-2.4700	-1.3264 to -0.5924	-2.6937 to -2.2463	0.2016	< 0.0001
BMD hip	0.8503	0.7121	0.8010 to 0.8996	0.6775 to 0.7467	0.02953	< 0.0001
BMD LS	0.9741	0.8304	0.9258 to 1.0223	0.8001 to 0.8606	0.02696	< 0.0001
FRAX hip	3.7406	5.4633	2.7457 to 4.7355	4.4098 to 6.5169	0.8051	0.03
FRAX major osteoporotic	9.3594	11.5400	7.8613 to 10.8574	10.1060 to 12.9740	1.1193	0.054

With the exception of the data of FRAX algorithm (hip fracture risk by FRAX and major osteoporotic fracture risk by FRAX), all osteoporosis quantification items (T score hip, T score lumbar spine, BMD hip, BMD lumbar spine) are statistically significantly different as mean values in patients with RA and osteoporosis (table 3).

In analyzing the correlation between disease activity objectified by DAS28 (mean of the group = 4.29 ± 1.24) and quality of life quantified by HAQ (mean of the group = 1.52 ± 0.61) for the whole group we obtained a direct relation proportional and highly significant statistical $r = 0.64$, $p < 0.0001$ (figure 1 and table 4).

TABLE 4. DAS28 and HAQ correlation

Sample size	85
Correlation coefficient r	0.6490
Significance level	$P < 0.0001$
95% Confidence interval for r	0.5132 to 0.7532

In order to analyze whether the coexistence of osteoporosis has an impact on the quality of life, we performed a t analysis for the independent variables for the two groups (figure 2).

Although it can be seen that patients in group B suffering from RA and osteoporosis have a poorer quality of life (1.44 ± 0.56 vs. 1.66 ± 0.68), the difference is not statistically significant ($p = 0.109$).

FIGURE 1. DAS28 and HAQ correlation

FIGURE 2. Comparative analysis of HAQ in groups A and B

FIGURE 3. HAQ and ACPA correlation

The only linear relationship that deserves to be emphasized is that between HAQ and ACPA. Between these two parameters there is a directly proportional correlation, statistically significant, described by a value of the correlation coefficient $r = 0.24$, $p = 0.01$. The quality of life objectified by HAQ does not correlate with the RF ($r = 0.1$; $p = 0.33$) or with the T score for the hip ($r = 0.07$; $p = 0.46$) and for the lumbar spine ($r = 0.08$; $p = 0.41$) (figure 3, table 5, figure 4, table 6).

TABLE 5. HAQ and ACPA correlation

Sample size	85
Correlation coefficient r	0.2448
Significance level	P = 0.0180
95% Confidence interval for r	0.04323 to 0.4272

TABLE 6. HAQ and RF correlation

Sample size	85
Correlation coefficient r	0.1007
Significance level	P = 0.3369
95% Confidence interval for r	-0.1052 to 0.2983

DISCUSSION

Osteoporosis is a chronic skeletal disorder resulting in impaired bone strength predisposing to an in-

creased risk of fractures at various sites (vertebral, hip, forearm) involved in increasing general morbidity and mortality. RA is a chronic inflammatory joint disease with systemic manifestations of unspecified etiology which has a fluctuating long-term evolution, also with implications for overall morbidity and mortality. In recent years, there has been a growing interest in incorporating the concept of quality of life into the clinical evaluation in patients with RA and osteoporosis in order to indicate appropriate medical interventions.

There are currently data in the literature on the quality of life in patients with osteoporosis (11), but there is little information on the extension of impaired quality of life by osteoporosis in patients with RA. That is why, the current study aims to analyze this aspect of the quality of life affected by osteoporosis in patients with RA.

According to the World Health Organization (WHO) (12), quality of life is a „broad concept that incorporates in a complex system physical health, psychological status, level of independence, social relationships and personal expectations of patient and with basic characteristics of the environment in which the patient lives“. Quality of life can be meas-

FIGURE 4. HAQ and RF correlation

ured with various instruments; in the current study that looked at the impact of osteoporosis on the quality of life in patients with RA we used the Health Assessment Questionnaire (HAQ) which is specific to RA given the known fact that the impairment of quality of life in these patients is reported in several areas such as physical health, level of independence, personal and environmental expectations compared to the healthy population (13,14). The following categories are evaluated by HAQ: dressing and grooming, arising, eating, walking, hygiene, reach, grip, common daily activities. Patients report the degree of difficulty on a scale of 0-3 if the respective categories can be performed without difficulty (scale 0) or cannot be performed at all (scale 3), the final score being generated by a computer-assisted system (6).

Considering that osteoporosis is a „silent disease“ for a long period of time and thus underdiagnosed and undertreated, the association of osteoporosis with RA does not seem to have a major impact on the quality of life in patients with RA, this being determined only by the respective inflammatory rheumatic disease. The development of osteoporotic fractures (vertebral, hip, forearm), either induced by minimal trauma or spontaneous, by association with thoraco-lumbar pain, kyphosis, prolonged immobilization and loss of self-care, has a major impact on the quality of life in patients with RA.

That is why there is currently a deep need for understanding the quality of life of osteoporotic patients with RA in view of the need for non-medical and medical therapeutic decisions with the major purpose of improving the quality of life of these patients.

This study included a total of 85 patients diagnosed with RA by a rheumatologist in accordance with the 2010 ACR / EULAR classification criteria, which was divided into two groups according to the presence or absence of osteoporosis: 52 (61.17%) patients with RA and osteoporosis and 33 (38.82%) patients with RA but without osteoporosis. It should be mentioned that in our total group of patients, according to the data from the specialized literature, women predominated over men: 79 (92.94%) were women and 6 (7.05%) were men (15); the average age of the whole group of patients was 67.64 years and the disease duration was 9.17 years.

The clinical and immunological characteristics of our RA patients are comparable to the most major studies in the literature. There are differences in the value of ESR, CRP and FI, in favor of patients with

RA and osteoporosis compared to patients with RA and without osteoporosis, but without statistically significant differences; all osteoporosis quantification items (T score hip, T score lumbar spine, BMD hip, BMD lumbar spine) are statistically significantly different as mean values in patients with RA and osteoporosis compared to the patients with RA and without osteoporosis, this confirming the correctness of the patients' selection in our study.

The results of our study shows that the patients with RA and osteoporosis have a lower quality of life evaluated by HAQ compared to patients with RA and without osteoporosis. In patients with RA and osteoporosis exists a statistically significant correlation between the quality of life of patients evaluated by HAQ and the activity of the disease evaluated by DAS28 compared to patients with RA and without osteoporosis ($p < 0.0001$), this supporting the idea that the more active the rheumatic disease, the lower the quality of the life is. There is no correlation between the quality of life of patients evaluated by HAQ and rheumatoid autoimmunity expressed by ACPA and RF for the whole group of patients.

Among the limitations of the study is the fact that in the group of patients the presence of fragility fractures or spontaneous fractures could not be identified. Thus, the quality of life of RA patients could not be correlated with the presence of osteoporotic fractures, either in the presence or absence of diagnosis of osteoporosis in patients with RA.

CONCLUSIONS

The patients with RA and osteoporosis tend to have a lower quality of life evaluated by HAQ compared to patients with RA and without osteoporosis, but the differences were not statistically significant ($p = 0.109$).

There is a statistically significant correlation with a strong level of significance between quality of life assessed by HAQ and disease activity of rheumatic disease evaluated by DAS28 in patients with RA and osteoporosis compared to patients with RA and without osteoporosis ($p < 0.0001$).

Regarding the relationship between quality of life assessed by HAQ and rheumatoid autoimmunity expressed by ACPA and RF, there is a statistically significant correlation trend between HAQ and ACPA ($p = 0.018$), but there is no statistical correlation between HAQ and RF ($p = 0.3369$).

The quality of life in patients with RA evaluated by HAQ is related to the activity of rheumatic dis-

ease evaluated by DAS28 and the overlap of osteoporosis, as a disease that has long been underdiagnosed and undertreated, does not lead to a statistically significant decrease in the quality of life; this makes us to conclude that osteoporosis cannot influence by itself the quality of life in patients with RA.

It is expected that osteoporotic fractures, through their clinical and functional manifestations, will influence the quality of life in patients with RA and osteoporosis.

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